Applicant's election of Group 1, in Paper No. 12, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. See M.P.E.P. 818.03(a).

Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject, matter which applicant regards as the invention. Claims 1, 3, 4, 5 and 7 are indefinite in the use of the language "import antibody" in that it is not clear what constitutes an important antibody, ie. what the determines what is to be an import antibody. Claim 1 step a) is indefinite in that it is not clear what is meant by a "consensus human variable domain". Claim 1 step d) is indefinite in that it is not clear what is actually taking place when one aligns the amino acid sequences of the FR, ie. is this a physical or mental step? Claim 1 step e) is unclear in what type of homology is indicated, ie. are conservative amino acids considered as homologs or should their be identical amino acid residues at the indicated portion of the framework. Claim 1 step f), 3 is indefinite in the use of the language "participates" in that the nature of participation is unclear. Claim 1 step f) is indefinite in that it is not clear how one of ordinary skill can determine the effects which are listed in steps 1-3, ie. through antigen binding, through hybridization? Claim 1 step g) is indefinite in that it is not clear what effects are reasonably expected to occur. Claim 2 is indefinite in that the antecedent basis for "the domain" is unclear. Claim 3 is indefinite in that it is not clear when in the process of making the antibody one would search for the glycosylation sites. Claim 4 is indefinite for the same reason that claim 3 is indefinite. Claim 5 is indefinite in that it is believed that the claims up to this point were directed to making a

"humanized antibody", and it is unclear how "preparing a humanized antibody" in claim 5 differs from the preparation of the antibody up to this point. Furthermore, it is not clear what is intended in the preparation of the antibody of claim 5. Claim 6 is vague in that it is not clear what the numbers are meant to designate. It is suggested that applicant clarify the nature of the numbers or point to a figure. Claim 7 is indefinite in that it is not clear what the method is drawn to. it is suggested that the language "a method of making a humanized antibody" be inserted within the claim.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately describe the invention and failing to adequately teach how to make and or use the invention, ie. failing to provide an enabling disclosure. The following terms lack enablement in the specification:.

Claims 1 and 7 lack enablement in the language "at least a portion of an import variable domain". Applicant has only indicated specific residues which may be transferred, but they are claiming an antibody wherein the a portion of the import antibody are to be transferred. There is no guidance in the specification which would enable one of skill in the art to make antibodies with

transferred variable domains other than CDRs. Applicant is aware that a portion of the variable domain can be any one of the CDRs as well as the framework regions. However, this language also reads on small amino acid sequences which are incomplete regions of the variable region of the antibody. There is no support in the specification for linking the variable region of the antibody to any or all of the myriad "portions" which are encompassed within this language. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. It is suggested that the specific portion of the human variable region which is described in the specification be recited within the claim or this language be removed completely in order to obviate this rejection.

Claim 1 step c) lacks enablement in that it is not clear how one would determine which amino acids are to be substituted. There is no specific recitation of what characteristics of the amino acids are necessary for deciding whether it is to be replaced or not. Without this description one of skill in the art would not be able to choose the appropriate amino acid residues without hindering the function of the antibody.

Claim 1 step f), lacks enablement in that the protocol for determining whether the amino acid residues in the import amino acid sequence are reasonably expected to interact with the antigen is not described anywhere in the specification. There is no

explicit step which enables one of ordinary skill in the art to determine the effects which are recited. It would require undue experimentation of one of ordinary skill in the art to make the variations which may be made in order to test the effects of the mutant antibodies.

Claim 2 lacks enablement in that there is no description in the specification of how to determine which residues are exposed on the surface or which residues are buried within the domain, is this through computer modeling or through x-ray crystallography or other methods?

Claim 3 lacks enablement in that there is no guidance in the specification on how one would determine which glycosylation site affects antigen binding, or what comprises "reasonable expectation".

Claims 6, 7 and 9 lack enablement in that it would appear that these amino acids are relevant to IgG and not to other isotypes. There is no indication that one of skill in the art would extrapolate the use of these amino acids to all or other isotypes of immunoglobulins. Furthermore, there is insufficient description and guidance in the specification with regards to the properties of these amino acids which would enable one of ordinary skill in the art to make humanized antibodies with other isotypes using these amino acid sequences.

Applicant has not shown that antibodies which have been modified as that which is claimed are capable of functioning as that which is being disclosed, ie. maintaining the binding affinity of the parent antibody. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Burgess et. al. Journal of Cell biology, 111: 2129-2138 (1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Lazar et. al. Molecular and Cellular Biology, 8:1247-1252 (1988). Similarly it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies. See Tao et. al. The Journal of Immunology, Vol. 143, No. 8. 2595-2601 (1989) and Gillies et. al. Human Antibodies and Hybridomas, Vol 1, no. 1, 47-54 (1990). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity and characteristic of a protein. Therefore, without sufficient guidance in the

specification to support the use of the above terms and for the reasons mentioned above one of ordinary skill in the art would forced into undue experimentation in order to practice the invention as is claimed.

Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

35 U.S.C. § 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.**

Claims 1-4, 6-8 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The above claims are drawn to a method of preparing an antibody, however, there is no indication within the claims that actual physical steps are taking place. For example, there is no step which includes isolating an antibody, rather obtaining an amino acid sequence. All of the steps which are listed in the claims can be done on paper as mental steps or on a computer terminal.

The specification is objected to under 35 U.S.C. § 112, first paragraph, and claims 9-13 are rejected under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 101 as the specification fails to adequately teach how to use the claimed monoclonal antibodies in the manner in which they are disclosed ie. for the therapeutic

purposes. Applicants claims are supported only by in vitro data showing the ability of muMab4D5, which is a humanized anti-p185 antibody which reacts with breast and ovarian cancers, to react with different cell lines (see page 88-90 of the specification). Applicant has made no showing that these data correlate with utility for in vivo therapy in humans of the complex array of diseases encompassed by the claims. In general, effective treatment of human cancers has not been routinely achieved in the art using monoclonal antibodies. Further, in vitro data such as that reported in the specification and animal model studies frequently do not correlate with clinical utility in in vivo trials in patients. Based on the evidence of record, the alleged utility of the claimed composition for the treatment of cancer would not be believable on its face to the person of skill in the art in view of the contemporary knowledge in the art. Applicant has not provided any showing of therapeutic utility of the subject monoclonal antibodies which would lead one of skill in the art to believe that the antibodies are broadly applicable for the treatment of all types of autoimmune diseases. Applicant is required to provide evidence commensurate with the scope of the claims, which would be convincing to those skilled in the art that the claimed compositions have utility for the treatment of malignant and autoimmune diseases in humans. See MPEP 608.01(p).

Waldmann, in a recent review of the literature pertaining to clinical applications of monoclonal antibodies for diagnosis and therapy of human disease, teaches that effective therapy using monoclonal antibodies has been elusive and indicates that hopes for antibody-based treatment methods engendered by in vitro studies have not correlated well with in vivo clinical trial results in patients with cancer. It does not appear that the exemplary material provided in the specification in support of the assertions that the claimed antibodies have therapeutic utility would be viewed by those skilled in the art as being predictive of their utility for treating humans. Applicant has not exemplified how to use the claimed antibodies in vivo and has not shown that the antibodies would be effective in vivo. It appears that undue experimentation would be required of one skilled in the art to practice the claimed invention for the single utility disclosed in the specification.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless--

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this country or a

> **foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> **A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**
>
> **Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.**

Claims 1, 2, 5-10 are rejected under 35 U.S.C. § 102(b) as being anticipated by Queen et. al.. The above claims are drawn to a method of producing a humanized antibody wherein the amino acid sequences of an import antibody and a consensus antibody are compared, wherein the CDRs of the import antibody are substituted for the antibody of the consensus antibody, and wherein certain framework residues which are responsible for the binding of antigen, interaction with CDR, or participating in the Vl-Vh interaction are also imported to the consensus antibody. In essence, residues of the framework region are also transferred with

the CDRs in order to retain the antigen binding affinity of the parent antibody.

Queen et. al. describe the production of humanized antibodies wherein the murine antibody is compared to human antibodies and the most homologous human antibody is chosen as the acceptor molecule. The CDRs of the murine antibody are then substituted for the CDRs of the human antibody and certain framework residues are also changed. Queen et. al. describe computer modeling and sequence comparison in order to determine the amino acid residues which are to be substituted (see page 10031-10033). Although the steps of the methods are not in exactly the same order, all of the claimed elements are present with in the reference.

Claims 1,2 and 5-10 are rejected under 35 U.S.C. § 102(a) as being anticipated by Co et. al.. See above discussion.

Co et. al. show the production of humanized anti-HSV using the general concept of Queen et. al. (see Results and Table 1).

Claims 3 and 4 are rejected under 35 U.S.C. § 103 as being unpatentable over Queen et. al. or Co et. al. in view of Wallick et. al.

The above claims are drawn to a method of making a humanized antibody wherein the CDRs of an import antibody are transferred to a consensus human antibody along with certain residues of the framework. Furthermore, the claims require that the glycosylation

sites, if any, of the import amino acid also be imported with the CDRs and framework regions if these sites have an affect on the binding of antigen.

Queen et. al. and Co et. al. both describe the production of humanized antibodies by transferring the CDRs and certain framework regions of the donor antibody to the human consensus antibody (see Queen et. al. pages 10031-10033 and Co et. al. page 2871). They further state that any residue which might have an affect on the antigen binding of the antibody should be changed substituted in order to maintain the binding affinity of the parent antibody (see page 10033 of Queen et. al. at the last paragraph on the page). They do not however, specifically discuss the glycosylation sites as potential targets for transfer. Wallick et. al. teach the importance of carbohydrate interaction with antigen for maintaining or increasing antigen binding affinity (see pages 1107-1108). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make humanized antibodies using the method of Queen et. al. or Co et. al. and further incorporating the concept taught by Wallick et. al.. One of ordinary skill in the art would have been motivated to combine the teachings of the two references in view of the teaching of Queen that retaining high antigen binding affinity is desirable in the production of humanized antibodies. Knowing the role of carbohydrates in antigen antibody interaction as was pointed out by

Wallick et. al. one of ordinary skill would have had the means and the motivation to make humanized antibodies using both of the teachings of the primary and secondary references.

Claim 11 is rejected under 35 U.S.C. § 103 as being unpatentable over Queen et. al. or Co et. al. in view of Reichmann et. al.

The above claim is drawn to a humanized antibody wherein only one amino acid (listed in claim 9) in the framework and the CDRs have been substituted in the consensus antibody.

Queen et. al. and Co et. al. both teach the production of humanized antibodies by transferring the CDRs of a murine antibody along with specific residues of the framework region to the acceptor antibody molecule. They do not however teach only substituting one of the framework residues among those listed in claim 9. Queen et. al. introduce the general concept of a scaffold wherein certain amino acid residues of the framework must be present and certain are dispensable. Reichmann et. al. teach that a single amino acid substitution in an antibody is sufficient to retain the antigen binding specificity of the parent antibody (see final paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make only a single substitution in the antibody of Queen et. al. or Co et. al. in positions among those listed in claim 9. It would have been obvious to one of ordinary skill to complete the

invention in light of the success of Reichmann et. al. in only mutating one amino acid of the framework. Knowing that each antibody varies slightly in the non-conserved region, and given the computer modelling protocol set forth by Queen et. al. one of ordinary skill would have been motivated to make a single mutation in the variable region with the expectation of obtaining a functional antibody.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lila Feisee whose telephone number is (703) 308-2731.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Feisee/lf
September 29, 1992

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
9/30/92

TO SEPARATE, HOLD TOP AND BOTTOM EDGES, SNAP–APART AND DISCARD CARBON

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

NOTICE OF REFERENCES CITED

SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
715272	1806	13

APPLICANT(S): Paul Carter et al.

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A						
	B						
	C						
	D						
	E						
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R Yoger et al. Molecular and cellular Biology 8: 1247 1988

S Burgess et al. The Journal of cell Biology 111: 2129 1990

T Tao et al. The Journal of Immunology. 143(8) 2595 1989

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EXAMINER L. B. DATE 9/29/92

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

FORM PTO-1449 | U.S. Dept. of Commerce Patent and Trademark Office

LIST OF PRIOR ART CITED BY APPLICANT

(Use several sheets if necessary)

Atty Docket No.	Serial No.
709	07/715,272
Applicant: Paul J. Carter et al.	
Filing Date: June 14, 1991	Group: 1806

#12 attach

*Examiner Initials		OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)
	A	Chothia et al., J. Mol. Biol. 186:651-663 (1985)
	B	Novotny and Haber, Proc. Natl. Acad. Sci. USA 82:4592-4596 (1985)
	C	Morrison, S. L. et al., Proc. Natl. Acad. Sci. USA 81:6851-6855 (1984)
	D	Boulianne, G. L. et al., Nature 312:643-646 (1984)
	E	Neuberger, M. S. et al., Nature 314:268-270 (1985)
	F	Brüggemann, M. et al., J. Exp. Med. 166:1351-1361 (1987)
	G	Riechmann, L. et al., Nature 332:323-327 (1988)
	H	Love et al., Methods in Enzymology 178:515-527 (1989)
	I	Bindon et al., J. Exp. Med. 168:127-142 (1988)
	J	Jones, P. T. et al., Nature 321:522-525 (1986)
	K	Verhoeyen, M. et al., Science 239:1534-1536 (1988)
	L	Hale, G. et al., Lancet i:1394-1399 (1988)
	M	Queen, C. et al., Proc. Natl. Acad. Sci. USA 86:10029-10033 (1989)
	N	Co et al., Proc. Natl. Acad. Sci. USA 88:2869-2873 (1991)
	O	Gorman et al., Proc. Natl. Acad. Sci. USA 88:4181-4185 (1991)
	P	Daugherty et al., Nucleic Acids Research 19(9):2471-2476 (1991)
	Q	Brown et al., Proc. Natl. Acad. Sci. USA 88:2663-2667 (1991)
	R	Junghans et al., Cancer Research 50:1495-1502 (1990)
	S	Davies, D. R. et al., Ann. Rev. Biochem. 59:439-473 (1990)
	T	Chothia, C. & Lesk, A. M., J. Mol. Biol. 196:901-917 (1987)

Examiner: [signature] | Date Considered: 9/29/92

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

USCOMM-DC 80-398

FORM PTO-1449 — U.S. Dept. of Commerce, Patent and Trademark Office

LIST OF PRIOR ART CITED BY APPLICANT

(Use several sheets if necessary)

Atty Docket No.	Serial No.
709	07/715272

Applicant: Paul J. Carter et al.

Filing Date	Group
June 14, 1991	1806

U.S. PATENT DOCUMENTS

*Examiner Initials		Document Number	Date	Name	Class	Subclass	Filing Date
	AA	4,816,567	3/28/89	Cabilly et al.	530	387.1	
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	AL							
	AM							
	AN							
	AO							
	AP							

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	AR	Chothia, C. et al., Nature 342:877-883 (1989)
	AS	Tramontano, A. et al., J. Mol. Biol. 215:175-182 (1990)
	AT	Margolies et al., Proc. Natl. Acad. Sci. USA 72:2180-2184 (1975)
	AU	Pluckthun, Biotechnology 9:545-51 (1991)
	AV	Spiegelberg et al., Biochemistry 9:4217-4223 (1970)
	AW	Wallick et al., J. Exp. Med. 168:1099-1109 (1988)
	AX	Sox et al., Proc. Natl. Acad. Sci. USA 66:975-982 (1970)

Examiner: [signature] — Date Considered: 9/29/92

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

USCOMM-DC 80-398.

FORM PTO-1449 | U.S. Dept. of Commerce Patent and Trademark Office | Atty Docket No. 709 | Serial No. 07/715272

LIST OF PRIOR ART CITED BY APPLICANT

(Use several sheets if necessary)

Applicant Paul J. Carter et al.

Filing Date June 14, 1991 | Group 806

U.S. PATENT DOCUMENTS

*Examiner Initials		Document Number	Date	Name	Class	Subclass	Filing Date
	BA						
	BB						
	BC						
	BD						
	BE						
	BF						
	BG						
	BH						
	BI						
	BJ						
	BK						

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
	BL	WO 91/09967	7/11/91	PCT				
	BM							
	BN							
	BO							
	BP							

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

BR	Margni et al., Ann. Rev. Immunol.6:535-554 (1988)
BS	Fendly, B. M. et al., Cancer Res. 50:1550-1558 (1990)
BT	Neuberger et al., Nature 312:604-608 (1984)
BU	Takeda et al., Nature 314:452-454 (1985)
BV	Snow and Amzel, Protein: Structure, Function, and Genetics 1:267-279, Alan R. Liss, Inc. pubs. (1986)
BW	Cheetham, J., Protein Engineering, 2(3): 170-172 (1988)
BX	

Examiner [signature] Date Considered 9/29/92

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

USCOMM-DC 80-398.

180.1.16 #14 Cl
1-25-93

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of)
Paul J. Carter et al.)
Serial No. 07/715,272)
Filed: 14 JUNE 1991)
For: IMMUNOGLOBULIN VARIANTS)

Art Unit: 1806

Examiner: L.FEISEE

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

The attached materials were received in connection with the prosecution of a foreign patent application corresponding to the captioned case. These materials contain at least two reference citations, the relevance of which is apparent from the communication from the foreign patent office that is also enclosed.

A PTO Form 1449 is submitted herewith to facilitate citation to the record of all references contained in these materials.

Respectfully submitted,
GENENTECH, INC.
Carolyn R. Adler
Carolyn R. Adler
Reg. No. 32,324

December 30, 1992
460 Point San Bruno Boulevard
South San Francisco, CA 94080
415-225-2614

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh
Louise Strasbaugh

Date: December 30, 1992

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Paul J. Carter et al.

Serial No. 07/715,272

Filed: June 14, 1991

For: Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. FEISEE

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-2614

CERTIFICATION UNDER 37 C.F.R. § 1.97(e)

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

I hereby certify that each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement. Pursuant to §1.97, this information disclosure has been filed in a timely fashion and no fees are required.

Respectfully submitted,

GENENTECH, INC.

Carolyn R. Adler
Reg. No. 32,324

Dated: December 30, 1992

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh
Louise Strasbaugh

Date: December 30, 1992

PR. 1806

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	Group Art Unit: 1806
Paul J. Carter et al.	Examiner: L. Feisee
Serial No. 07/715,272	
Filed: 14 June 1991	
For: Immunoglobulin Variants	460 Point San Bruno Boulevard South San Francisco, CA 94080 (415) 225-2614

#16

Amendment and Response

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Responsive to the Office Action mailed 5 October 1992, please amend the claims as follows:

---

1. (Amended) A method for making at least a portion of a humanized antibody variable domain comprising amino acid sequence of a non-human[, import] antibody which is desired to be humanized (import antibody) and a human antibody, comprising the steps of:

a. obtaining the amino acid sequences of [at least a portion of] an import variable domain and of a consensus human variable domain;

b. identifying Complementarity-Determining Region (CDR) amino acid sequences in the import and the human amino variable domain sequences;

c. substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence;

d. aligning the amino acid sequences of a Framework Region (FR) of the import antibody and the corresponding FR of the consensus antibody;

e. identifying import antibody FR residues in the aligned FR sequences that are non-homologous to the corresponding consensus antibody residues;

f. determining if the non-homologous import amino acid residue is reasonably expected to have at least one of the following effects:

1. non-covalently binds antigen directly,

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2. interacts with a CDR; or

3. participates in the V_L - V_H interface by affecting the proximity or orientation of the V_L and V_H regions with respect to one another; [and]

g. for any non-homologous import antibody amino acid residue which is [reasonably] expected to have at least one of these effects, substituting that residue for the corresponding amino acid residue in the consensus antibody FR sequence; and

h. preparing a humanized antibody variable domain having amino acid sequences determined in steps a-g.

2. (Amended) The method of claim 1, having an additional step of determining if any such non-homologous residues are exposed on the surface of the consensus human antibody variable domain or buried within it, and if the residue is exposed, retaining the consensus residue.

3. (Amended) The method of claim 1, having the additional steps, which may be taken between any two steps in the method of claim 1, of searching the import antibody variable domain amino acid sequence for glycosylation sites, determining if any such glycosylation site is reasonably expected to affect the antigen binding or affinity of the antibody, and if so, substituting the glycosylation site into the consensus amino acid sequence.

4. (Amended) The method of claim 1, having the additional steps, which may be taken between any two steps in the method of claim 1, of searching the consensus variable domain amino acid sequence for glycosylation sites which are not present at the corresponding amino acid in the import antibody amino acid sequence, and if the glycosylation site is not present in the import sequence, substituting the import amino acid residues for the amino acid residues comprising the consensus glycosylation site.

5. (Amended) The method of claim 1, having an additional step which comprises aligning import antibody and consensus antibody FR amino acid sequences, identifying import antibody FR amino acid residues which are non-homologous with the aligned consensus FR sequence, and for each such non-homologous import antibody FR amino acid residue, determining if the corresponding consensus antibody amino acid residue represents a residue which is highly conserved across all species at that site, and if it is so conserved, preparing a humanized antibody which comprises the consensus antibody amino acid residue at that site.

7. (Amended) A method for making a humanized antibody comprising providing [at least a portion of] a non-human antibody variable domain amino acid sequence which is desired to be humanized (import antibody) having a CDR and a FR, obtaining the amino acid sequence of at least a portion of a consensus human antibody variable domain having a CDR and a FR, substituting the non-human CDR for the human CDR in the consensus human antibody variable domain, and then substituting an amino acid residue for the consensus amino acid residue at at least one of the following sites:
4L, 35L, 36L, 38L, 43L, 44L, 46L, 58L, 62L, 63L, 64L, 65L, 66L, 67L, 68L, 69L, 70L, 71L, 73L, 85L, 87L, 98L, 2H, 4H, 24H, 36H, 37H, 39H, 43H, 45H, 49H, 58H, 60H, 68H, 69H, 70H, 73H, 74H, 75H, 76H, 78H, 91H, 92H, 93H, and 103H.

[Please add the following new claims 17-21:]

--17. A method of using a consensus human antibody variable domain amino acid sequence in the preparation of a humanized antibody.-- 112/2nd no method steps.

--18. In a method for making a humanized antibody variable domain, the improvement consisting of using consensus human antibody variable domain amino acid sequence.--

--19. A method for making an improved antibody, comprising amino acid sequence from a non-human (import) antibody and a human antibody, comprising the steps of:

a. obtaining the amino acid sequences of at least a portion of an import antibody variable domain and of a consensus human antibody variable domain;

b. identifying Complementarity Determining Region (CDR) amino acid sequences in the import and the human amino variable domain sequences;

c. substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence;

d. aligning the amino acid sequences of a Framework Region (FR) of the import antibody and the corresponding FR of the consensus antibody;

e. identifying import antibody FR residues in the aligned FR sequences that are non-homologous to the corresponding consensus antibody residues;

f. determining if the non-homologous import amino acid residue is reasonably expected to have at least one of the following effects:

1. non-covalently binds antigen directly,

2. interacts with a CDR; or

3. participates in the V_L - V_H interface by affecting the proximity or orientation of the V_L and V_H regions with respect to one another;

g. for any non-homologous import antibody amino acid residue which is reasonably expected to have at least one of these effects, substituting that residue for the corresponding amino acid residue in the consensus antibody FR sequence; and

h. preparing an improved, humanized antibody having amino acid sequences determined in steps a-g; and

i. evaluating the antigen binding or immunogenicity of the improved, humanized antibody with respect to the parental antibody.--

--20. A method comprising, following the identification of an antibody by the method of any one of claims 1, 7, or 17-19, the manufacture of the antibody.--

--21. A method comprising, following the identification of an antibody by the method of any one of claims 1, 7, or 17-19, the expression of nucleic acid encoding the antibody.--

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Remarks

Claims 1-13, and 17-21 are presented herein for examination. Reconsideration of the outstanding rejections is respectfully requested for the reasons that follow. A request for a one-month extension of time to respond is submitted herewith, bringing the due date for this response to 5 February 1993. This response is timely filed.

Amendments

Claims 1, 3, 4, 5 and 7 have been amended to indicate that an import antibody is a non-human antibody which is desired to be humanized. Support for this language is found in the specification at page 6, line 27 to page 7, line 3.

Claim 1, step (f) has been amended to clarify that the word "participates" in the V_L - V_H interface means to affect the proximity or orientation of the V_L and V_H regions with respect to one another. Support for this amendment is found on page 15, lines 30-32. New step (h) has been added to claim 1, directed to the physical step of preparation of a humanized antibody variable domain. Support for this step appear throughout the specification.

Claims 3 and 4 have been amended to provide that the additional steps may be taken between

any two steps in the method of claim 1. Claims 2-7 have been amended to clarify that the residues or sequences referred to relate to amino acids.

New claims 17 - 21 have been added. These claims are alternate approaches to claiming the subject matter claimed in claim 1. Additional support for claims 20-21 is found in Example 1.

It is believed that these amendments introduce no new matter. The inventors respectfully request entry of these amendments.

The rejection under 35 U.S.C. § 112, second paragraph

Claims 1-10 were rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. Claims 1, 3, 4, 5 and 7 were rejected for use of the term "import antibody". These claims have been amended to indicate that the import antibody is a non-human antibody which is desired to be humanized.

Claim 1 step (a) was rejected because of the term "consensus human variable domain". The terms "consensus sequence", "consensus antibody" and "consensus human variable domain" are defined at specification page 16, line 29 to page 17, line 17:

> The terms "consensus sequence" and "consensus antibody" as used herein refers to an amino acid sequence which comprises the most frequently occurring amino acid residues at each location in all human immunoglobulins of any particular subclass. In preferred embodiments, the consensus human variable domain sequences are derived from the most abundant subclasses in the sequence compilation of Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, National Institutes of Health, Bethesda MD (1987), namely V_L κ subgroup I and V_H group III....

As described in the specification, a "consensus human variable domain" would have an amino acid sequence comprising, amino acid residue by residue, the most frequently occurring amino acid residue gathered from a group of human immunoglobulins. The identity of each amino acid residue making up the consensus sequence is determined separately, requiring merely routine tabulation of the amino acids present in each member of a particular immunoglobulin subclass. To expedite the routine tabulation of the most commonly occurring amino acids, workers in the field are referred to the Kabat *et al.* publication cited in the quoted material above, which presents such tabulations.

Claim 1 step (d) was rejected as indefinite as to whether the alignment of the amino acid sequences is a physical or mental step. This rejection is somewhat confusing. The inventors intend claim 1, step (d) to refer to a maximal homology alignment of representations of amino acid sequences, as described in the specification at page 17, lines 18-27. Preparing such a homology alignment typically combines physical and mental actions. This connotation for the phrase "alignment of sequences" is common in the art to which this invention pertains. Step (d) of claim 1 does not require

manipulation of the actual, tangible amino acids, merely manipulation of symbolic representations of the actual amino acids.

Claim 1 step (e) was rejected because of the term "homology"; the Examiner questioned whether conservative amino acids are to be considered as homologs. Identity or homology with respect to a specified amino acid sequence of this invention is defined on page 17, lines 18-27. At lines 22-23, the specification indicates that this invention does "not consider[ing] any conservative substitutions as part of the sequence identity". Conservative substitutions are therefore not considered as homologs.

Claim 1 step (f) was rejected for use of the language "participates". Step (f) of claim 1 refers to an amino acid residue which "participates in the in the V_L - V_H interface". This step has been amended to clarify that immunoglobulin residues which so participate are those that affect the proximity or orientation of the V_L and V_H regions with respect to one another.

Claim 1 step (f) was also rejected as indefinite as to how one of ordinary skill can determine the effects listed in steps 1-3. Steps 1-3 presently list the following effects an import amino acid residue might have:

1. non-covalently binds antigen directly,
2. interacts with a CDR; or
3. participates in the V_L - V_H interface by affecting the proximity or orientation of the V_L and V_H regions with respect to one another.

The specification discusses, at pages 13-16, the interactions of amino acid residues within an immunoglobulin and describes at least two methods for evaluating the role of any particular amino acid residue: three dimensional models and assays. As stated at page 14, lines 2-9:

> "Three dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of the residues in the functioning of the candidate immunoglobulin sequence, i.e., the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen."

The specification provides detailed information how to evaluate the three-dimensional models to determine the various potential effects of amino acid residue changes.

The specification also suggests an alternate method for evaluating the effect of an amino acid residue change. On page 16, lines 14-18, the specification teaches:

> "Since it is not entirely possible to predict in advance what the exact impact of a given substitution will be it may be necessary to make the substitution and assay the candidate antibody for the desired characteristic. These steps, however, are *per se*

routine and well within the ordinary skill of the art."

The inventors submit that methods for determining the effects of amino acid changes are known in the art, and that those skilled in the art would understand what is claimed in step (f).

Claim 1 step (g) was rejected as being indefinite as to what effects are reasonably expected to occur. The word "reasonably" has been deleted from the claim.

Claim 2 was rejected as lacking antecedent basis for "the domain". This claim has been amended to clarify that the intended domain is the consensus human antibody variable domain.

Claims 3 and 4 were rejected as indefinite for not specifying when in the process one would search for the glycosylation sites. These claims have been amended to indicate that one would search for glycosylation sites between any two steps in the method of claim 1.

Claim 5 was rejected as unclear in the use of the phrase "preparing a humanized antibody"; this phrase has now been added by amendment as the last step of claim 1. The phrase is intended to mean the physical making of a humanized antibody, methods for which are described in the specification, including *in vitro* mutagenesis and recombinant engineering. The Examiner also seems to be questioning how claim 5 differs from the previous claims. Claim 5 adds an additional step of determining if a particular amino acid residue in the consensus human variable domain--which differs from the import antibody amino acid residue at that site--also appears at that site in antibodies of other species at that particular site (is conserved). If the particular amino acid residue is conserved across species at that site, than that residue is retained in the humanized antibody, and not substituted by the import antibody amino acid residue at that site, and without requiring evaluation of the impact of such a change on the antibody's characteristics.

Claim 6 was rejected as vague for unclear use of numbers. These numbers refer to particular amino acids in the light (L) and heavy (H) chains of immunoglobulins. By convention, workers in this field generally utilize the immunoglobulin numbering system set forth in Kabat, E. A. *et al.*, *Sequences of Proteins of Immunological Interest* (National Institutes of Health, Bethesda, MD, 1987)), as described in the specification at page 8, lines 19-21. The Examiner's attention is drawn to Queen *et al.*, already of record in this case, especially at page 10032 column 1 first paragraph (and reference 38 therein) where antibody amino acid residues are referred to with numbers representing certain positions. It is submitted that workers in the field will understand clearly what is claimed in claim 5.

Claim 7 was rejected as indefinite as to what the method is drawn, and has been amended according to the Examiner's suggestion.

According to the CAFC, a decision as to whether a claim is invalid for indefiniteness "requires a determination whether those skilled in the art would understand what is claimed", Amgen v. Chugai,

18 USPQ2d 1116, 1030 (CAFC 1991). The presently pending claims use terminology with clear meanings in the field, especially in light of the definitions provided in the specification. The wordings of the claims comply with the requirements of 35 USC § 112, and this rejection should be reconsidered and withdrawn.

The rejection under 35 U.S.C. § 112, first paragraph

Claims 1-11 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement.

Claims 1 and 7 were rejected as lacking enablement in the language "at least a portion of an import variable domain". These terms have been deleted from the claims.

Claim 1 step (c) was rejected for being unclear as to how one would determine which amino acids are to be substituted. This step recites "substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence". The identification of the Complementarity Determining Region (CDR) amino acid sequence of the import and the human amino variable domain sequences is made in previous step (b). To accomplish step (c), therefore, one substitutes the amino acids identified in step (b).

Methods for identifying CDRs and distinguishing them from Framework Residues (FRs) are known in the art. As the specification describes on page two, antibody variable domains of natural light and heavy chains have the same general structure, and each domain comprises four framework (FR) regions, whose sequences are somewhat conserved, connected by three hyper-variable or complementarity determining regions (CDRs) (see Kabat, E. A. *et al.*, *Sequences of Proteins of Immunological Interest*, National Institutes of Health, Bethesda, MD, (1987)). The four framework regions largely adopt a β-sheet conformation and the CDRs form loops connecting, and in some cases forming part of, the β-sheet structure. The CDRs in each chain are held in close proximity by the framework regions and, with the CDRs from the other chain, contribute to the formation of the antigen binding site. The CDR may be identified following three-dimensional modeling of the antibody. The CDRs may also be identified based on comparison of the an antibody amino acid sequence with a known antibody.

Attached as Exhibit A for the Examiner's convenience are pages from the Introduction to Kabat, E. A. *et al.*, *Sequences of Proteins of Immunological Interest, Fifth Edition*, National Institutes of Health, Bethesda, MD, (1991). This work, along with the earlier Kabat compendiums referred to in the specification and other references, guide the practitioner in the numbering of antibody amino acid sequences, and the assignment of particular amino acids to one of the FR or CDR regions. The Examiner's attention is drawn the sections beginning on page xv, the section entitled "Variable Region Sequence" and especially to Table I, page xvi. Table I presents the amino acid residues associated

with FRs and CDRs of the variable domains of immunoglobulin light and heavy chains. See also Figure 1. page xviii, which shows a schematic view of an immunoglobulin; please note the mention in that figure description to the use of a maximum homology alignment to determine the proper numbering of the amino acids (as referred to in the response to the previous § 112 rejection). The inventors submit that the identification of immunoglobulin amino acid residues as belonging to a CDR or to the framework is routine in the art, requiring no undue experimentation.

The specification teaches, in detail, several ways to substitute amino acid residues, including mutagenesis and the construction of nucleic acid encoding the desired sequence. Alanine scanning mutagenesis is described at page 36, line 20 to page 37, line 3. Oligonucleotide-mediated mutagenesis, PCT mutagenesis and cassette mutagenesis are described in the specification at page 39, line 10 through page 44, line 10. The inventors submit that steps (b) and (c) of claim 1 are fully enabled by the specification.

Claim 1 step (f) was rejected as lacking enablement for determining which amino acid residues may be expected to interact with the antigen. At page 29, lines 4-10, the specification teaches that:

> "Differences between the non-human import and the human consensus framework residues are individually investigated to determine their possible influence on CDR conformation and/or binding to antigen. Investigation of such possible influences is desirably performed through modeling, by examination of the characteristics of the amino acids at particular locations, or determined experimentally through evaluating the effects of substitution or mutagenesis of particular amino acids."

Techniques for molecular modeling are described on pages 27-28. Experimental evaluation of the role of particular amino acids will utilize assays tailored to the activities of the antibody to be humanized.

More detailed teaching on identifying residues that influence antigen binding is contained in the specification at page 14, line 10 through page 15, line 6, where it is stated:

> "A residue that noncovalently directly binds to antigen is one that, by three dimensional analysis, is reasonably expected to noncovalently directly bind to antigen. Typically, it is necessary to impute the position of antigen from the spatial location of neighboring CDRs and the dimensions and structure of the target antigen. In general, only those humanized antibody residues that are capable of forming salt bridges, hydrogen bonds, or hydrophobic interactions are likely to be involved in non-covalent antigen binding, however residues which are separated spatially by 3.2 Angstroms or less may also non-covalently interact. Such residues typically are the relatively larger amino acids, such as tyrosine, arginine, and lysine. Antigen-binding FR residues also typically will

have side chains that are oriented into an envelope surrounding the solvent oriented face of a CDR which extends about 7 Angstroms into the solvent from the CDR domain and about 7 Angstroms on either side of the CDR domain, again as visualized by three dimensional modeling.

The inventors submit that determining whether a residue may be expected to influence antigen binding is routine in the art, in light of the detailed teachings of the specification.

Claim 2 was rejected as lacking enablement for determining which residues are exposed on the surface or buried within the domain. As indicated in the specification, for example at page 91, lines 18-21, the worker in this field would examine the structural models of the import and human sequences to determine if an amino acid residue is exposed on the surface of the domain or is buried within. Evaluation of structural models, preparation of which are described in the specification, to determine whether a residue is exposed or buried is routine and within the ordinary skill in the art.

Claim 3 was rejected as lacking enablement for how one would determine which glycosylation site affects antigen binding, or what comprises "reasonable expectation". The specification teaches, at page 8, lines 22-32, teaches that determining if the glycosylation is reasonably expected to be important for the desired antigen binding and biological activity of the antibody involves determining if the glycosylation site binds to antigen or changes a side chain of an amino acid residue that binds to antigen, or if the glycosylation enhances or weakens antigen binding, or is important for maintaining antibody affinity. As with other aspects of this invention, evaluation of the impact of glycosylation typically is performed by evaluation of molecular models, or experimental evaluation of a modified polypeptide. Such evaluation is routine within the field.

Claims 6, 7 and 9 were rejected as being enabled only with respect to IgG and not other antibody isotypes. The specification, at page 13 lines 14-22, states:

"The humanized antibody will be selected from any class of immunoglobulins, including IgM, IgG, IgD, IgA and IgE, and any isotype, including IgG1, IgG2, IgG3 and IgG4. Usually the constant domain is a complement fixing constant domain where it is desired that the humanized antibody exhibit cytotoxic activity, and the class is typically IgG_1. Where such cytotoxic activity is not desirable, the constant domain may be of the IgG_2 class. The humanized antibody may comprise sequences from more than one class or isotype, and selecting particular constant domains to optimize desired effector functions is within the ordinary skill in the art."

The Examples presented in the specification involve the use of a IgG_1 constant domain. As noted in the specification, specific method steps and illustrative reagents for the use of IgG_1 are taught, as well

as their applicability to other antibody isotypes. The inventors respectfully reminds the Examiner that working examples are not a required component of a patent application. As stated in MPEP § 608.01(h), "There is no statutory requirement for the disclosure of a specific example." Thus, the absence of a working example describing particular embodiments of the invention cannot negative the patentability of the invention. The examples included in the specification, which illustrate the preparation of IgG_1 antibodies, are representative of the manner in which the invention may be practiced. From reading these examples and the detailed description of the invention, the ordinarily skilled artisan would immediately deduce the applicability of the methods described in the specification to other immunoglobulin isotypes.

The Examiner has not made a prima facie case for the § 112, first paragraph rejections, supplying no basis for her skepticism about the scope of the claims. The burden is on the Examiner to provide evidence to support rejections of this sort. "Mere broad generalizations and allegations are insufficient for holding of non-enablement," Ex parte Goeddel, 5 U.S.P.Q. 1449, 1450 (TTAB 1987).

If the Examiner is only prepared to allow claims to exemplified embodiments, what incentive exists for an inventor to disclose the invention to the public? Trade secret protection obviously would be superior to the following circumstances foreseen by the CCPA in In re Goffe, 191 USPQ 429, 431 (CCPA 1976):

> For all practical purposes, the board would limit appellant to claims involving the specific materials disclosed in the examples, so that a competitor seeking to avoid [literally] infringing the claims would merely have to follow the disclosure in the subsequently-issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. See In re Fuetterer, 50 CCPA 1453, 1462, 319 F.2d 259, 265, 138 USPQ 217, 223 (1963).

For a similar case, see In re Strahilevitz, 212 USPQ 561 (P.O.B.A. 1982), where the Board was reversed for rejecting as non-enabling an application that was devoid of even a single working example.

The first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. Whether this is achieved by the use of illustrative examples or by broad terminology is of no importance, In re Marzocchi et al., 169 USPQ 267 (CCPA 1971). Further, an assertion by the Examiner that the enabling disclosure is not commensurate with the protection being sought must be supported by reasons for doubting the truth or accuracy of any statement in the presumptively accurate supporting disclosure. It is also incumbent upon the Examiner to back up such assertions with acceptable evidence or reasoning to substantiate the doubts so expressed, In re Armbruster, 185

USPQ 152 (CCPA 1975), In re Strahilevitz, *op cit.*

Se also In re Smith, *supra*, wherein the CCPA reversed an Office ruling that the description in the specification of two categories of prepolymers was not sufficient to support the broad claim for all polymers having a certain desired property. In this case, the court even acknowledged that the specification did not contain language that was precisely identical to the language of the claims. However, the tenor of the specification was that the applicant had made a generic invention rather than one limited to two categories of polymers.

In the present situation, the Examiner has provided no evidence to support the assertion that the invention is not enabled for the preparation of humanized antibodies. Broad claims should be allowed if there is adequate disclosure and where, as in the present situation, there is no pertinent art to prevent such claims. As stated in In re Sus and Schaefer, 134 USPQ 301, 304 (CCPA 1962) (emphasis added):

> The public purpose on which the patent law rests required the granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions. It is neither contemplated by the public purpose of the patent laws nor required by the statute that an inventor shall be forced to accept claims narrower than his invention in order to secure allowance of his patent.

The inventors submit that in view of the detailed information provided in the specification as discussed above, the specification adequately teaches how to practice the claimed invention. The rejections under 35 USC § 112, first paragraph, should be reconsidered and withdrawn, as they are not statutorily based, are inconsistent with court and Patent Office decisions on the subject, and are contrary to public policy.

The rejection under 35 U.S.C. § 101

Claims 1-4, and 6-8 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. It is believed that the amendments to the claims made above render moot this ground of rejection.

The rejection under 35 U.S.C. § 112, first paragraph and under 35 U.S.C. § 101

Claims 9-13 were rejected under 35 U.S.C. § 112, first paragraph and under 35 U.S.C. § 101 as lacking utility for the treatment of malignant and autoimmune diseases in humans. The inventors request clarification of this rejection, because none of claims 9-13 are directed to methods of treatment. These claims are directed to humanized antibody variable domains and the polypeptides

of recited sequences. These polypeptides are useful as probes, and in diagnostic assays, as described in the specification at pages 65-66, and need not rely on therapeutic utility.

The rejections under 35 U.S.C. § 102(b) and § 102(a)

Claims 1, 2, and 5-10 were rejected under 35 U.S.C. § 102(b) as being anticipated by Queen *et al.*, and under 35 U.S.C. § 102(a) as being anticipated by Co *et al.*. The inventors respectfully traverse these rejections.

To constitute anticipation, all material elements of a claim must be found in one prior art source. In re Marshall, 198 USPQ 344 (CCPA 1978); In re Kalm, 154 USPQ 10 (CCPA 1967). The inventors will show that neither Queen nor Coe contains all the material elements of these claims, particularly the limitation regarding the use of a consensus sequence.

The rejected claims are directed to the humanization an antibody, namely the combination of amino acid sequence from a non-human antibody desired to be humanized, and from a consensus human variable domain. Methods for preparing such a consensus sequence are fully described in the specification and are discussed above. The inventors believe that the use of a such a consensus sequence achieve a superior result, or a "better" humanized antibody.

The cited prior art utilizes a different approach, which approach had apparently been taken by all other workers in the field prior to the present invention. These workers did not prepare a consensus human antibody to combine with their non-human antibody. Instead, they selected only one human antibody for use, based on the similarity of that human antibody to their non-human antibody. Queen *et al.* state this objective explicitly, at page 10031, column 2 of their paper:

> "In selecting a human antibody to provide the variable region framework for the humanized anti-Tac antibody, we reasoned that the more homologous the human antibody was to the original anti-Tac antibody, the less likely would combining the anti-Tac CDRs with the human framework be to introduce distortions into the CDRs."

Queen continues to describe selecting a human heavy chain V region which was 57% identical to their non-human antibody, after dismissing all other candidate as between 30-52% identical to their non-human. They selected the human light chain V region from the same human antibody for their use.

Co *et al.* are equally explicit describing their similar reasoning. At page 2871, column 1 they state:

> "First, a human antibody variable region with maximal homology to the mouse antibody is selected to provide the framework sequence for humanization of the mouse antibody. Normally the heavy chain and light chain from the same human antibody are

chosen so as to reduce the possibility of incompatibility in the assembly of the two chains. Based on a sequence homology search against the NBRF protein sequence data base, the antibody Pom was chosen to provide the framework sequences for humanization of Fd79."

The approach of the present invention is quite distinct, in its use of a consensus human variable domain sequence. This consensus sequence might or might not have a high degree of homology with the non-human antibody. Neither Queen *et al.* or Coe *et al.* supply this teaching, and therefore do not anticipate the claimed invention. This rejection should be reconsidered and withdrawn.

The rejection under 35 U.S.C. § 103

Claims 3 and 4 were rejected under 35 U.S.C. § 103 as being obvious over Queen *et al.* or Co *et al.* in view of Wallick *et al.*. Claim 11 was rejected under 35 U.S.C. § 103 as being unpatentable over Queen *et al.* or Co *et al.* in view of Reichmann *et al.*

None of the cited references teaches or suggests the claimed invention, which involves the preparation humanized antibodies using a consensus human antibody variable domain. Such a method is not suggested in any of the prior references, and absent such a teaching there was no motivation to try the methods described in the present specification.

The Obviousness Rejections Do Not Meet the Test of Graham v. Deere

The proper context for determining the issue of obviousness is provided in the seminal decision of Graham v. John Deere, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). In that case, the U.S. Supreme Court set forth the following considerations for deciding this issue:

(1) The scope and the content of the prior art;

(2) The difference between the prior art and the claims at issue;

(3) The level of ordinary skill in the pertinent art; and

(4) Secondary considerations such as commercial success, long-felt and unresolved needs, failure of others, etc.

a. Scope and Content of the Prior Art.

1. Queen *et al.* teach the humanization of an anti-Tac antibody. They do not teach the use of a human consensus variable domain to provide the framework for their non-human CDRs.

2. Co *et al.* teach the humanization of an anti-HSV antibody. They do not teach the use of a human consensus variable domain to provide the framework for their non-human CDRs.

3. Wallick *et al.* teach the importance of glycosylation for maintaining the affinity of a monoclonal antibody for its antigen. They do not teach methods for humanization of antibodies, nor teach the creation of a human antibody variable domain consensus sequence.

4. Reichmann *et al.* teach the humanization of an anti-CAMPATH-1 antibody. They do not teach the creation of a human antibody variable domain consensus sequence, or suggest that such might be desirable to provide the framework for their non-human antibody CDRs.

b. The Differences Between the Prior Art and the Claims at Issue

The Examiner has chosen various pieces of prior art and concludes that the combination of these references would have rendered the invention obvious.

The prior art shows that it was known as of the filing date to produce antibody fragments comprising sequence from a non-human antibody and from a human antibody. Prior to the present filing date, however, methods were not known which included the use of a consensus human variable domain for mounting the non-human CDRs. There would have been no impetus on the part of the skilled artisan at the filing date to attempt to produce such a consensus sequence or use it in antibody humanization, in view of the teachings of the prior art literature. The cited references do not teach or suggest the claimed invention, alone or in any combination, nor would there have been any reason from these references to practice the claimed methods. The absence of a suggestion of the claimed invention in the art of record precludes the Patent Office from satisfying its initial burden of showing prima facie obviousness.

c. Level of Ordinary Skill in the Art.

The Graham inquiries point to a conclusion of non-obviousness of the present claims regardless of the presumed level of skill in the art. However, absent evidence to the contrary, a person of ordinary skill in the art is presumed to be one who essentially follows conventional wisdom and does not undertake to innovate. As stated by the Federal Circuit in Standard Co. v. American Cyanamid Co., 227 U.S.P.Q. 293, 298 (Fed. Cir. 1985):

> A person of ordinary skill in the art is also presumed to be one who thinks along the line of convention wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights, it makes no difference which.

The inventors submit that one who followed the conventional wisdom would not have

extrapolated from the teachings of the cited references methods for using a consensus human antibody variable domain for humanizing a non-human antibody. Such an extension of the prior art teachings is based entirely upon hindsight analysis of the inventors' methods. The teachings of this invention should not be considered sufficient to support a conclusion of obviousness in this regard.

The inventors submit that in light of the foregoing amendments and remarks the subject matter defined by the pending claims is useful, enabled, and patentable over the references relied upon by the Examiner, which in no way teach or suggest the invention. The inventors believe the claims are now in condition for allowance and earnestly solicit a Notice to that effect. If the Examiner has any questions, she should feel free to contact the undersigned attorney at the telephone number indicated above.

Respectfully Submitted,
GENENTECH, INC.

Carolyn R. Adler
Reg. No. 32,324

29 January 1993

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 29 January 1993.

Dated: 29 January 1993

Carolyn R. Adler

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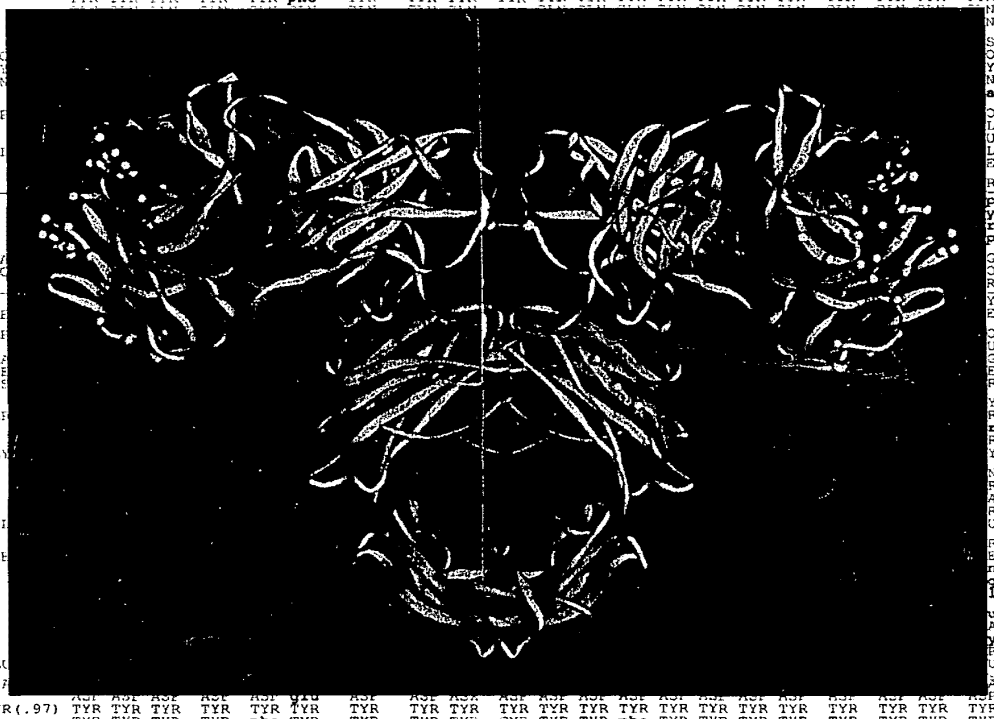
SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST

VOL I

FIFTH EDITION



1991

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

EXHIBIT A

SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST

FIFTH EDITION

Tabulation and Analysis of
Amino Acid and Nucleic Acid Sequences of Precursors,
V-Regions, C-Regions, J-Chain, T-Cell Receptors for Antigen,
T-Cell Surface Antigens, β_2-Microglobulins,
Major Histocompatibility Antigens, Thy-1, Complement,
C-Reactive Protein, Thymopoietin, Integrins, Post-gamma Globulin,
α_2-Macroglobulins, and Other Related Proteins

1991

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The collection and maintenance of this data base is sponsored under grant 5R01 AI-125616 to E.A. Kabat of Columbia University by the following components of the National Institutes of Health, Bethesda, MD 20892:

Office of the Director
National Center for Research Resources
National Cancer Institute
National Institute of Allergy and Infectious Diseases
National Institute of Diabetes, Digestive and Kidney Diseases
National Institute of General Medical Sciences
National Library of Medicine

Work with the PROPHET software package is supported by a subcontract from Columbia University to BBN Systems and Techologies, Cambridge, MA 02138

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

Public Health Service
National Institutes of Health

NIH Publication No. 91-3242

INTRODUCTION

Our earlier "Variable Regions of Immunoglobulin Chains" (1), the second edition "Sequences of Immunoglobulin Chains" (2) and the third edition "Sequences of Proteins of Immunological Interest" (3) have been further exixpanded in the Fourth Edition (4) and now in the Fifth Edition to include amino acid and nucleotide sequences of precursors, variable regions, constant regions, J-chains of immunoglobulins, β2-microglobulins, antigens of the major histocompatibility complex (HLA, H-2, Ia, DR) as well as of Thy-1, complement, T-lymphocyte receptors for antigens, other T-cell antigens of the immunoglobulin superfamily, interleukins, integrins and various other proteins related to immune functions. The identification and sequencing of clones obtained using recombinant DNA techniques has yielded nucleotide sequences of signal, variable, and constant regions of immunoglobulins (5,6), and these nucleotide sequences have been translated into amino acid sequences. The latter have been included in the tables of amino acid sequences with those determined earlier directly by amino acid sequencing and are indicated by an apostrophe followed by CL after the name of the clone. We have continued to use the PROPHET Software Package of the National Center for Research Resources, National Institutes of Health (7,8) to tabulate the sequences.

In compiling the data for this Fifth Edition we have tried to be as up-to-date as possible and have included only sequences which have been published or which have been accepted for publication. Residues which have not been definitely determined have been excluded. It should be remembered that sequences are often published in review articles without detailed documentary evidence. These have often been revised. We have listed such revisions in the notes in many instances; others can readily be found by comparison with sequences in previous editions. We have compiled sequences determined directly as amino acids and have merged with them those translated from the nucleotide sequences thus making all comparable data available. When antibody activities were known, they have been listed after the amino acid and nucleotide sequence tables and are included in the indexes.

When doubts arise as to the validity of any residue in a sequence, the original reference should be examined to ascertain whether definitive evidence for the sequence has been provided. In earlier editions, we have sent the amino acid and nucleotide sequences as stored in the computer to the original authors for verification. If so verified, this was denoted by "checked by author" at the end of each reference and except for the earliest sequences, the date on which the checked sequence was returned to us is given. Whenever possible, nucleotide sequences from GenBank (9) have been used. Programs for converting a GenBank sequence to the codon format of our tables have been developed. The correctness of the table sequence has been verified by converting back into the linear form and comparing with GenBank. When this has been done the sequence is listed as "from GenBank". Recently we have developed newer programs that automatically process a GenBank entry completely - e.g.: extract the relevant feature, determine the appropriate table, and perform alignment. In such cases, the reference will end with "processed automatically from GenBank:" followed by a list of the GenBank accession numbers from which the data was obtained. Some nucleotide sequences were transmitted to us by electronic mail, and they are indicated by "received from authors through e-mail." If the sequences were entered by us from the literature and then checked with GenBank, this is indicated by "checked with GenBank". We have entered many nucleotide sequences which were not then available from GenBank. In general, we have not included stretches of sequence such as enhancers, switch regions and introns. Much information about such sequences may be found in references (10-13). We have also had access to the Protein Information Resource (14) and to the European Molecular Biology Laboratories Data Base (15).

It is also possible, by examining the numbers of sequences at the

end of each table and the summary tables, to evaluate the probability that a given amino acid at a given position may not be correct. This is most readily done for the framework residues of the V-region and for the C-region; in the complementarity-determining regions this is more difficult because of the high variability.

AMINO ACID SEQUENCES

The first column in each table gives the residue number. Except for complement, T-cell surface antigens, integrins and miscellaneous proteins, the second column is a tabulation of invariant residues. Since exceptions to invariance are found, the frequency, if less than 1.0 and greater than or equal to 0.95, is indicated alongside the residue listed as invariant; when only a single sequence is available, this is not given. These rows are shaded in grey. Each sequence is tabulated in each subsequent column. Three dashes (---) indicate that no amino acid is present at that position and that the sequence continues. In all instances residues considered uncertain by the authors have not been included in the table. In some instances the symbol # is used to indicate that several amino acid residues were found in one position, and these residues are listed in the notes. The four columns at the end of each table give:

1. the number of residues sequenced at that position,
2. the number of different amino acids found at that position,
3. the number of times the most common amino acid occurred and that amino acid in parentheses, and
4. the variability.

These columns are included only in tables with more than five sequences. Miscellaneous tables have only columns corresponding to the first two above.

Variability is calculated (16) as:

$$\text{Variability} = \frac{\text{Number of different amino acids occurring at a given position}}{\text{Frequency of the most common amino acid at that position}}$$

An invariant position would have a variability of one; if 20 amino acids occurred with equal frequency, the variability would be 20 divided by 0.05 equals 400. If, for example, four different amino acids Ser, Asp, Pro, and Thr occurred at a given position, and of 100 sequences available at that position, Ser occurred 80 times, the variability would be 4/0.8 = 5. When any of the amino acid residues, sequenced directly as amino acids, were not identified completely and are listed as Glx (or Asx), two values, separated by a comma, are given in the last three columns. The first value in each of these columns is calculated assuming that only one of the two possibilities, e.g., Glu or Gln (or Asp or Asn) occurred, while the second considers that both were present and maximizes variability. In the variability plots, the horizontal bars indicate the two values.

When two or more amino acids are most common and occur with equal frequency, they are tabulated as a note, and the symbol + is used in the next to last column. If no sequence data have been reported for any position, there are no entries in the last four columns. Variability is not calculated for insertions or if only a single sequence is known. When the translated sequence of a clone corresponds to a previously listed sequence of a plasmacytoma from

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Table I.

which it was prepared, only one sequence is listed so that the variability computations are not affected, and a note is included. If a given sequence is associated with any antibody activity, this is indicated by an asterisk alongside the protein heading, and the antibody specificities are given in a separate list with binding constants if available. The notes list the a-allotypes for the rabbit heavy chain V-region and the b-allotypes for the constant domain of the rabbit kappa light chain. A key reference to the sequence is given; generally the most recent reference since it is usually the most nearly complete, but often several references are included, especially when revisions of a sequence have been made. Notes are of two types: general notes about a table indicated by the symbol #, and specific notes indicated by the sequence number.

Signal Sequences

The signal (precursor) amino acid sequences of immunoglobulin chains are listed as human, mouse, and miscellaneous for kappa light chains, for lambda light chains, and for heavy chains for a total of nine precursor tables. They were obtained either by direct sequencing of signal proteins (17-19) or by translating nucleotide sequences from DNA clones. Signal segments range from 17-29 amino acid residues in length and are thus numbered from -29 to -1. Genomic DNA clones contain introns of varying length that interrupt the coding sequence of the precursor within the codon for position -4, and in rare cases for position -6. Thus, the L-gene encodes the leader peptide to position -4 and the 5' end of the V-gene codes for positions -4 to -1.

The signal amino acid sequences of the T-cell receptors for antigens, β2-microglobulins, major histocompatibility complex proteins, complement components, integrins, and other related proteins are listed in separate tables.

By conformational energy calculations, the core V_κ hydrophobic Leu-Leu-Leu-Trp-Val-Leu-Leu-Leu (MOPC321, MOPC63) exists in an alpha helical conformation, terminated by chain reversal conformations in the four C-terminal residues Trp-Val-Pro-Gly; the four amino terminal residues are compatible with the alpha helix (20).

Variable Region Sequences

The variable regions (21) of immunoglobulins have been shown to contain hypervariable segments in their light (16,22-26) and heavy (27-30) chains, of which certain residues have been affinity labeled with haptenic determinants (31-44). Three hypervariable segments of light chain were delineated from a statistical examination of sequences of human V_κ, human V_λ, and mouse V_κ light chains aligned for maximum sequence similarity (16,23,24,27). These and the three corresponding segments of the heavy chains (27) were hypothesized (16,27) to be the complementarity-determining regions or segments (CDR) containing the residues which make contact with various antigenic determinants, several years before high resolution x-ray structures were determined, and this has now been verified by X-ray diffraction studies at high resolution for all antibodies examined Figures 3-47. The proposed fourth hypervariable region (cf. 30) of heavy chains is not part of the antibody combining site (27). The rest of the V-region constitutes the framework (16,27,45-54). It is convenient to identify the framework segments (FR1, FR2, FR3, and FR4) and the complementarity-determining segments (CDR1, CDR2, and CDR3) with the three CDRs separating the four FRs. The CDRs in the stereo Figures 3-47 have solid circles for each residue. References and comments are given with each figure and are not listed in the bibliography. The residue numbers for these segments are given in Table I.

TABLE I

Amino Acid Residues Associated with Framework(FR) and Complementarity Determining Regions (CDR) of the Variable Domains of Immunoglobulin Light (V_L) and Heavy (V_H) Chains

Segment	Light Chain	Heavy Chain
FR1	1-23 (with an occasional residue at 0, and a deletion at 10 in V_λ chains)	1-30 (with an occasional residue at 0)
CDR1	24-34 (with possible insertions numbered as 27A,B,C,D,E,F)	31-35(with possible insertions numbered as 35A,B)
FR2[a]	35-49[a]	36-49
CDR2	50-56	50-65 (with possible insertions numbered as 52A,B,C)[b]
FR3	57-88	66-94 (with possible insertions numbered as 82A,B,C)
CDR3	89-97 (with possible insertions numbered as 95A,B,C,D,E,F)	95-102 (with possible insertions numbered as 100A,B,C,D,E,F,G,H,I,J,K)
FR4	98-107 (with a possible insertion numbered as 106A)	103-113

[a] Five Basilea rabbits (λ) immunized with type II pneumococci and which produced anti-type II pneumococcal polysaccharide had Met at position 48 and an insertion of four amino acid residues between positions 48 and 49; in four of the five the sequence was Glu, Leu, Lys, Ser and the fifth was Trp, Leu, Arg, Lys (53,54,63,64); the others were not sequenced at these positions (for references see table of rabbit λ amino acid sequences.)

[b] In the rabbit, Mage et al. (65) consider position 65 in V_H to be in FR3, since it is allotype related.

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The V-genes for the light chains code to amino acid position 95, and the J-minigenes from position 97 to 107 for lambda and 108 for kappa light chains. Position 96 is usually the site of V-J joining by recombination and may be coded partly by the V-gene and partly by the J-minigene. Because the site of V-J recombination could occur at different positions within a codon, different amino acid residues may result at this position. We have changed the location of the inserted residues from 97A-F (2) to 95A-F, since it makes for better alignment by confining chains of different lengths to the V-gene region. In mouse V_κ chains, J1 and J2 were used 5 to 10 times more frequently than J4 and J5 (55).

The V-genes for the heavy chains code up to amino acid position 94 and are followed by the D- and J-minigenes. Because of the extensive variation in the lengths of D-minigenes, and their ability to be read in different reading frames (56), the exact boundary between D and J is not always located at the same amino acid position. In addition, the lengths of the J encoded amino acid sequences vary by a few amino acid residues. Moreover, the process of D-J joining appears to involve insertions of extra nucleotides between V and D and between D and J, termed the N region (57-61) and correlates with the appearance of terminal deoxytransferase in B cells (60). The original numbering system for the heavy chains has therefore been retained. Wysocki et al. (61) have provided some evidence suggesting a non-random origin for the V_H-D_H junction, perhaps a minigene, rather than random addition of the N nucleotides. Light chains do not appear to have N sequences at the V_L-J_L junction (62), but show an additional residue 95A which probably results from V_L-J_L joining. N sequences are generally rare in fetal and neonatal mouse V_H-D-J_H junctions (62), only 1/87 DNA and 17/146 RNA sequences contained N regions, an incidence much lower than in adults indicating that N insertion is developmentally regulated both in T and B cells. P elements also contribute to diversity but are templated (62a).

In the tables of V-regions, the FR and CDR are separated by horizontal lines for convenience in reading. One mouse kappa light chain, MPC 11, has an extra segment of 12 amino acid residues between position 1 and the signal sequence (66). Several chains have internal deletions.

Figure 1 (50) shows the domain structure for IgG1 protein EU. Numbering on the left half indicates the CDR for the light and heavy chains (50), while that on the right half gives the EU numbering (67).

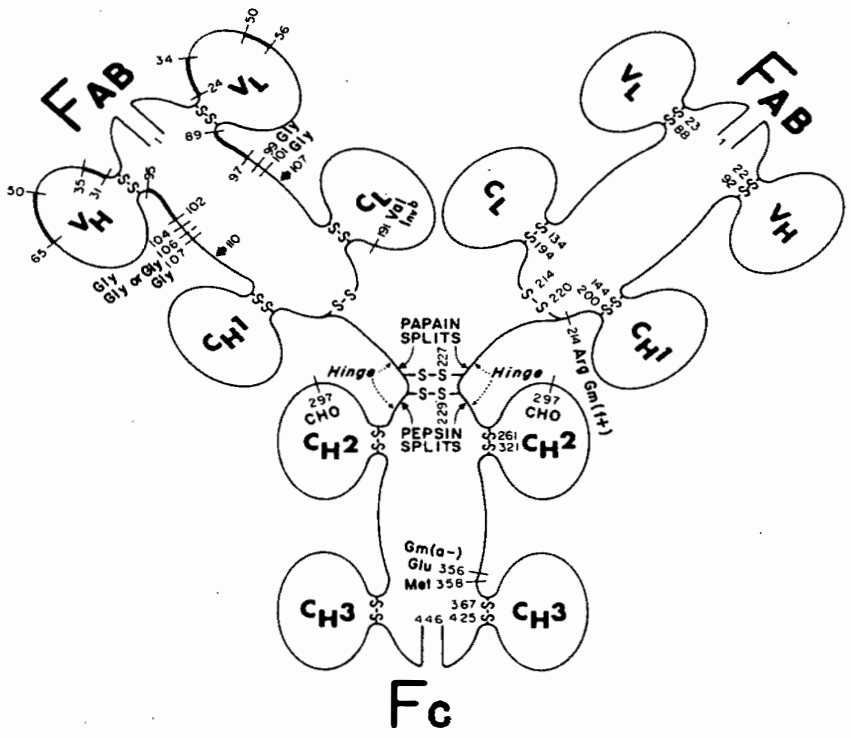

FIG. 1. Schematic view of four-chain structure of human IgG1$_\kappa$ molecule. *Numbers on right side:* actual residue numbers in protein EU [Edelman *et al.* (67)]; *Numbers* of Fab fragment on *left side* aligned for maximum homology; light chains numbered as in Wu and Kabat (16) and heavy chains as in Kabat and Wu (27). Heavy chains of EU have residue 52A, three residues 82A,B,C, and lack residues termed 100A,B,C,D,E,F,G,H,I,J,K, and 35A,B. Thus residue 110 (end of variable region) is 114 in actual sequence. Hypervariable regions, complementarity-determining segments or regions (CDR): *heavier lines.* V_L and V_H: light and heavy chain variable region; C_H1, C_H2, C_H3: domains of constant region of heavy chain; C_L: constant region of light chain. *Hinge region* in which two heavy chains are linked by disulfide bonds is indicated approximately. Attachment of carbohydrate is at residue 297. *Arrows* at residues 107 and 110 denote transition from variable to constant regions. Sites of action of papain and pepsin and locations of a number of genetic factors are given. Modified from 50.

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Critical understanding of the architecture of antibody combining sites and the genetics of the generation of diversity and of antibody complementarity depends to a great extent on the evaluation of a large number of sequences of the variable regions and especially of the complementarity-determining segments of light and heavy chains of immunoglobulins of different species. Ability to locate residues in the site making contact with antigenic determinants (68,69) and to predict (70) the structures of antibody combining sites will depend heavily upon such sequences. The role and scope V_H and V_L chains in contributing to binding of the epitope must be resolved. This can be often accomplished by use of immunochemical data in defining antibody combining sites (68,70-73) in addition to other methodologies such as 2D-NMR (71,51) or high resolution X-ray crystallography.

Through the generous cooperation of X-ray crystallographers we have been provided with the α-carbon coordinates of almost all available Fab molecules, V_H dimers and antigen-antibody complexes from which Drs. Eduardo Padlan and Chantal Abergal made the stereo models shown. Legends and key references for each are listed with the model.

E. Long, R. Mage, C. ub and L. Steiner for rlier editions.

s of Fab and antigen as α-carbon coordinates in the text where these an and Chantal Abergel (stereodiagrams from indebted to them. Dr. the x-ray structure of bted to Drs. Rose Mage the introduction and to tions to organizing the Margulies made helpful text. Dr. Lawrence A. se V_H and V_κ families as V_H and V_κ sequences into

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PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Paul J. Carter et al.

Serial No. 07/715,272

Filed: 14 June 1991

For:Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. Feisee

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-2614

PETITION AND FEE FOR EXTENSION OF TIME (37 CFR 1.136(a))

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Applicant petitions the Commissioner of Patents and Trademarks to extend the time for response to the Office action dated 05 October 1992 for one month(s) from 5 January 1993 to 5 February 1993. The extended time for response does not exceed the statutory period.

Please charge Deposit Account Number 07-0630 in the amount of $110. to cover the cost of the extension. Any deficiency or overpayment should be charged or credited to this deposit account. A duplicate of this sheet is enclosed.

Respectfully submitted,
GENENTECH, INC.

Carolyn R. Adler
Reg. No. 32,324

Date: 29 January 1993

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Carolyn R. Adler

Date: 29 January 1993

Carolyn R. Adler

c124.u

GENENTECH, INC.
460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-2614

#15 J. 8995 2293

Attorney Docket No. 709
Examiner: L. Feisee
Group Art Unit 1806

In re Application of: Paul J. Carter et al.

Serial No.: 07/715,272

Filed: 14 June 1991

For: Immunoglobulin Variants

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Transmitted herewith is an amendment in the above-identified application.

The fee has been calculated as shown below.

	(Col. 1) Claims Remaining After Amendment		(Col. 2) Highest No. Previously Paid For	(Col. 3) Present Extra	Rate	Addit. Fee
Total	* 21	Minus	** 21	= 0	x 20=	$ 0
Indep.	* 10	Minus	*** 8	= 2	x 72=	$ 144
_____ First Presentation of Multiple Dep. Claim					+ 220=	$ 0
					TOTAL . . .	$ 144.

*If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.
**If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
***If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space.
The "Highest Number Previously Paid For" (Total or Independent is the highest number found from the equivalent box in col. 1 of a prior amendment or the number of claims originally filed.)

1. __ No additional fee is required.

2. x Please charge any additional fees, including any fees necessary for extensions of time, or credit overpayment to Deposit Account No. 07-0630. A duplicate copy of this sheet is enclosed.

x Any additional filing fees required under 37 CFR 1.16.
x Any patent application processing fees under 37 CFR 1.17.

Dated: 29 January 1993

Carolyn R. Adler
(Attorney of Record)

Carolyn R. Adler
Registration No. 32,324

SC13193 02/17/93 07715272 07-0630 130 115 110.00CH

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service on the date below as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Dated: 29 January 1993

Carolyn R. Adler

c124.u

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address : COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/715,272	06/14/91	CARTER	P 709

EXAMINER
PEISEL, L

18M2

GENENTECH, INC.
ATTN: CAROLYN R. ADLER
460 POINT SAN BRUNO BLVD.
SOUTH SAN FRANCISCO, CA 94080

ART UNIT	PAPER NUMBER
1806	17

DATE MAILED: 05/19/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 2/3/93 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-23 are pending in the application.
   Of the above, claims 14-16 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☒ Claims 12 and 13 are allowed.
4. ☒ Claims 1-13, 17-21 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Some of the rejections under 35 USC 112 second paragraph have been obviated in view of the amendments to the claims. However, the following rejection still remain. The language "consensus human variable domain" is still unclear despite the description in the specification. It is unclear whether the consensus human variable domain is a culmination of different variable domains or a single universal variable domain which is homologous to other human variable domains.

With regards to the langauge "import amino acid", it is suggested the import amino acid be described in the following manner: "an import antibody comprising the amino acid sequence of a non-human antibody which binds to ...". The language "reasonably expected" is unclear since it is not known what criteria determines what is "reasonable".

Claim 1 remains rejected and new claims 19-21 are rejected under 35 USC 112 first paragraph as lacking enablement for the language "at least a portion" for the same reasons as set forth in pages 3 and 4 of paper #13.

Applicant states that this language has been deleted from claim 1, but, this is not the case. This language has been moved to the beginning of the claim and the claim contains the same objectionalble language, therefore, the rejection set forth

previously still applies.

The rejection of claims 1-4, 6-8 under 35 USC 101 is withdrawn in view of the amendment to the claims.

The rejection of claims 9-13 as lacking utility is withdrawn in view of the argument set forth in the letter of 2/3/93.

The objection to the specification and the rejection of claims 1-11 under 35 USC 112 first paragraph is maintained and newly added claims 17-21 are rejected for the reasons of record.

The language "at least a portion" still remains in claim 1 and newly added claims 19-21. Therefore, the rejection set forth previously on pages 3-4 of paper #13 still applies. With regards to substituting an import CDR in place of the human CDR, the rejection still applies, since there is no clear guidance in the specification to enable one of ordinary skill in the art to make the human "consensus variable region" which is to contain the claimed substitution. It is true that once the amino acid sequences are known, it is routine to determine the CDRs according to Kabat, and substitute the rodent CDRs in place of the human CDRs. However, the only guidance presented in the specification with regards to the substitutions is the amino acid sequences of SEQ ID NO: 3 and 4, which are specific variable regions. The specification vaguely alludes to variable domain sequences which are derived from the most abundant subclasses but shows no way of making such variable domains. The fact remains

that applicant has not clearly taught how to determine which amino acids are the ones to be substituted since there is only a single example of the appropriate variable region which is to support the substitutions.

The rejection of claim 2 with regards to determining which residues are surface or buried residues is withdrawn in view of the argument presented explaining that computer modeling is well known in the art to determine the position of various amino acid residues.

The rejection of claims 1 and 3 with regards to the language "reasonably" and newly added claim 19 is maintained, since there is no set standard for determining what is reasonable interaction, or interfacing or what amount of glycosylation reasonably affects binding.

The rejection of claims 6,7 and 9 based on the specific amino acids sequences which are only relevant to IgG is maintained. Applicant argues that he is not required to exemplify every embodiment, however, if the claim requires the presence of a certain sequence which does not exist in a particular isotype, than clearly there is a lack of enablement for making that particular embodiment of the claim.

The rejections of claims 1,2,5-10 under 35 USC 102(a) and 102(b) is maintained and newly added claims 17-21 are rejected under 35 USC 102(a) and 35 USC 102(b) as being anticipated by

Queen et. al. or Co et. al. for the same reasons as set forth in the previous Office action.

Applicant argues that the distinction between the prior art and the instant invention is that the framework amino acids are chosen from a consensus human variable region. However, as previously mentioned there is no clear indication of what is meant by consensus variable regions and as it is stated by applicant on page 14 of the response the chosen amino acids in the references may indeed be the same as what applicant calls consensus variable domain sequences.

The rejection of claims 3 and 4 under 35 USC 103 is maintained for the same reasons as set forth in the previous Office action. Applicant again argues that the use of "consensus region variable domains" is different from the prior art methods, however, as previously mentioned, the consensus amino acids may be the same as the most homologous murine antibodies of the references. The lack of clarity of the language "consensus" amino acid region" is what allows this particular interpretation of the claims.

Claims 17,18, 20 and 21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject, matter which applicant regards as the invention. New claims 17,18,20 and 21 are indefinite in that there are no discrete method steps.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lila Feisee whose telephone number is (703) 308-2731.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Feisee/em
May 18, 1993

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
5/19/93

FORM PTO-1449 | U.S. Dept. of Commerce, Patent and Trademark Office

Atty Docket No.	Serial No.
709	07/715,272

LIST OF DISCLOSURES CITED BY APPLICANT

(Use several sheets if necessary)

Applicant: Paul J. Carter et al. #14

Filing Date	Group
June 14, 1991	1806

U.S. PATENT DOCUMENTS

*Examiner Initials		Document Number	Date	Name	Class	Subclass	Filing Date
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes	Translation No
CR	AL	WO 90/07861	7/26/90	PCT	—	—		
	AM							
	AN							
	AO							
	AP							

OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, Etc.)

CR	AR	Carter et al., Proc. Natl. Acad. Sci., 89: 4285-4289 (1992)
	AS	
	AT	
	AU	
	AV	
	AW	
	AX	

Examiner: [signature] Date Considered: 4/29/93

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

GENENTECH, INC.
460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-2614

Corres. and Mail
BOX AF

Attorney Docket No. 709
Examiner: L. FEISEE
Group Art Unit 1806

In re Application of: Paul J. Carter et al.

Serial No.: 07/715272

Filed: June 14, 1991

For: Immunoglobulin Variants

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Transmitted herewith is an amendment in the above-identified application.

The fee has been calculated as shown below.

	(Col. 1) Claims Remaining After Amendment		(Col. 2) Highest No. Previously Paid For	(Col. 3) Present Extra	Rate	Addit. Fee
Total	* 17	Minus	** 21	= 0	x 22=	$ 0
Indep.	* 6	Minus	*** 10	= 0	x 74=	$ 0
_____	First Presentation of Multiple Dep. Claim				+ 230=	$
					TOTAL . . .	$ 0

*If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.
**If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
***If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space.
The "Highest Number Previously Paid For" (Total or Independent is the highest number found from the equivalent box in col. 1 of a prior amendment or the number of claims originally filed.)

1. x No additional fee is required.

2. x Please charge any additional fees, including any fees necessary for extensions of time, or credit overpayment to Deposit Account No. 07-0630. **A duplicate copy of this sheet is enclosed.**

x Any additional filing fees required under 37 CFR 1.16.
x Any patent application processing fees under 37 CFR 1.17.

Dated: September 20, 1993

Janet E. Hasak
(Attorney of Record)

Janet E. Hasak
Registration No. 28,616

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service on the date below as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Dated: 20 Sept 1993

Louise Strasbaugh
Louise Strasbaugh

Corres. and Mail

BOX AF

1806

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Carter et al.

Serial No. 07/715272

Filed: June 14, 1991

For: Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. FEISEE

#18 Supp 9-28-93

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-1896

PETITION AND FEE FOR EXTENSION OF TIME (37 CFR 1.136(a))

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Applicant petitions the Commissioner of Patents and Trademarks to extend the time for response to the Office action dated 19 May 1993 for one month(s) from 19 August 1993 to 19 September 1993. The extended time for response does not exceed the statutory period.

Please charge Deposit Account Number 07-0630 in the amount of $110 to cover the cost of the extension. Any deficiency or overpayment should be charged or credited to this deposit account. A duplicate of this sheet is enclosed.

Respectfully submitted,

GENENTECH, INC.

Janet E. Hasak

Janet E. Hasak
Reg. No. 28,616

Date: September 20, 1993

07-0630 140 115 110.00CH

CS14005 09/24/93 07715272

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh

Louise Strasbaugh

Date: September 20, 1993

Amendment under 37 CFR 1.116
Expedited Procedure
Examining Group 1806

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	Group Art Unit: 1806
Paul J. Carter et al.	)	Examiner: L. FEISEE
Serial No. 07/715272	)	
Filed: June 14, 1991	)	
For: Immunoglobulin Variants	)	460 Point San Bruno Boulevard South San Francisco, CA 94080 (415) 225-1896

19(c)(ne) sucks 9-30-93

AMENDMENT AFTER FINAL REJECTION PURSUANT TO 37 CFR § 1.116

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

This is responsive to the Office Action mailed May 19, 1993, which is a final rejection of claims 1 to 11 and 17 to 21. Claims 12 & 13 have been allowed. A request for a one-month extension of time to respond is submitted herewith, bringing the due date for this response to September 20, 1993 as September 19 is a Sunday. This response is timely filed.

Do not enter

IN THE SPECIFICATION:

On page 19, line 3, please delete "effect or" and insert --effector--.

On page 87, please amend Table 1 as follows:

line 6, please amend the heading of the second to last column to read --$K_d^{\dagger}$--;

lines 6 & 7, please amend the heading of the last column to read --Relative

cell proliferation‡--;

line 8, please delete "proliferation‡";

line 10, please amend the second to last column to read --25-- and the last column to read --102--.

IN THE CLAIMS:

Please cancel claims 14-16 and 18 from the application, without prejudice. Please amend claims 1, 3, 7, 17, 19, 20 and 21 as follows:

1. (Twice amended) A method for making [at least a portion of] a humanized antibody variable domain comprising amino acid sequences of an import antibody comprising a non-human antibody which is desired to be humanized [(import antibody)] and a human antibody, comprising the steps of:

a. obtaining the amino acid sequences of an import variable domain and of a consensus human variable domain of a human immunoglobulin subgroup; New

b. identifying Complementarity Determining Region (CDR) amino acid sequences in the import and the human amino variable domain sequences;

c. substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence;

d. aligning the amino acid sequences of a Framework Region (FR) of the import antibody and the corresponding FR of the consensus antibody;

e. identifying import antibody FR residues in the aligned FR sequences that are non-homologous to the corresponding consensus antibody residues;

f. determining if the non-homologous import amino acid residue is [reasonably] expected to have at least one of the following effects:

1. non-covalently binds antigen directly,

2. interacts with a CDR; or

3. participates in the V_L - V_H interface by affecting the proximity or orientation of the V_L and V_H regions with respect to one another;

g. for any non-homologous import antibody amino acid residue which is expected to have at least one of these effects, substituting that residue for the corresponding amino acid residue in the consensus antibody FR sequence; and

h. preparing a humanized antibody variable domain having amino acid sequences determined in steps a-g.

In claim 3, line 4, please delete "reasonably".

7. (Twice amended) A method for making a humanized antibody comprising providing an import antibody comprising a non-human antibody variable domain amino acid sequence which is desired to be humanized [(import antibody)] having a CDR and a FR, obtaining the amino acid sequence of [at least a portion of] a consensus human antibody variable domain of a human immunoglobulin subgroup, having a CDR and a FR, substituting the non-human CDR for the human CDR in the consensus human antibody variable domain, and then substituting an amino acid residue for the consensus amino acid residue at at least one of the following sites:
4L, 35L, 36L, 38L, 43L, 44L, 46L, 58L, 62L, 63L, 64L, 65L, 66L, 67L, 68L, 69L, 70L, 71L, 73L, 85L, 87L, 98L, 2H, 4H, 24H, 36H, 37H, 39H, 43H, 45H, 49H, 58H, 60H, 68H, 69H, 70H, 73H, 74H, 75H, 76H, 78H, 91H, 92H, 93H, and 103H.

17. (Amended) A method of making a humanized antibody variable domain comprising the step of substituting Complementary Determining Region (CDR) amino acid residues of a variable domain of a non-human antibody for the corresponding CDR amino acid residues of [using] a consensus human antibody variable domain amino acid sequence of a human immunoglobulin subgroup [in the preparation of a humanized antibody].

19. (Amended) A method for making an improved antibody, comprising amino acid sequences from an import antibody comprising a non-human [(import)] antibody and a human antibody, comprising the steps of:

a. obtaining the amino acid sequences of [at least a portion of] an import antibody variable domain and of a consensus human antibody variable domain of a human immunoglobulin subgroup;

b. identifying Complementarity Determining Region (CDR) amino acid sequences in the import and the human [amino] variable domain sequences;

c. substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence;

d. aligning the amino acid sequences of a Framework Region (FR) of the import antibody and the corresponding FR of the consensus antibody;

e. identifying import antibody FR residues in the aligned FR sequences that are non-homologous to the corresponding consensus antibody residues;

f. determining if the non-homologous import amino acid residue is [reasonably] expected to have at least one of the following effects:

1. non-covalently binds antigen directly,

2. interacts with a CDR; or

3. participates in the V_L - V_H interface by affecting the proximity or orientation of the V_L and V_H regions with respect to one another;

g. for any non-homologous import antibody amino acid residue which is [reasonably] expected to have at least one of these effects, substituting that residue for the corresponding amino acid residue in the consensus antibody FR sequence[; and] ; and

h. preparing an improved, humanized antibody having amino acid sequences determined in steps a-g; and

i. evaluating the antigen binding or immunogenicity of the improved,

humanized antibody with respect to the parental antibody.

20. A method of making a humanized antibody comprising the step of making the antibody identified [, following the identification of an antibody] by the method of any one of claims [1,] 7[,] or 17 [-19, the manufacture of the antibody].

21. A method of making a humanized antibody comprising the step of expressing nucleic acid encoding the antibody identified [, following the identification of an antibody] by the method of any one of claims 1, 7, [or] 17, [-] or 19 [, the expression of nucleic acid encoding the antibody].

REMARKS

The claims pending in this application are claims 1 to 13, 17 and 19 to 21. Applicants have canceled claims 14 to 16 and 18, without prejudice to file divisional applications directed thereto.

The proposed amendments to the claims are purely in response to the rejections of the Final Action. No new matter has been introduced by the claim amendments. These amendments should be considered under Rule 116 because they do not introduce issues not already fully joined in this case and because they are believed to place the claims in better condition for appeal. Further, they are offered in a good faith effort to place this case in condition for allowance.

I. Amendments

The specification has been amended to correct obvious typographical errors. With respect to the amendment to Table 1 on page 87, a copy of Carter *et al., Proc. Natl. Acad. Sci.,* **89,** (1992) is attached, which is a publication of the experimental data disclosed in the above application, and was published after the filing date thereof. It is clear that the

last two column headings of Table 1 were inadvertently superimposed and the amendment to the specification serves merely to correct these errors. It would have been obvious from the information provided on page 87 of the specification, that the last two headings were intended to be "Kd nM", and "Relative cell proliferation", respectively, as the key under Table 1 discloses what the headings indicated by † and ‡ are. Also, it is clear that the figures in the last two columns of the first line of data in Table 1 were intended to be 25 and 102 respectively, and were inadvertently superimposed. Applicants respectfully request that the specification be amended to correct the obvious typographical errors discussed above.

Claims 1, 7, 17 and 19 have been amended to refer to the consensus human variable domain "of a human immunoglobulin subgroup", with support for the amendment found on at least page 16, lines 29-32 and page 17, line 4. Claim 17, 19, and 20 have been amended to recite a preamble and a positive step, which steps are clear from at least the original set of claims filed.

II. Rejections under 35 U.S.C. § 112, second paragraph

Most of the rejections under 35 U.S.C. § 112, second paragraph, which were raised in the earlier Office Action dated October 5, 1992 have been withdrawn. Applicants thank the Examiner for withdrawing these rejections.

The Examiner has, however, maintained some of the rejections under 35 U.S.C. § 112, second paragraph, which relate to claims 1, 3-5 and 7. The separate sets of rejections are addressed separately below.

A. The Examiner has maintained the rejection of claim 1 with respect to the phrase "consensus human variable domain" because it is allegedly not clear whether the consensus domain is a culmination of different variable domains or a single universal variable domain which is homologous to other human variable domains.

In the interests of expediting examination, claims 1, 7, 17 and 19 have been amended to recite that the consensus human variable domain is "of a human

immunoglobulin subgroup". Information concerning the amino acid sequences of the *variable* domains of antibodies belonging to various human immunoglobulin subgroups was compiled by Kabat *et al., Sequences of Proteins of Immunological Interest,* Fourth Edition, U.S. Dept. of Health & Human Services, pubs., (1987), a copy of which is attached to the enclosed Kelley Declaration as Exhibit "B". Kabat *et al.* grouped various heavy and light chain variable domains according to their amino acid sequence identity to form several human immunoglobulin "subgroups" i.e. human kappa light chains subgroups I to IV, human lambda light chains subgroups I to VI and human heavy chains subgroups I to III (see pages 41-76 and 160-167 of Kabat *et al.*). The "occurrences of most common amino acids" at each position of the variable domain are provided in the second to last column for each immunoglobulin subgroup in Kabat *et al.* The consensus human variable domain claimed in the above application is an amino acid sequence comprising the most commonly occurring amino acid residues at each position of the variable domain for a particular human immunoglobulin subgroup as defined by Kabat *et al.* It would have been readily apparent, to the ordinarily skilled biochemist, what constitutes a consensus human variable domain of a human immunoglobulin subgroup upon reading the above application.

Applicants respectfully request the withdrawal of the rejection of claim 1 as indefinite in light of the above submissions.

B. The Examiner has suggested that the "import amino acid" be described as "an import antibody comprising the amino acid sequence of a non-human antibody which binds to ...". Applicants understand that the Examiner considers that inclusion of the wording "import antibody" in parentheses is unclear and that the rejection relates to claims 1, 3, 4, 5 and 7. In order to overcome the rejection, claims 1, 7 and 19 have been amended to recite "an import antibody comprising a non-human antibody...". The non-human, import antibody may be the muMAb4D5 disclosed in Example 1 of the application, for example. Claims 3-5 depend on claim 1 and because there is clear antecedence basis for the phrases "import antibody variable domain amino acid

sequence", "import sequence" and "import antibody" in claim 1, the rejection of these claims is also rendered moot.

C. The Examiner has maintained the rejection of claim 1 under 35 U.S.C. §112, second paragraph, with respect to the wording "reasonably expected" on the grounds that it is not known what criteria determines what is "reasonable". In order to obviate the rejection, Applicants have deleted the word "reasonably" from claims 1, 3 and 19. Applicants respectfully submit that the amendment to the claims renders the rejection moot.

Applicants respectfully request that the maintained rejections of claims 1, 3-5 and 7 under 35 U.S.C. § 112, second paragraph, be withdrawn in light of the amendments to the claims and the submissions under paragraphs A to C above.

III. Objection and Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the objection to the specification and the rejection of claims 1 to 11 under 35 U.S.C. § 112, first paragraph as lacking enablement. New claims 17 to 21 have also been rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The various sets of rejections are addressed separately below.

A. The Examiner has maintained the rejection of claim 1 and has rejected claims 19 to 21 for including the language "at least a portion". In the interests of expediting examination, claims 1, 7 and 19 have been amended by deleting the wording "at least a portion of" therefrom. Applicants submit that the amendment of the claims renders the rejection of claims 1 and 19-20 under 35 U.S.C. § 112, first paragraph, moot and respectfully request the withdrawal thereof.

B. The Examiner has maintained the rejection that step c) of claim 1 (i.e. the step of substituting an import CDR amino acid sequence for the corresponding human CDR amino acid sequence) is not enabled by the specification. The Examiner asserts that there is no clear guidance in the specification to enable one of ordinary skill in the art to make the human "consensus variable domain". The Examiner further asserts that the

only guidance presented in the specification with regards to the substitutions is the amino acid sequences of SEQ ID NO: 3 and 4. Applicants understand that the basis for the Examiner's rejection is that the information provided in the specification would not have enabled the ordinarily skilled biochemist to carry out the methods claimed in order to produce a humanized antibody.

Applicants respectfully traverse this rejection on the grounds that the specification is enabling for the method claimed. In support of the above position, a Declaration pursuant to 37 C.F.R. § 1.132 by Robert Kelley is attached. See specifically his opinion in paragraph 3 and the bases for this opinion set forth in paragraphs 4 to 7.

This Declaration was not earlier submitted because it was believed, in good faith, that the rejection would be overcome without the need for a Declaration. Applicants respectfully request the entry of this Declaration in the above application pursuant to Rule 116, because it does not introduce issues not already fully joined in this case. The Declaration is offered in a good faith effort to place this case in condition for allowance.

As discussed under section II (A) above and in paragraph 4 of the Kelley Declaration, the consensus human variable domain constitutes an amino acid sequence comprising the most commonly occurring amino acids at each position in the variable domain of a particular human immunoglobulin subgroup as defined by Kabat *et al.* The immunoglobulin subgroups referred to in Kabat *et al.* were grouped according to the amino acid sequence homology between human immunoglobulin *variable* domains, and the most commonly occurring amino acids at each position in the variable domain for each subgroup were identified (i.e. the "consensus human variable domain"). The skilled biochemist could have used the consensus human variable domains of the light chain and heavy chain subgroups having the greatest number of sequences therein (i.e. light chains kappa subgroup I and heavy chains subgroup III) as disclosed in Kabat *et al.* (see page 17, first paragraph of the specification) to humanize the non-human antibody of interest. Alternatively, the skilled biochemist could have chosen the consensus human variable domain of another human immunoglobulin subgroup as defined in Kabat *et al.*

i.e. the consensus human variable domain for human kappa light chains subgroups II to IV, human lambda light chains subgroups I to VI, or human heavy chains subgroups I or II (see pages 41-76 and 160-167 of Kabat *et al.*). Therefore, the skilled biochemist could have elected to use a consensus human variable domain other than those defined as SEQ ID NO: 3 & 4 on page 17 of the above application, as the consensus human variable domains for other subgroups were compiled in Kabat *et al.* Page ix of Kabat *et al.* identifies the residues forming the CDR regions of heavy and light chain variable domains tabulated from human and mouse variable domains. Kabat *et al.* have adopted standardized numbering for each of the residue locations. Accordingly, the skilled biochemist could have identified the CDR regions of the consensus human variable domain and the import variable domain using the teachings of Kabat *et al.* Alternatively, the structural definition of Chothia *et al., J. Mol. Biol.*, **196:** 901-917 (1987) (see page 16, third paragraph of the specification) could have been adopted to identify the CDR regions of the consensus and import variable domains. See paragraph 4 of the Kelley Declaration. The above submissions show that steps a & b of claim 1 were enabled by the specification as filed.

Also, step c of claim 1 could have been carried out by the ordinarily skilled biochemist using the information provided in the specification and techniques such as manual tabulation of amino acid sequences or a computer program which was known in the art prior to June 14, 1991. See paragraph 5 of the Kelley Declaration.

Steps d to g of claim 1 would similarly have been straightforward to perform. These steps of claim 1 relate to the identification of Framework Region (FR) residues in the consensus human variable domain which are non-homologous to the corresponding import FR residues and replacement of such non-homologous human residues with corresponding import residues, if the residues are expected to have any one of the effects specified in step f. The locations of FR residues in human and mouse variable domains are indicated in Kabat *et al.* (see page ix) and the structural definition of the FR's was available (see Chothia *et al.*) Hence, it would have been straightforward for the skilled

immunologist to identify the FR residues in the consensus human variable domain and the import sequence. Using computer programs available before June 14, 1991, the skilled biochemist would have been able to study the 3-dimensional structure of the antibody in order to establish whether a particular non-homologous import amino acid residue is likely to have one of the effects discussed in section f of claim 1. Information is provided on pages 14 to 16 of the specification which would have enabled the skilled biochemist to determine whether any non-homologous residue(s) would be expected to have the effects claimed. The techniques claimed in steps d to g of claim 1 could have been carried out routinely by a person versed in the relevant art, prior to June 14, 1991. See paragraph 6 of the Declaration.

As discussed in paragraph 7 of the Declaration, once the primary amino acid sequence of the antibody had been characterized, it would have been routine to make the protein using recombinant techniques or a peptide synthesizer, which techniques were well known in the art prior to the filing date of the above application.

Applicants conclude that, contrary to the Examiner's assertions, the ordinarily skilled biochemist would have been able to carry out the method claimed in the above application, using the information provided in the specification and techniques which were well known in the relevant art, prior to June 14, 1991.

Accordingly, Applicants request that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn in light of the above submissions and the Declaration.

C. The Examiner has maintained the rejection of claims 1 and 3, and has rejected claim 19 under 35 U.S.C. § 112, first paragraph, with respect to the wording "reasonably" therein. In order to obviate the rejection, the wording "reasonably" has been deleted from claims 1, 3 and 19.

Accordingly, Applicants request that the rejection of claims 1, 3 and 19 under 35 U.S.C. § 112, first paragraph, be withdrawn.

D. The Examiner has maintained the rejection of claims 6, 7 and 9 as lacking

enablement under 35 U.S.C. § 112, first paragraph, the Examiner's position being that the amino acids are relevant to IgG only and not to other isotypes. Applicants respectfully traverse this rejection on the basis that the immunoglobulin *sites* claimed would have been relevant with respect to antibodies, other than IgG antibodies. Applicants refer the Examiner to paragraphs 8 & 9 of the Kelley Declaration which support this position. The Examiner appears to suggest that the rejected claims cover *sequences* which would not be found in immunoglobulin isotypes, other than IgG isotypes. However, as pointed out in paragraph 9 of the Kelley Declaration, the claims refer to *positions* or *sites* of the variable domain, not specific amino acid residues. These sites relate to the position of a residue in the 3-D structure of the variable domain. Kabat *et al.* have used universal numbering for the amino acid residue locations of the variable domains for each of the immunoglobulin subgroups mentioned therein. The FR residue sites indicated may be occupied by an amino acid residue which is non-homologous to the corresponding consensus human variable domain residue, and which residue is likely to have at least one of the effects discussed in step f of claim 1. The residue at the particular site can be any amino acid residue, depending on the antibody in which it is located. These residue locations or sites are applicable *across species* (see page 16, line 8). Accordingly, it is likely that an amino acid residue located at one of the sites indicated in claims 6, 7 and 9 will have one of the effects of claim 1 (step f) regardless of the antibody in which it is located. It is apparent that the particular sites claimed are applicable to immunoglobulins other than IgG.

Accordingly, Applicants submit that the rejection of claims 6, 7 & 9 under 35 U.S.C. § 112, first paragraph, should be reconsidered and withdrawn in light of the above submissions and Declaration.

In light of the submissions presented in paragraphs A to D above, Applicants respectfully request that the objection to the specification and the rejection of claims 1-11 and 17-21 under 35 U.S.C. §112, first paragraph, be withdrawn.

Applicants thank the Examiner for withdrawing the rejections which were raised

under 35 U.S.C. § 101 in the earlier Office Action dated October 5, 1992 .

IV. Rejection of claims 1, 2 and 5-10 under 35 U.S.C. 102 (a) and 102(b)

The rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 102(a) and 102(b) has been maintained and newly added claims 17-21 have been rejected under 35 U.S.C. § 102(a) and 102(b) as being anticipated by Queen *et al., Proc. Natl. Acad. Sci.*, **86:**10029-10033 (1989) and Co *et al., Proc. Natl. Acad. Sci.*, **88:**2869-2873 (1991). The basis for the rejection is that there is allegedly no clear indication as to what is meant by the consensus human variable domain claimed in the above application.

To constitute anticipation, all material elements of a claim must be found in one prior art source. *In re Marshall*, 198 USPQ 344 (CCPA 1978), *In re Kalm*, 154 USPQ 10 (CCPA 1967). Applicants will show that Queen *et al.* and Co *et al.* do not contain all material elements of claims 1, 2, 5-10 and 17-21.

The nature of the "consensus human variable domain of a human immunoglobulin subgroup" as defined in the claims as amended has been discussed above under Section II(A) of this response and in paragraph 4 of the Kelley Declaration, those discussions being incorporated herein. Applicants submit that the meaning of the phrase consensus human variable domain of a human immunoglobulin subgroup would have been clearly understood by those skilled in the art upon reading the specification. The prior art relied upon in the Office Action fails to disclose a method of making a humanized antibody using a consensus human variable domain to "humanize" a non-human antibody. The Declaration by Kelley supports this position. In particular, Applicants direct the Office's attention to paragraphs 11-13 of the attached Declaration. It is apparent from the information given in Table 1 of Exhibit C and in the Figures of Exhibits D and E of the Kelley Declaration (see paragraphs 12 & 13 thereof), that the variable domains of the human immunoglobulin sequences used by Queen *et al.* and Co *et al.* are not a consensus human variable domain of any human immunoglobulin subgroup as set forth in the claims of the above application.

Since, as shown above, Queen *et al.* and Co *et al.* do not teach all the material elements of the instant claims as required under *Marshall* and *Kalm, supra,* Applicants respectfully submit that the rejection of claims 1, 2, 5-10 and 17-21 under 35 U.S.C. § 102(a) and (b) can not be upheld and therefore request that the rejections be withdrawn.

V. Rejection of claims 3 and 4 under 35 U.S.C. § 103

The rejection of claims 3 and 4 as unpatentable under 35 U.S.C. § 103 over Queen *et al.* or Co *et al., supra,* in view of Wallick *et al., J. Exp. Med.,* **168** (1988) has been maintained. The basis for the rejection relates to the alleged lack of clarity of the language "consensus human variable domain" in the claims of the above application. The consensus human variable domain as defined in the above application would have been readily understood by the ordinarily skilled biochemist (see paragraph 4 of the Kelley Declaration). Claim 1 of the above application relates to a method of using a consensus human variable domain to "humanize" a non-human antibody (e.g. muMAb4D5). As established in section IV above, use of a consensus human variable domain from a human immunoglobulin subgroup is not disclosed in Queen *et al.* or Co *et al.*

The publication by Wallick *et al.* does not compensate for the deficiencies in the primary references. Wallick *et al.* refer to the importance of glycosylation for maintaining antigen binding affinity of monoclonal antibodies. Wallick *et al.* fail to disclose or suggest a method of humanizing a non-human antibody, much less a method of humanizing a non-human antibody using a consensus human variable domain of a immunoglobulin subgroup. The skilled biochemist would have had no motivation to use a consensus human variable domain based on the prior art referred to in the Office Action, because the prior art techniques had all relied upon using a human variable domain sequence which has the closest sequence homology to the non-human variable sequence (to be humanized) in order to reduce the likelihood of introducing distortions into the CDR's (see column 2 on page 10031 of Queen *et al.*) and "to retain high binding affinity in the humanized antibody" (see column 1 on page 2871 of Co *et al.*). The method claimed in

the above application does not rely on a high degree of homology between the variable domain of the non-human sequence and the consensus variable domain which is used to humanize the non-human sequence.

Also, as supported by paragraph 15 of the Kelley Declaration, the invention claimed in the above application resulted in an unexpected result which could not have been reasonably predicted from the prior art. It was surprising that a consensus variable domain of a selected immunoglobulin subgroup could be used to humanize a non-human antibody, regardless of the degree of homology between the human and non-human amino acid sequences. It was also surprising that the humanized antibody so formed retained, and in some instances, had increased antigen binding affinity compared to the non-human antibody from which it was derived. The above application shows that the huMAb4D5-8 variant actually binds the $p185^{HER2}$ ECD 3-fold more tightly than muMAb4D5 (see page 82 lines 31 & 32 to page 83, line 1 of the specification) which could not have been predicted by the ordinarily skilled biochemist. See paragraph 15 of the Kelley Declaration. The evidence of unexpected results in Applicants' application is sufficient to support a conclusion of nonobviousness. *Ralston Purina Co. Far-Mar-Co., Inc.*, 222 USPQ 863 (DC KS, 1984).

It is apparent that the invention claimed in claim 1 was novel and nonobvious over the citations because the combination of the prior art failed to disclose, or suggest, the invention claimed in claim 1 and, moreover, the method resulted in a new and unexpected result which could not have been reasonably predicted from the art.

Claims 3 & 4 depend on claim 1 which, as established above, is novel and nonobvious over the citations. Claim 3 refers to the step of finding any glycosylation site which is likely to affect the antigen binding or affinity in the import antibody and substituting the glycosylation site *into* the *consensus* amino acid sequence. Claim 4 refers to the step of *replacing* glycosylation sites of the consensus domain with the corresponding import amino acid residues if such glycosylation sites are not present in the import sequence. These claims would not have been obvious over the prior art of

record because the prior art failed to disclose the use of a human consensus variable domain to humanize the non-human antibody. Accordingly, the skilled biochemist would have had no motivation to replace or insert glycosylation sites into a consensus amino acid sequence, as claimed in claims 3 and 4 of the application. See paragraph 15 of the Kelley Declaration.

The law is clear that obviousness cannot be established by combining the teachings of the references to produce the claimed invention, absent some teaching, suggestion, or incentive supporting the combination. *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 221 USPQ 929, 933 (Fed. Cir. 1984). The above discussion shows that the cited references, alone or in combination, lack the requisite teaching of the use of a consensus human variable domain to humanize a non-human antibody. In this case, the combined art would not have reasonably enabled or motivated the skilled practitioner to use a human consensus variable domain in this manner, which provides a method of making improved humanized antibodies. Accordingly, it is clear that the invention claimed in claims 3 & 4 is novel and nonobvious over the prior art of record.

Applicants submit that the rejection of claims 3 and 4 under 35 U.S.C. § 103 should be reconsidered and withdrawn in light of the above submissions and the Declaration.

VI. Rejection of claims 17,18, 20 and 21 under 35 U.S.C. §112, second paragraph.

Claims 17, 18, 20 and 21 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in that there are allegedly no discrete method steps. In order to obviate the rejection, claims 17, 20 and 21 have been amended to each recite a definite method step and claim 18 has been deleted.

Applicants respectfully request the withdrawal of the rejection of claims 17, 20, and 21 under 35 U.S.C. § 112, second paragraph, in light of the amendments to the claims.

As all objections and rejections have been addressed and overcome, Applicants

believe that the claims are now in condition for allowance. Notice to that effect is respectfully requested. If the Examiner has any questions concerning the response, she should feel free to call the undersigned attorney at the number indicated above.

Respectfully submitted,
GENENTECH, INC.

Janet E. Hasak

Janet E. Hasak
Reg. No. 28,616

Date: September 20, 1993

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh
Louise Strasbaugh

Date: September 20, 1993

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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9-30-93

In re Application of	)	Group Art Unit: 1806
Paul J. Carter et al.	)	Examiner: L. FEISEE
Serial No. 07/715272	)	
Filed: June 14, 1991	)	
For: Immunoglobulin Variants	)	460 Point San Bruno Boulevard South San Francisco, CA 94080

DECLARATION OF ROBERT F. KELLEY PURSUANT TO 37 CFR §1.132

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

I, ROBERT F. KELLEY, do hereby declare as follows:

1. I received my Ph.D. in Biochemistry in 1984 from the University of Iowa. Following my Ph.D, I was a NIH postdoctoral fellow in the Department of Molecular Biophysics & Biochemistry at Yale University from July 1984 to December 1985. In 1986, I joined the Biocatalysis Department at Genentech, Inc. as an Associate Scientist. In September 1988, I was promoted to Scientist and I am employed in that capacity at present. (The Biocatalysis Department has been renamed "Protein Engineering"). I am the author or co-author of 22 publications relating to the 3-D structures and folding of various proteins. A copy of my curriculum vitae is attached as Exhibit "A".

2. I understand that the Patent Office has rejected the above application on the basis that the application as filed does not provide sufficient disclosure to enable a skilled biochemist to carry out the method of claim 1 because the Examiner believes no clear guidance exists in the specification to allow a skilled biochemist to make the "consensus human variable domain" and substitute an import (i.e. non-human) Complementary Determining Region (CDR) amino acid sequence for the corresponding human CDR amino acid sequence, as set forth in claim 1. I further understand that the Office considers that

the only guidance in the specification with regards to the substitutions is the amino acid sequences of SEQ ID NO: 3 and 4.

3. I have read the above application, the Office Action date May 19, 1992 (Paper # 17) rejecting the claims of the application, and the proposed amendment of the claims in response to the rejection. In my opinion, the skilled biochemist could have readily carried out the method of claim 1 in order to make a humanized antibody, using the general knowledge available in the field on and before June 14, 1991, and the information given in the above application. The bases for my opinion are given in paragraphs 4 to 7 below.

4. Claim 1 relates to a method of making a humanized antibody. Steps a and b of claim 1, as amended, discuss identification of the CDR amino acid sequences of a non-human import antibody (to be humanized) and a consensus human variable domain of a human immunoglobulin subgroup. The consensus human variable domain constitutes an amino acid sequence comprising the most commonly occurring amino acids at each position in the variable domain of a particular human immunoglobulin subgroup as defined by Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, Fourth Edition, U.S. Dept. of Health & Human Services, pubs., (1987), a copy of which is attached as Exhibit "B". The immunoglobulin subgroups referred to in Kabat *et al.* were grouped according to the amino acid sequence homology between human immunoglobulin *variable* domains, and the most commonly occurring amino acids at each position in the variable domain for each subgroup were identified (i.e. the "consensus human variable domain"). The skilled biochemist could have used the consensus human variable domains of the light chain and heavy chain subgroups having the greatest number of sequences (i.e. light chains kappa subgroup I and heavy chains subgroup III) as disclosed in Kabat *et al.* (see page 17, first paragraph of the specification) to humanize the non-human antibody of interest. Alternatively, the skilled biochemist could have chosen the consensus human variable domain of another human immunoglobulin subgroup as defined in Kabat *et al.* (i.e. the consensus human variable domain for human kappa light chains subgroups II to IV, human lambda light chains subgroups I to VI, or human

heavy chains subgroups I or II [see pages 41-76 and 160-167 of Kabat *et al.*]). Therefore, the skilled biochemist could have elected to use a consensus human variable domain other than those defined as SEQ ID NO: 3 & 4 on page 17 of the above application, as the consensus human variable domains for other subgroups were compiled in Kabat *et al.* Page ix of Kabat *et al.* identifies the residues forming the CDR regions of heavy and light chain variable domains tabulated from human and mouse variable domains. Kabat *et al.* have adopted standardized numbering for each of the residue locations. Accordingly, the skilled biochemist could have identified the CDR regions of the consensus human variable domain and the import variable domain using the teachings of Kabat *et al.* Alternatively, the structural definition of Chothia *et al.*, *J. Mol. Biol.*, **196:** 901-917 (1987) (see page 16, third paragraph of the specification) could have been adopted to identify the CDR regions of the consensus and import variable domains. Hence, it would have been straightforward for the skilled biochemist to carry out steps a and b of claim 1 using the information provided in the specification.

5. Step c of claim 1 discloses the step of replacing the corresponding human CDR sequence with the import CDR amino acid sequence. This step could have been carried out routinely by the skilled biochemist by manual tabulation or using a computer program such as the ALIGN program, (Dayhoff *et al.*, *Meth. Enzymol.*, **91:**524-545 [1983]) which was available prior to June 14, 1991. Steps a to c of claim 1 would have resulted in the characterization of a primary amino acid sequence encoding a humanized variable domain with import (non-human) CDR regions.

6. Steps d to g of claim 1 relate to the identification of Framework Region (FR) residues in the consensus human variable domain which are non-homologous to the corresponding import FR residues and replacement of such non-homologous human residues with corresponding import residues, if the residues are expected to have any one of the effects specified in step f. The locations of FR residues in human and mouse variable domains are indicated in Kabat *et al.* (see page ix) and the structural definition of the FR's was available (see Chothia *et al.*) Hence, it would have been straightforward for the skilled immunologist to identify the FR residues in the consensus human variable domain and the

import sequence. Using computer programs (such as the INSIGHT program [Biosym Technologies], available before June 14, 1991), the skilled biochemist would have been able to study the 3-dimensional structure of an antibody in order to establish whether a particular non-homologous import amino acid residue is likely to have one of the effects discussed in section f of claim 1. Information is provided on pages 14 to 16 of the specification which would have enabled the skilled biochemist to determine whether any non-homologous residue(s) would be expected to have the effects claimed. The techniques claimed in steps d to g of claim 1 could have been carried out routinely by a person versed in the relevant art, prior to June 14, 1991.

7. Steps a to g of claim 1 would have lead to the characterization of an amino acid sequence of a humanized antibody having non-human CDR amino acid residues and, optionally, having one or more non-human FR residues. In order to prepare the humanized antibody as claimed in claim 1, step h, the skilled biochemist could have synthesized the antibody using a peptide synthesizer which was commercially available before June 14, 1991. Alternatively, the antibody could have been made in recombinant cell culture (see page 26, last paragraph of the specification). Preparation of the antibody would have been straightforward to perform by the person skilled in the art, once the amino acid sequence of the humanized antibody had been characterized.

8. I understand that the Patent Office has rejected the above application on the basis that the sites in the variable domain referred to in claims 6, 7, and 9 are relevant to IgG antibodies only. It is my opinion that the sites referred to in claims 6, 7, and 9 would be relevant to other immunoglobulins. The basis for my opinion is given in paragraph 9 below.

9. The sites referred to in claims 6, 7, and 9 are the residue locations, or sites, of the FR residues in the heavy or light chain forming the variable domain of immunoglobulins. The residue sites referred to in claims 6, 7 & 9 relate to the position of a residue in the 3-D structure of the variable domain. Kabat *et al.* have used universal numbering for the amino acid residue locations of the variable domains for each of the immunoglobulin subgroups mentioned in the reference. The FR residue sites

indicated may be occupied by an amino acid residue which is non-homologous to the corresponding consensus human variable domain residue, and which is likely to have at least one of the effects discussed in step f of claim 1. These residue locations or sites are applicable *across species* (see page 16, line 8 of the specification). Accordingly, it is likely that an amino acid residue located at one of the sites indicated in claims 6, 7 and 9 will have one of the effects of claim 1 (step f), regardless of the antibody in which it is located, because it will be in the same position in the 3-D structure of the antibody variable domain as the residue sites referred to in the rejected claims. Accordingly, the examples of residue locations to be substituted in the variable domains would be applicable to antibodies, other than IgG antibodies.

10. I understand that the Patent Office has rejected the above application on the grounds that the invention as claimed is disclosed in Queen *et al.*, *Proc. Natl. Acad. Sci.*, 86:10029-10033 (1989) or Co *et al.*, *Proc. Natl. Acad. Sci.*, 88:2869-2873 (1991) and that the Office has suggested that the human variable domains disclosed in these references may have the same amino acid sequences as one of the consensus human variable domains disclosed in Kabat *et al.*

11. The above statements regarding the state of knowledge as of June 14, 1991, do not establish that the invention claimed in this application was known, or would have been obvious, to the skilled biochemist at the time the invention was made. To the contrary, after having read the citations relied upon by the Patent Office, it is my judgement that these documents would not have disclosed, nor suggested, the methods claimed. The basis for my opinion is given below.

12. The invention of the above application can be distinguished on the basis that a *consensus human variable domain* is used to "humanize" a non-human antibody of interest. The Queen *et al.* and Co *et al.* publications fail to disclose a consensus human variable domain. Instead, these publications refer to the use of a human variable domain having the closest sequence homology to the variable domain of the non-human antibody to be humanized. Queen *et al.* used the Eu human variable domain sequence (see Fig 2 thereof) and Co *et al.* used the variable domains of the Pom or Eu human

antibodies (see Fig 1 thereof). The sequences used in Queen *et al.* and Co *et al.* do not constitute a consensus human variable domain of a human immunoglobulin subgroup. The sequence identity between the amino acid sequences of the FR residues of the variable domains of the Pom or Eu heavy or light chains compared to the FR residues of the consensus human variable domains of each of the human immunoglobulin subgroups as defined by Kabat *et al.* is illustrated in Table 1 (see Exhibit "C", attached hereto). The CDR residues were not used in the comparison because of the large number of differences between these residues for variable domains of different antibodies. The Pom and Eu variable domain sequences were taken from Kabat *et al.* The consensus human variable domains of the V_L lambda subgroups IV and V were not compared, as these subgroups have too few members. While the variable domain of Eu is classified in subgroups V_L kappa I and V_H I, and the variable domain of Pom is classified in subgroups V_L kappa III and V_H III, it is apparent that the Eu and Pom variable domain amino acid sequences are not consensus human variable domains of any immunoglobulin subgroup. This is further demonstrated in the following paragraph.

13. Exhibits "D" and "C" attached hereto, show the differences in the amino acid sequences of the Pom and Eu heavy and light chain variable domains compared to the consensus human variable domain of the subgroup in which they are classified. Exhibit D illustrates an alignment of the amino acid sequences of the light chain variable domains of Eu, Pom and the consensus variable domain of the V_L kappa subgroup I (in which the light chain variable domain of Eu is classified). Exhibit E illustrates an alignment of the amino acid sequences of the heavy chain variable domains of Eu, Pom and the consensus variable domain of the V_H subgroup III (in which the heavy chain variable domain of Pom is classified). Even though Eu is classified in V_L kappa I, it has seven framework residues which are different from the framework residues of the kappa I consensus sequence. Furthermore, while Pom is classified in the V_H III subgroup, eight of its framework residues differ from the corresponding framework residues of the V_H III consensus sequence. There are, of course, many differences between the CDR residues of the consensus sequences and the corresponding CDR residues of Pom and Eu.

It is clear from the information in Exhibits C, D, & E that the Queen *et al.* and Co *et al.* publications fail to disclose a method wherein a non-human import antibody is humanized using a consensus human variable domain of an immunoglobulin subgroup.

14. I understand the Patent Office has rejected the above application on the basis that the invention claimed in claims 3 & 4 would have been obvious in light of Queen *et al.*, or Co *et al.*, when read in conjunction with Wallick *et al., J. Exp. Med.*, **168** (1988). After reading these references, it is my opinion that the invention claimed in claims 3 and 4 is novel and would not have been obvious in light of the citations. The basis for my opinion is given in the following paragraph.

15. Claim 1 of the above application relates to a method of using a consensus human variable domain to "humanize" a non-human antibody (e.g. muMAb4D5). Use of a consensus human variable domain from a human immunoglobulin subgroup to humanize a non-human antibody is not disclosed in Queen *et al.*, Co *et al.* or Wallick *et al.* Wallick *et al.* does not relate to a method of humanizing a non-human antibody, much less a method of humanizing a non-human antibody using a consensus human variable domain of a human immunoglobulin subgroup. The skilled biochemist would have had no motivation at the filing date of this application to use a consensus human variable domain to humanize a non-human antibody, because the techniques in the prior literature had all relied upon using a human variable domain sequence which has the closest sequence homology to the non-human variable sequence (to be humanized) in order to reduce the likelihood of introducing distortions into the CDR's (see column 2 on page 10031 of Queen *et al.*) or to "retain high binding affinity in the humanized antibodies" (see column 1 on page 2871 of Co *et al.*). The method claimed in the above application does not rely on a high degree of homology between the variable domain of the non-human sequence and the consensus variable domain which is used to humanize the non-human sequence. It was surprising that a consensus variable domain of a selected immunoglobulin subgroup could be used to humanize a non-human antibody, regardless of the degree of homology between the human and non-human amino acid sequences. It was also surprising that the humanized antibody so formed retained,

and in some instances, had increased antigen binding affinity compared to the non-human antibody from which it was derived. The above application shows that the huMAb4D5-8 variant actually binds the $p185^{HER2}$ ECD 3-fold more tightly than muMAb4D5 (see page 82 lines 31 & 32 to page 83, line 1 of the specification), which could not have been predicted by the ordinarily skilled biochemist at the time the specification was filed. Claim 3 refers to the step of finding any glycosylation site which is likely to affect the antigen binding or affinity in the import antibody and substituting the glycosylation site *into* the *consensus* amino acid sequence. Claim 4 refers to the step of *replacing* glycosylation sites of the consensus domain with the corresponding import amino acid residues if such glycosylation sites are not present in the import sequence. In my opinion, these claims would not have been obvious over the prior literature because the reference failed to disclose the use of a human consensus variable domain to humanize the non-human antibody. Accordingly, the skilled biochemist would have had no motivation to replace or insert glycosylation sites into a consensus amino acid sequence, as claimed in claims 3 and 4 of the application.

16. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 9/20/93 Signed: Robert F. Kelley
ROBERT F. KELLEY

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on September 20, 1993.

Dated: September 20, 1993

Louise Strasbaugh
Louise Strasbaugh

w012.u

EXHIBIT A

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Personal information:

Birthdate: November 7, 1957
Married, Wife's name: Wendy L. Kelley
One child: Brian F. Kelley

Education:

B.S., Biochemistry, Michigan State University, 1979
Ph. D., Biochemistry, University of Iowa, 1984

Employment positions:

Teaching assistant, Chemistry Dept., Michigan State Univ., 1978-1979
Teaching assistant, Biochemistry Dept., University of Iowa, 1979-1981
Graduate research assistant, Biochemistry Dept., University of Iowa, 1982-April 1984
Postdoctoral associate, Biochemistry Dept., University of Iowa, May 1984-June 1984
NIH postdoctoral fellow, Dept. of Molecular Biophysics & Biochemistry, Yale University, July 1984-Dec. 1985
Associate Scientist, Biocatalysis Dept., Genentech, Inc., January 1986-September 1988
Scientist, Biomolecular Chemistry Dept., Genentech, Inc., September 1988-present

Awards and membership in professional organizations:

Biophysical Society, 1983-present
American Chemical Society, 1991-present

Scientific publications

Kelley, R.F., & Stellwagen, E. (1984) "Conformational transitions of thioredoxin in guanidine hydrochloride", Biochemistry 23, 5095-5102.

Kelley, R.F., Wilson, J., Bryant, C., & Stellwagen, E. (1986)"Effects of guanidine hydrochloride on the refolding kinetics of denatured thioredoxin", Biochemistry 25, 728-732.

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TABLE 1
SEQUENCE IDENTITY - (%)

CONSENSUS VARIABLE DOMAIN SUBGROUP	EU	POM
V_L kappa I	92	76
V_L kappa II	61	71
V_L kappa III	72	85
V_L kappa IV	73	78
V_L lambda I	61	59
V_L lambda II	57	54
V_L lambda III	59	56
V_L lambda VI	52	49
V_H I	83	64
V_H II	53	62
V_H III	61	91

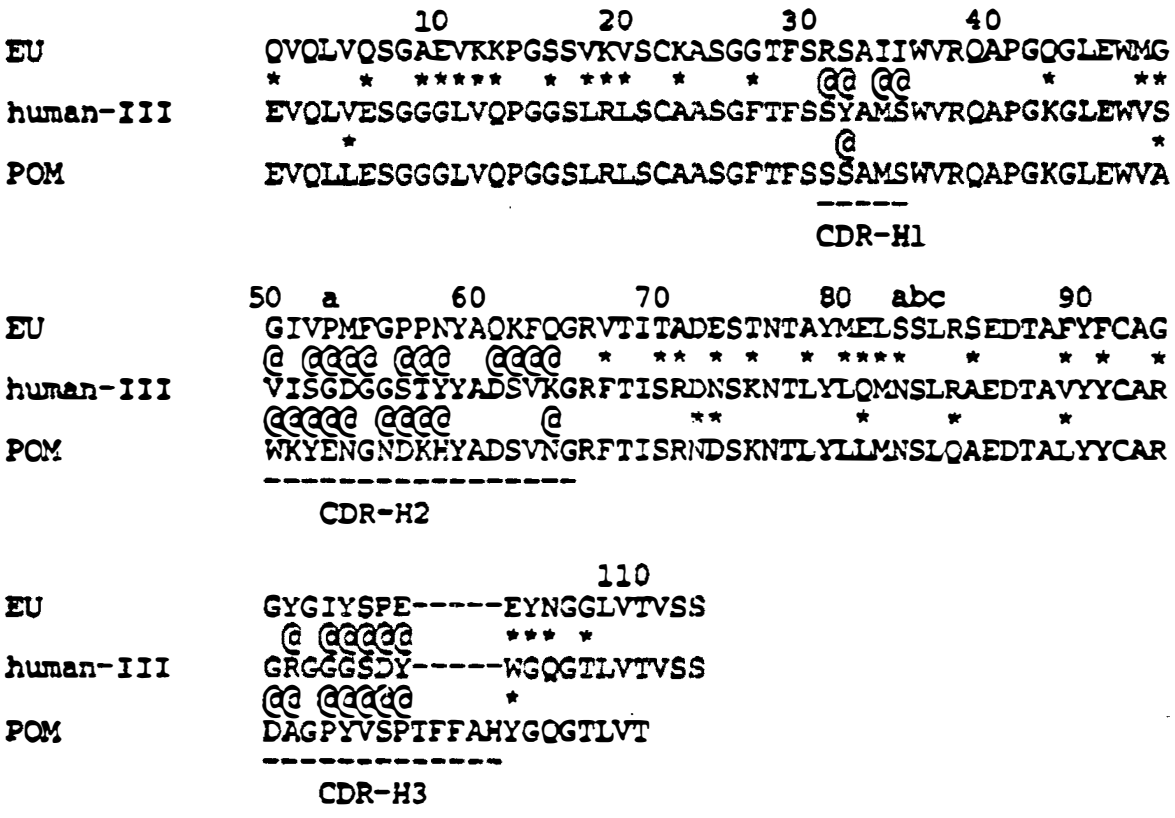
Variable Light Domain

```
                    10        20        30        40
EU          DIQMTQSPSTLSASVGDRVTITCRASQ-SINTWLAWYQQKPGKAPKLLMY
                     *                 @ @@@                 *
Kappa-I     DIQMTQSPSSLSASVGDRVTITCRASQ--ISNYLAWYQQKPGKAPKLLIY
            * *     **  * * * * **     @@@@@      *** *
POM         EIVMTQSPVTLSVSPGERATLSCRASQSISNSYLAWYQQKPSGSPRLLIY
                                 ----------
                                 CDR-L1

           50        60        70        80        90        100
EU          KASSLESGVPSRFIGSGSGTEFTLTISSLQPDDFATYYCQQYNSDSKMFGQ
            @           *       *         *             @@@@
Kappa-I     AASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSLPWTFGQ
            @  @@@@ * *         *         *     *       @@ @
POM         GASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWPPTFGQ
            -------                                   ---------
            CDR-L2                                    CDR-L3

EU          GTKVEVKGT
                 * *
Kappa-I     GTKVEIKRT
              *
POM         GTRVEIKR
```

KEY: * = differences in FR residues

@ = differences in CDR residues

Variable Heavy Domain



KEY: * = differences in FR residues

@ = differences in CDR residues

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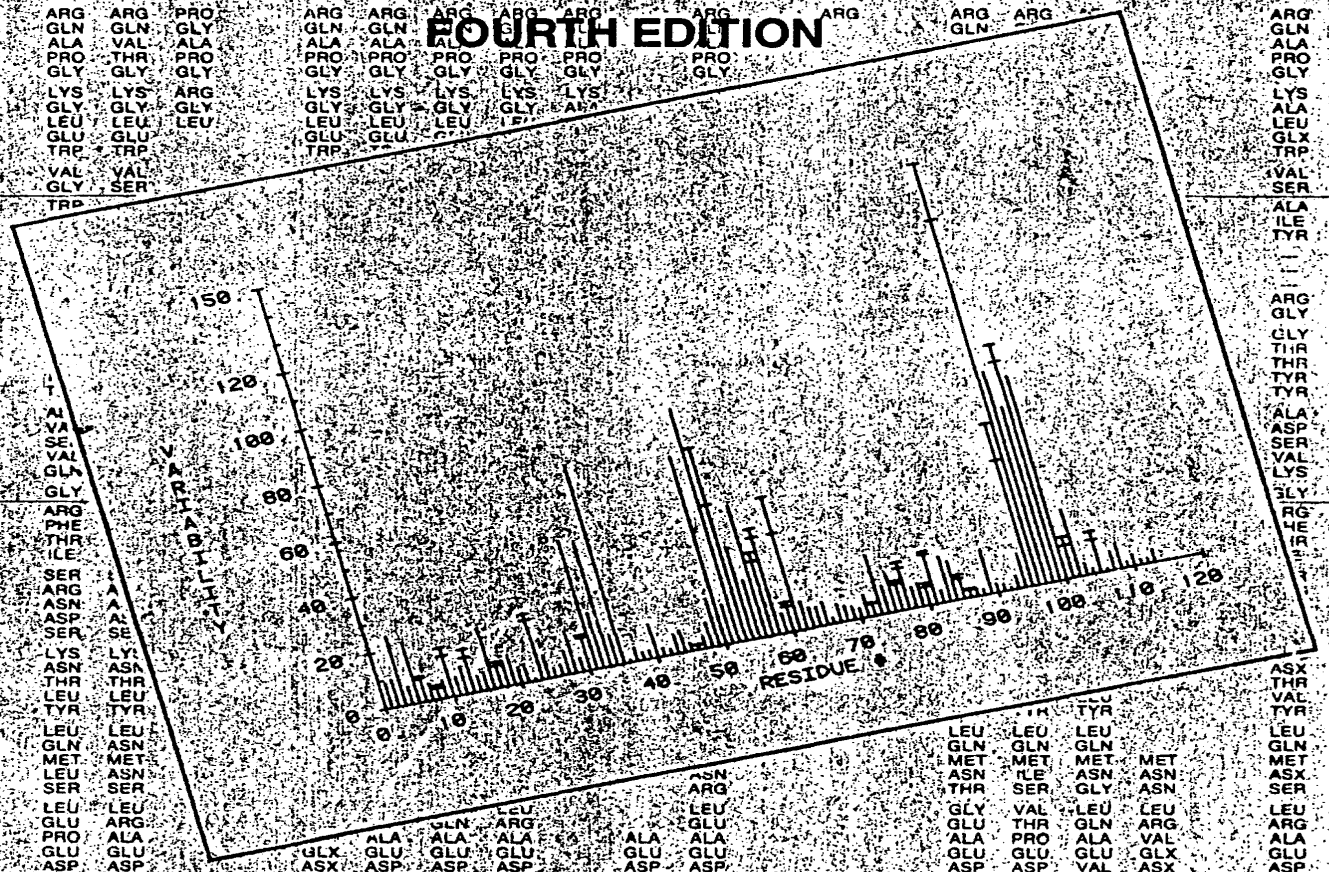
SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST

FOURTH EDITION



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Public Health Service
National Institutes of Health

SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST

FOURTH EDITION

Tabulation and Analysis of
Amino Acid and Nucleic Acid Sequences of
Precursors, V-Regions, C-Regions, J-Chain,
T-Cell Receptor for Antigen, T-Cell Surface Antigens,
β_2-Microglobulins, Major Histocompatibility Antigens,
Thy-1, Complement, C-Reactive Protein, Thymopoietin,
Post-gamma Globulin, and α_2-Macroglobulin

1987

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The collection and maintenance of this data base is sponsored through Contract N01-RR-8-2158 by the following components of the National Institutes of Health, Bethesda, MD 20892:

Division of Research Resources
National Cancer Institute
National Institute of Allergy and Infectious Diseases
National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases
National Institute of General Medical Sciences

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health
(1987)

TABLE OF CONTENTS

considered uncertain by the authors have not been included in the table. In some instances the symbol # is used to indicate that several amino acid residues were found in one position, and these residues are listed in the notes. The four columns at the end of each table give:

1. the number of residues sequenced at that position,
2. the number of different amino acids found at that position,
3. the number of times the most common amino acid occurred and that amino acid in parentheses, and
4. the variability.

Variability is calculated (11) as:

$$\text{Variability} = \frac{\text{Number of different amino acids occurring at a given position}}{\text{Frequency of the most common amino acid at that position}}$$

An invariant position would have a variability of one; if 20 amino acids occurred with equal frequency, the variability would be 20 divided by 0.05 equals 400. If, for example, four different amino acids Ser, Asp, Pro, and Thr occurred at a given position, and of 100 sequences available at that position, Ser occurred 80 times, the variability would be 4/0.8 = 5. When any of the amino acid residues sequenced were not identified completely and are listed as Glx (or Asx), two values, separated by a colon, are given in the last three columns. The first value in each of these columns is calculated assuming that only one of the two possibilities, e.g., Glu or Gln (or Asp or Asn) occurred, while the second considers that both were present and maximizes variability. In the variability plots, the horizontal bars indicate the two values.

When two or more amino acids are most common and occur with equal frequency, they are tabulated as a note, and the symbol + is used in the next to last column. If no sequence data have been reported for any position, there are no entries in the last four columns. Variability is not calculated for insertions or if only a single sequence is known. When the translated sequence of a clone corresponds to a previously listed sequence of a plasmacytoma from which it was prepared, only one sequence is listed so that the variability computations are not affected, and a note is included.

If a given sequence is associated with any antibody activity, this is indicated by an asterisk alongside the protein heading, and the antibody specificities are given in a separate list with binding constants if available. The notes list the a-allotypes for the rabbit heavy chain V-region and the b-allotypes for the constant domain of the rabbit kappa light chain. A key reference to the sequence is given; generally the most recent reference since it is usually the most nearly complete, but often several references are included, especially when revisions of a sequence have been made. Notes are now of two types; general notes about a table indicated by the symbol #, and specific notes indicated by the sequence number.

Signal Sequences

The signal (precursor) amino acid sequences of immunoglobulin chains are listed in three tables: one for kappa light chains, one for lambda light chains, and one for heavy chains. They were obtained either by direct sequencing of signal proteins (12-14) or by translating nucleotide sequences from DNA clones. Signal segments range from 17-29 amino acid residues in length and are thus numbered from -29 to -1. Genomic DNA clones contain introns of varying length that interrupt the coding sequence of the precursor within the codon for position -4, and in rare cases for position -6. Thus, the L-gene encodes the leader peptide to position -4 and the 5′ end of the V-gene codes for positions -4 to -1.

The signal amino acid sequences of the T-cell receptors for antigens, β_2-microglobulins, major histocompatibility complex proteins, and complement components are listed in separate tables.

By conformational energy calculations, the core V_κ hydrophobic Leu-Leu-Leu-Trp-Val-Leu-Leu-Leu (MOPC321, MOPC63) exists in an alpha helical conformation, terminated by chain reversal conformations in the four C-terminal residues Trp-Val-Pro-Gly; the four amino terminal residues are compatible with the alpha helix (15).

Variable Region Sequences

The variable regions (16) of immunoglobulins have been shown to contain hypervariable segments in their light (11,17-23) and heavy (22,24-27) chains, of which certain residues have been affinity labeled (28-41). Three hypervariable segments of light chain were delineated from a statistical examination

of sequences of human V_κ, human V_λ, and mouse V_κ light chains aligned for maximum homology (11,22). These and the three corresponding segments of the heavy chains (22,26,27) were hypothesized (11,22) to be the complementarity-determining regions or segments (CDR) containing the residues which make contact with various antigenic determinants, and this has been verified by X-ray diffraction studies at high resolution (42-67). The rest of the V-region constitutes the framework (11,22,66-68). It is convenient to identify the framework segments (FR1, FR2, FR3, and FR4) and the complementarity-determining segments (CDR1, CDR2, and CDR3) with the three CDRs separating the four FRs. The residue numbers for these segments are as follows:

Segment	*Light Chain*	*Heavy Chain*
FR1	1-23 (with an occasional residue at 0, and a deletion at 10 in V_λ chains)	1-30 (with an occasional residue at 0)
CDR1	24-34 (with possible insertions numbered as 27A,B,C,D,E,F)	31-35 (with possible insertions numbered as 35A,B)
FR2	35-49	36-49
CDR2	50-56	50-65 (with possible insertions numbered as 52A,B,C)[a]
FR3	57-88	66-94 (with possible insertions numbered as 82A,B,C)
CDR3	89-97 (with possible insertions numbered as 95A,B,C,D,E,F)	95-102 (with possible insertions numbered as 100A,B,C,D,E,F,G,H,I,J,K)
FR4	98-107 (with a possible insertion numbered as 106A)	103-113

[a] In the rabbit, Mage *et al.* (69) consider position 65 in V_H to be in FR3, since it is allotype related.

In the tables of V-regions, the FR and CDR are separated by horizontal lines for convenience in reading. One mouse kappa light chain, MPC11, has an extra segment of 12 amino acid residues between position 1 and the signal sequence (70). Several chains have internal deletions.

In the tables, the V-genes for the light chains code to amino acid position 95, and the J-minigenes from position 97 to 107 for lambda and 108 for kappa light chains. Position 96 is usually the site of V-J joining by recombination and may be coded partly by the V-gene and partly by the J-minigene. Because the site of V-J recombination could occur at different positions within a codon, different amino acid residues may result at this position. We have changed the location of the inserted residues from 97A-F (2) to 95A-F, since it makes for better alignment by confining chains of different lengths to the V-gene region. In V_κ chains, J1 and J2 were used 5 to 10 times more frequently than J4 and J5 (71).

The V-genes for the heavy chains code up to amino acid position 94 and are followed by the D- and J-minigenes. Because of the extensive variation in the lengths of D-minigenes, the exact boundary between D and J is not always located at the same amino acid position. In addition, the lengths of the J encoded amino acid sequences vary by a few amino acid residues. Moreover, the process of D-J joining appears to involve insertions of extra nucleotides between V and D and between D and J, termed the N region (72-76) and correlates with the appearance of terminal deoxytransferase in B cells (75). The original numbering system for the heavy chains has therefore been retained. Wysocki *et al.* (76) have provided some evidence suggesting a non-random origin for the V_H-D_H junction, perhaps a minigene, rather than random addition of the N nucleotides.

It has become evident that a critical understanding of the architecture of antibody combining sites and the genetics of the generation of diversity and of antibody complementarity will depend to a great extent on the evaluation of a large number of sequences of the variable regions and especially of the complementarity-determining segments of light and heavy chains of immunoglobulins of different species. Ability to locate residues in the site making contact with antigenic determinants (77) and to predict (67,78-82) the structures of antibody combining sites will depend heavily upon such sequences.

Figures 1 and 2 are stereoviews of the α-carbon skeletons of the four Fv regions for which high resolution X-ray structures have been determined, NEWM (44), KOL (62), MCPC603 (47, 48, 63), and J539 (64). The residues in the CDRs are shown as solid circles. In Fig. 1 the combining site is at the

HUMAN KAPPA LIGHT CHAINS SUBGROUP I

		INVARIANT RESIDUES	1 ROY	2 AU	3 REI	4 HAU	5 HK101 CL #	6 SCW	7 AG #	8* WEA	9 HK 137 CL #	10 HK 134 CL #	11 DAUDI CL	12 WALKER CL	13 HF3-16/6	14 HF2-1/13B	15 HF2-18/2	16 HF2-1/17	17 BJ 26 #	18 RFZ	19 PSM	20 HOM	21 ESM IGG	22 ESM IGM	23 WAT
	0		---	---	---	---	#	---	---	---	---	#	---	---	---	---	---	---	---	---	---	---	---	---	---
	1		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	2		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	4		MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET
	5	THR(.98)	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	7	SER(.95)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO(.98)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
FR1	10		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	11		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12	SER(.96)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	14		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	15	VAL(.96)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	16	GLY(.99)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	18		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	19	VAL(.97)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	20	THR(.96)	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	21	ILE(.95)	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	22		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS
	24		GLN	GLN	GLN	ARG	ARG	GLN	GLN	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	GLN	GLN	GLN	GLN	ARG	ARG	GLX
	25	ALA(.95)	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	26		SER	SER	SER	SER	ARG	SER	SER	SER	SER	SER	SER	GLY	SER	SER	SER	SER	SER	ASN	SER	ARG	SER	SER	SER
	27		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	HIS	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	HIS	GLX	GLX	GLN
	27A		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	27B		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
CDR1	27C		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	27D		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	27E		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	27F		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	28		ASP	ASP	ASP	SER	GLY	ASP	ASP	GLY	GLY	GLY	ASN	SER	GLY	GLY	GLY	GLY	SER	VAL	ASP	ASP	SER	SER	ASP
	29		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	30		SER	SER	ILE	SER	SER	ARG	ASN	ARG	SER	SER	THR	SER	ARG	ARG	ARG	ARG	ASN	SER	ARG	SER	SER	SER	SER
	31		ILE	ASP	LYS	SER	SER	LYS	HIS	ASN	ASN	SER	ASN	ASN	ASN	ASN	ASN	ASN	LYS	SER	ASN	SER	SER	SER	ASP
	32		PHE	TYR	TYR	TYR	TRP	HIS	TYR	ASP	TYR	TRP	PHE	TYR	ASP	ASP	ASP	ASP	TYR	SER	TYR	TYR	TYR	TYR	TYR
	33		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	ALA	LEU	LEU	LEU	LEU	LEU	VAL
	34		ASN	ASN	ASN	SER	ALA	ASN	ASN	THR	ALA	ALA	SER	ASN	GLY	GLY	GLY	GLY	ASN	ASN	ASN	ASN	ASX	ASX	ASN
	35	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP
	36		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	PHE	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	PHE	TYR	TYR	
	37		GLN	GLN	GLN	GLN	GLN	ASP	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLU	GLN	GLN	GLN	GLX	GLX	
	38		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN			
	39		LYS	LYS	THR	LYS	LYS	LYS	#	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	#	ARG	LYS	LYS			
	40	PRO(.95)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	GLN	PRO			
FR2	41		GLY	GLY	GLY	GLY	GLU	GLY	#	GLY	GLY	GLU	GLY	GLY					#	GLY	GLY	GLY			
	42		LYS	LYS	LYS	LYS	LYS	LYS	LYS	THR	LYS	LYS	LYS	LYS					LYS	GLN	LYS				
	43		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA					ALA	ALA	ALA				
	44	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO					PRO	PRO	PRO				
	45		LYS	LYS	LYS	GLN	LYS	ARG	LYS	LYS	LYS	LYS	THR	LYS					LYS	LYS	LYS				
	46		LEU	LEU	LEU	VAL	SER	LEU	ILE	ARG	SER	SER	LEU	LEU					LEU	LEU	LEU				
	47	LEU(.98)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU						LEU	LEU				
	48	ILE(.98)	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE						ILE	ILE				
	49		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR						TYR	TYR				
	50		ASP	ASP	GLU	ALA	ALA	GLY	ASP	GLY	ALA	ALA	ALA	ALA						ASP	ASP				
	51		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	VAL	ALA						ALA	ALA				
	52		SER	SER	SER	SER	SER	SER	SER	THR	SER	SER	SER	SER						ALA	SER				
CDR2	53		LYS	ASN	ASN	SER	SER	THR	ASN	SER	SER	SER	SER	ASN						ARG	ASX				
	54	LEU(.98)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU						LEU	LEU	LEU			
	55		GLU	GLU	GLN	PRO	GLN	GLU	GLU	GLN	GLN	GLN	GLN	GLN						GLU	GLU	GLU			
	56		ALA	SER	ALA	SER	SER	THR	THR	SER	SER	SER	VAL	SER						THR					
	57	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY						GLY	GLY				
	58	VAL(.98)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL						ASX	VAL				
	59		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	THR						PRO	PRO				
	60	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER						SER					
	61	ARG(.95)	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG						LYS	ARG				
	62	PHE(.95)	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE						VAL	PHE				
	63		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER						SER	THR				
	64	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY						GLY	GLY				
	65		THR	GLY	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER						SER					
	66	GLY(.95)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY						GLY	GLY				
	67		SER	SER	SER	SER	SER	SER	PHE	SER	SER	SER	SER	SER						SER					
	68		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY						GLU					
	69		THR	ALA	THR	THR	THR	THR	THR	THR	THR	THR	ALA	THR						THR					
	70		ASP	HIS	ASP	ASP	ASP	ASP	ASP	GLU	ASP	ASP	GLU	ASP						ASP					
	71		PHE	PHE	TYR	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE						VAL					
FR3	72		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR						THR					
	73		PHE	PHE	PHE	LEU	LEU	LEU	PHE	LEU	LEU	LEU	LEU	LEU						VAL					
	74		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR						ASX					
	75	ILE(.95)	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE						GLX					
	76	SER(.95)	SER	SER	SER	SER	SER	SER	SER	ASN	SER	SER	SER	SER						SER					
	77		GLY	SER	SER	SER	SER	THR	GLY	SER	SER	SER	SER	SER						SER					
	78		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU						LEU					
	79		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN						GLN					
	80		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO						PRO					
	81		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU						GLU					
	82		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP						ASP					
	83		ILE	ILE	ILE	PHE	PHE	ILE	ILE	PHE	PHE	PHE	PHE	SER						ILE					
	84	ALA(.98)	ALA	ALA	ALA	ALA	ALA	GLY	ALA	ALA	ALA	ALA	ALA	ALA						ALA					
	85		THR	THR	THR	THR	THR	ASN	THR	THR	THR	THR	THR	THR						PRO					
	86	TYR(.98)	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR						LYS					
	87	TYR(.98)	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR											
	88	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS											
	89		GLN	GLN	GLN	GLN	GLN	GLN	GLN	LEU	GLN	GLN	GLN	GLN					GLN						
	90		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN					GLN						
	91		PHE	TYR	TYR	ASN	TYR	TYR	TYR	TYR	TYR	TYR	ASN	SER					ARG						
	92		ASP	ASP	GLN	TYR	ASN	ASP	ASP	SER	ASN	ASN	TYR	TYR					ASP						
	93		ASN	TYR	SER	ILE	SER	ASN	THR	SER	SER	SER	ASN	SER					ASP						
	94		LEU	LEU	LEU	THR	TYR	VAL	LEU	PHE	TYR	TYR	PHE	THR					LEU						
CDR3	95		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	SER	LEU					PRO						
	95A		---	---	---	---	#	---	---	---	---	#	---	---					---						
	95B		---	---	---	---	---	---	---	---	---	---	---	---					---						
	95C		---	---	---	---	---	---	---	---	---	---	---	---					---						
	95D		---	---	---	---	---	---	---	---	---	---	---	---					---						
	95E		---	---	---	---	---	---	---	---	---	---	---	---					---						
	95F		---	---	---	---	---	---	---	---	---	---	---	---					---						
	96		LEU	TRP	TYR	THR	---	ILE	ARG	TRP	---	---	PHE	ILE					TYR						
	97		THR	THR	THR	SER	---	THR	THR	THR	---	---	THR	THR					THR						
	98		PHE	PHE	PHE	PHE	---	PHE	PHE	PHE	---	---	PHE	PHE					LEU						
	99	GLY	GLY	GLY	GLY	GLY	---	GLY	GLY	GLY	---	---	GLY	GLY					GLY						
	100		GLY	GLN	GLN	GLN	---	GLN	GLN	GLN	---	---	GLY	GLN					GLY						
	101	GLY	GLY	GLY	GLY	GLY	---	GLY	GLY	GLY	---	---	GLY	GLY					GLY						
	102	THR(.97)	THR	THR	THR	THR	---	THR	THR	THR	---	---	THR	THR					THR						
FR4	103		LYS	LYS	LYS	ARG	---	ARG	LYS	LYS	---	---	LYS	ARG					LYS						
	104		VAL	VAL	LEU	VAL	---	VAL	LEU	VAL	---	---	VAL	LEU					VAL						
	105		ASP	GLU	GLN	GLU	---	GLU	GLU	GLU	---	---	ASP	GLU					GLU						
	106		PHE	ILE	ILE	ILE	---	ASN	ILE	VAL	---	---	ASN	ILE					MET						
	106A		---	---	---	---	---	---	---	---	---	---	---	---					---						
	107		LYS	LYS	THR	LYS	---	LYS	LYS	LYS	---	---	LYS	LYS					LYS						
	108		ARG	ARG	ARG	ARG	---	GLY	ARG	ARG	---	---	---	---											
	109	THR	THR	THR	THR	THR	---	THR	THR	THR	---	---	---	---											

HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

		24 AMYLOID VIII-B	25* LOW	26 DIE	27 CAR A	28 TEI	29 BJ 48	30 CON	31 TRA	32 AMYLOID LEP	33 F-GUI #	34 OU (IOC)	35 DEE	36 GAL (I)	37 JOH	38 KER	39* LAY	40 BRA	41 WES	42 Vb 'CL	43 Vb' 'CL	44 HK102 'CL #	45 EU	46 DEN	47 PAU
	0	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	#	---	---	---
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASX	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	4	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
FR1	10	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	thr	thr	thr	thr
FR1	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	val	val	val	LEU	LEU	LEU	LEU
FR1	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
FR1	13	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	val	val	ALA	ALA	ALA	ALA	ALA	ALA	ALA
FR1	14	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	15	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASX	ASP	ASP	ASP	ASP	ASP	glx	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	18	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	19	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ile	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	20	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	21	ILE	ILE	THR	ILE	ILE	ILE	ILE	ILE		THR	ILE	ILE	ILE	ILE	THR	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	22	THR	THR	ILE	THR	THR	THR	THR	THR		THR	THR	THR	ile	ser	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	23	CYS	CYS	CYS	CYS	CYS	CYS				CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS
	24	GLN	ALA									ARG	ARG	ARG		GLN	GLN		ARG	ARG	ARG	ARG	ARG	ARG	ARG
	25	ALA	ALA								ALA	ALA	ALA	ALA		ALA	ALA		ALA	ALA	ALA	ALA	ALA	THR	ALA
	26	SER	SER									SER	GLY	SER		SER	SER		SER	SER	SER	SER	SER	SER	SER
	27	GLN	GLN									GLX	GLN	GLN		GLN	GLN		GLN	GLN	GLN	GLN	GLN	GLN	GLN
	27A	---	---									---	---	---		---	---		---	---	---	---	---	---	---
	27B	---	---									---	---	---		---	---		---	---	---	---	---	---	---
CDR1	27C	---	---									---	---	---		---	---		---	---	---	---	---	---	---
CDR1	27D	---	---									---	---	---		---	---		---	---	---	---	---	---	---
CDR1	27E	---	---									---	---	---		---	---		---	---	---	---	---	---	---
CDR1	27F	---	---									---	---	---		---	---		---	---	---	---	---	---	---
CDR1	28	ASX	ASX									THR	SER	GLY		ASP	ASN		ASP	GLY	GLY	SER	SER	SER	SER
	29	ILE	ILE									ILE	VAL	ILE		ILE	VAL		ILE	ILE	ILE	ILE	ILE	ILE	ILE
	30	GLY	SER									SER	ASN	ARG		LYS	ASN		SER	SER	SER	SER	ASN	SER	SER
	31											SER	LYS	ASN			ALA		HIS	SER	SER	SER	THR	ARG	SER
	32	TYR										TYR	TYR	ASP			TYR		TRP	TRP	TRP	TRP	TRP	TRP	SER
	33	LEU										LEU	LEU	LEU			LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU
	34											ASX	ASN	THR			ASN		ALA	ALA	ALA	ALA	ALA	ALA	ALA
	35	TRP										TRP	TRP	TRP			TRP		TRP	TRP	TRP	TRP	TRP	TRP	TRP
	36											TYR	TYR	TYR			TYR		TYR	TYR	TYR	TYR	TYR	TYR	TYR
	37											GLX	GLN	GLN			GLN		GLN	GLN	GLN	GLN	GLN	GLN	GLX
	38											GLX	GLN	GLN			GLN		GLN	GLN	GLN	GLN	GLN	GLN	GLX
	39											LYS	LYS	LYS			LYS		LYS	LYS	LYS	LYS	LYS	LYS	LYS
	40											PRO	PRO	PRO			PRO		SER	PRO	PRO	PRO	PRO	PRO	PRO
FR2	41											GLY	GLY	GLY			GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY
FR2	42											LYS	LYS	LYS			LEU		LYS	LYS	LYS	LYS	LYS	GLU	GLX
FR2	43						ALA					ALA	ALA	ALA			ALA		ALA	ALA	ALA	ALA	ALA	ALA	ALA
	44						PRO					PRO	PRO	PRO			PRO		PRO	PRO	PRO	PRO	PRO	PRO	PRO
	45						LYS					ASX	LYS	LYS			LYS		LYS	LYS	LYS	LYS	LYS	LYS	LYS
	46											LEU	VAL	GLU			LEU		LEU	LEU	LEU	LEU	LEU	VAL	LEU
	47											LEU	LEU	LEU			LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU
	48											ILE		ILE			ILE		ILE	ILE	ILE	ILE	MET	ILE	ILE
	49						GLY					TYR		TYR			TYR		TYR	TYR	TYR	TYR	TYR	TYR	TYR
	50						ASP					ALA	ALA	ALA			GLY		SER	ALA	ALA	ASP	LYS	GLY	GLX
	51						ALA					ALA	ALA	ALA			ALA		ALA	ALA	ALA	ALA	ALA	ALA	
	52						SER					SER	SER	SER			SER		SER	SER	SER	SER	SER	SER	
	53						SER					ASX	SER	ASN			THR		SER	SER	SER	SER	SER	ASN	
CDR2	54						LEU					LEU	LEU	LEU			ARG		LEU	LEU	LEU	LEU	LEU	LEU	
CDR2	55						ASX					HIS	LYS	GLN			GLU		GLU	GLN	GLN	GLU	GLU	GLU	
CDR2	56						SER					SER	SER	SER			ALA		ASN	SER	SER	SER	SER	SER	
	57						GLY					GLY	GLY	GLY			GLY		GLY	GLY	GLY	GLY	GLY	GLY	
	58						VAL					VAL	VAL	VAL			VAL		VAL	VAL	VAL	VAL	VAL	VAL	
	59						VAL					PRO	PRO	PRO			PRO		PRO	PRO	PRO	PRO	PRO	PRO	
	60						SER					SER	SER	SER			SER		SER	SER	SER	SER	SER	SER	
	61						ARG					ARG	ARG	ARG			ARG		ARG	ARG	ARG	SER	ARG	ARG	
	62						GLN					PHE	PHE	PHE			PHE		PHE	PHE	PHE	PHE	PHE	PHE	
	63						SER					SER	SER	SER			SER		SER	SER	SER	SER	ILE	SER	
	64						GLY					GLY	GLY	GLY			GLY		GLY	GLY	GLY	GLY	GLY	GLY	
	65						SER					SER	SER	SER			SER		SER	SER	SER	SER	SER	SER	
	66						GLY					GLY	GLY	GLY			GLY		GLY	GLY	GLY	GLY	GLY	GLY	
	67						SER					SER	SER	ALA			SER		SER	SER	SER	SER	SER	SER	
	68						GLY					GLY	GLY	GLY			GLY		GLY	GLY	GLY	GLY	GLY	GLY	
	69						THR					THR	THR	THR			THR		THR	THR	THR	THR	THR	THR	
	70						ASP					ASX	ASP	GLU			ASP		GLU	ASP	ASP	GLU	GLU	GLU	
FR3	71						PRO					PHE	PHE	PHE			PHE		PHE	PHE	PHE	PHE	PHE	PHE	
FR3	72						SER					THR	THR	THR			THR		THR	THR	THR	THR	THR	THR	
FR3	73						LEU					PHE	LEU	LEU			PHE		LEU	LEU	LEU	LEU	LEU	LEU	
	74						ALA					THR	THR	THR			THR		THR	THR	THR	THR	THR	THR	
	75						VAL					ILE	ILE	ILE			ILE		ILE	ILE	ILE	ILE	ILE	ILE	
	76						SER					SER	SER	SER			SER		SER	SER	SER	SER	SER	SER	
	77						ARG					GLY	GLY	SER			SER		SER	SER	SER	SER	SER	SER	
	78											LEU	LEU	LEU			LEU		LEU	LEU	LEU	LEU	LEU	LEU	
	79											GLX	LEU	GLN			GLN		GLN	GLN	GLN	GLN	GLN	GLN	
	80											PRO	PRO	PRO			PRO		PRO	PRO	PRO	PRO	PRO	SER	
	81											GLX	GLU	GLU			GLU		GLU	GLU	GLU	ASP	ASP	ASP	
	82											ASP	ASP	ASP			ASP		ASP	ASP	ASP	ASP	ASP	ASP	
	83											PHE	PHE	PHE			ILE		PHE	PHE	PHE	PHE	PHE	PHE	
	84											ALA	ALA	ALA			ALA		ALA	ALA	ALA	ALA	ALA	ALA	
	85											THR	THR	THR			THR		THR	THR	THR	THR	THR	THR	
	86											TYR	TYR	TYR		TYR	TYR		TYR	TYR	TYR	TYR	TYR	TYR	
	87											TYR	TYR	TYR		TYR	TYR		PHE	TYR	TYR	TYR	TYR	TYR	
	88											CYS	CYS	CYS		CYS	CYS		CYS	CYS	CYS	CYS	CYS	CYS	
	89											GLX	GLX	LEU		GLN	GLN		GLN	GLN	GLN	GLN	GLN	GLN	
	90											GLX	GLX	GLN		GLN	GLN		GLN	GLN	GLN	GLN	GLN	GLN	
	91						GLY					SER	SER	GLN		TYR	TYR		ALA	ALA	ALA	TYR	TYR	TYR	
	92						GLU					TYR	TYR	ASN		ASP	ASN		HIS	ASN	ASN	ASN	ASN	ASP	
	93						SER					SER	THR	SER		ASP	ASN		SER	SER	SER	SER	SER	SER	
	94						ASP					SER	THR	TYR		LEU	TRP		VAL	PHE	PHE	TYR	ASP	PHE	
CDR3	95						SER					PRO	PRO	PRO		PRO	PRO		PRO	PRO	PRO	SER	SER	PRO	
CDR3	95A						---					---	---	---		---	---		---	---	---	#	---	---	
CDR3	95B						---					---	---	---		---	---		---	---	---	---	---	---	
CDR3	95C						---					---	---	---		---	---		---	---	---	---	---	---	
CDR3	95D						---					---	---	---		---	---		---	---	---	---	---	---	
CDR3	95E						---					---	---	---		---	---		---	---	---	---	---	---	
CDR3	95F						---					---	---	---		---	---		---	---	---	---	---	---	
CDR3	96						ARG					THR	TYR	ARG		PRO	PRO		LEU	---	---	---	LYS	TYR	
CDR3	97						THR					THR	THR	SER		THR	THR		THR	---	---	---	MET	THR	
	98						PHE					PHE	PHE	PHE		PHE	PHE		PHE	---	---	---	PHE	PHE	
	99						GLY					GLY	GLY	GLY		GLY	GLY		GLY	---	---	---	GLY	GLY	
	100						GLN					GLX	PRO	GLN		PRO	GLN		GLY	---	---	---	GLN	GLN	
	101						GLY					GLY	GLY	GLY		GLY	GLY		GLY	---	---	---	GLY	GLY	
FR4	102						THR					THR	THR	THR		THR	THR		THR	---	---	---	THR	THR	
FR4	103						LYS					ARG	LYS	LYS		LYS	LYS		THR	---	---	---	LYS	LYS	
FR4	104						VAL					LEU	VAL	VAL		VAL	VAL		VAL	---	---	---	VAL	LEU	
FR4	105						GLU					GLX	GLU	GLU		ASP	GLU		ASP	---	---	---	GLU	GLU	
FR4	106						VAL					ILE	MET	ILE		LEU	VAL		ILE	---	---	---	VAL	ILE	
FR4	106A						---					---	---	---		---	---		---	---	---	---	---	---	
FR4	107						LYS					LYS	THR	LYS		LYS	LYS		LYS	---	---	---	LYS	LYS	
	108											ARG	ARG	ARG			ARG		ARG	---	---	---	GLY	ARG	
	109											THR	THR	THR						---	---	---	THR	THR	

HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

		48 HBJ 4	49 FRA	50 GR*	51 PAUL	52 MON	53* HEI	54 POT	55 S-GUI #	56 AMYLOID BAN #	57 BJ 19 #	58 BEL	59 JBL #	60 PAP	61 CAR	62 MEV	63 BI	64 AMYLOID ES305 #	65 CRA	66* DAV	67* FIN	68 KA	69 Vd *CL	70 LUX	71 NE	72 Va* CL
	0	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ala
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	his	GLN
	4	MET	MET	MET	MET	MET	MET	MET	MET	leu	leu	leu	MET	MET	MET	MET	MET	leu	MET	MET	MET	MET	leu	leu	leu	leu
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	7	SER	SER	SER	SER	SER	SER	SER	ala	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9	SER	SER	SER	SER	SER	SER	ala	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
FR1	10	thr	thr	thr	thr	thr	thr	SER	SER	SER	SER	SER	SER	SER	thr	SER	pro	SER	SER	SER	thr	phe	phe	SER	SER	SER
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	val	ALA	ALA	ALA	ALA	ALA	thr	thr	val	ALA	ALA	ALA	ALA
	14	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	tyr	SER	SER	SER	SER	SER	SER	val	val	SER	SER	SER	SER	SER
	15	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	leu	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	VAL	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	arg	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASX	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASX	ASP
	18	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ser	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	19	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	20	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	ala	ile	THR	#	THR	THR	THR	THR	THR	THR	THR	THR
	21	ILE	ILE	ILE	ILE	ILE		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	THR	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	22	THR	THR	THR	THR	THR		THR	THR	THR	THR	THR	ala	ala	THR	THR	THR	CYS	THR	THR	THR	THR	THR	THR	THR	THR
	23	CYS	CYS	CYS	CYS			CYS	CYS	CYS	CYS	CYS	CYS		CYS	CYS	CYS		CYS	CYS	CYS	CYS	CYS		CYS	CYS
	24	ARG	ARG	ARG	ARG				ARG	ARG	GLN	GLX	ARG		ARG	ARG	GLN	GLN		ASP	ASP	GLU	ARG		GLX	ARG
	25	ALA	ALA	ALA	ALA				ALA	ALA	ALA	ALA	ALA		ALA	ALA	ALA	ALA		ALA	ALA	ALA	ALA		ALA	ALA
	26	SER	SER	SER	SER					SER	SER	SER	SER		SER	SER	SER	SER		SER	SER	SER	SER		SER	SER
	27	GLN	GLX	ARG	GLN					GLN	GLN	GLX	GLN		GLN	GLN	GLN	GLU		GLN	GLN	GLN	GLN		GLX	GLN
	27A	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
	27B	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
CDR1	27C	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
	27D	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
	27E	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
	27F	---	---	---	---					---	---	---	---		---	---	---	---		---	---	---	---		---	---
	28	SER	ASX	SER	SER					SER	ASP	ASX	SER		ASN	SER	ASP	ALA		ASX	ASX	THR	GLY		ASX	GLY
	29	VAL	ILE	ILE	ILE					VAL	ILE	ILE	ILE		ILE	SER	ILE	#		ILE	ILE	VAL	ILE		ILE	ILE
	30	ASN	ASX	SER	SER					TYR	ASN	SER	SER		SER	VAL	ARG			ASX	ASX	LEU	SER		SER	SER
	31	ASN	ASX	SER	SER					ASN	THR	LYS	THR		SER	ASP	ASN	ASN		SER	SER	SER	SER		ASX	SER
	32	TRP	TYR	TRP	SER					TYR	PHE		PHE		TRP	TYR	SER	TYR		TRP	TRP	TYR	TYR		TYR	ALA
	33	LEU	LEU	LEU						VAL	LEU		LEU		LEU	LEU	LEU	LEU		LEU	LEU	LEU	LEU		LEU	LEU
	34	ALA	ALA	ALA						ALA	ASN		#		ALA	ASN	ILE			ILE	ILE	ASN	ALA		ASX	ALA
	35	TRP	TRP	TRP						TRP	TRP		TRP		TRP	TRP	TRP	TRP		TRP	TRP	TRP	TRP		TRP	TRP
	36	TYR	TYR	TYR						PHE	TYR		TYR		TYR	TYR	TYR	TYR		TYR	TYR	TYR	TYR		TYR	TYR
	37	GLN	GLX	GLN						GLN	GLU		GLN		GLN	GLN	GLN			GLN	GLN	GLN	GLN		GLX	GLN
	38	GLU	GLX	GLY						GLN	GLN		GLN		GLN	GLN	GLN			GLN	GLN	GLN	GLN		GLX	GLN
	39	LYS	LYS	ARG						LYS	#		LYS		LYS	LYS	LYS			TYR	TYR	LYS	LYS		LYS	LYS
	40	PRO	PRO	PRO						PRO	PRO		PRO		PRO	PRO	PRO			PRO	PRO	PRO	PRO		PRO	PRO
FR2	41	GLY								GLY	#	GLY	GLY		GLY	GLY	GLY					GLY	GLY		GLY	GLY
	42	GLX								LYS	LYS	LYS	LYS		LYS	LYS	LYS					LYS	LYS		GLX	LYS
	43	ALA								ALA	ALA	PRO	ALA		ALA	ALA	ALA					ALA	ALA		ALA	ALA
	44	PRO								PRO	PRO	PRO	PRO		PRO	PRO	PRO					PRO	PRO		PRO	PRO
	45	LYS								LYS	LYS	GLU	LYS		LYS	LYS	LYS					LYS	LYS		LYS	LYS
	46	LEU								SER	LEU	LEU	LEU		VAL	LEU	PHE					LEU	LEU		VAL	LEU
	47	LEU								LEU	LEU	LEU	LEU		LEU	LEU	LEU					LEU	LEU		MET	LEU
	48	ILE								ILE	ILE	ILE			ILE	ILE	ILE					ILE	ILE		ILE	ILE
	49	SER								TYR	TYR	TYR	TYR		TYR	PHE	TYR					TYR	TYR		TYR	TYR
	50	LYS								ASP	ASP	ASP			LYS	ASP	ASP					ALA	ALA			ASP
	51	THR								ALA	ALA	ALA			SER	THR	ALA					ALA	ALA			ALA
CDR2	52	SER								SER	SER	SER			SER	SER	GLU					SER	SER			SER
	53	SER								THR	SER	THR			SER	ASN	ASN					SER	THR			SER
	54	LEU								LEU	LEU	LEU			LEU	LEU	LEU					LEU	LEU			LEU
	55	GLU								GLN	GLU	LYS			GLU	GLN	GLU					GLU	GLN			GLU
	56	ARG								SER	THR	THR			SER	SER	ILE					THR	SER			SER
	57	GLY								GLY	GLY	GLY			GLY	GLY	GLY					GLY	GLY			GLY
	58	VAL								VAL	VAL	VAL			VAL	VAL	VAL					VAL	VAL			VAL
	59	PRO								PRO	GLX	PRO			PRO	PRO						PRO	PRO			PRO
	60	SER								SER	SER	SER			SER	SER	SER					SER	SER			SER
	61	ARG								ASN	ARG	ARG			ARG	ARG	ARG					ARG	ARG			ARG
	62	PHE								PHE	PHE	PHE			PHE	PHE	PHE					PHE	PHE			PHE
	63	ALA								THR	LEU	SER			SER	SER	ARG					SER	SER			SER
	64	GLY								GLY	GLY	GLY			GLY	GLY	GLY					GLY	GLY			GLY
	65	SER								SER	SER	SER			SER	GLY	SER					GLN	SER			SER
	66	GLY								GLY	ASX	GLY			GLY	ARG	GLY					GLY	GLY			GLY
	67									SER	PHE	SER			SER	SER	SER					SER	SER			SER
	68									GLY	ASX	GLU			GLY	GLY	GLY					GLY	GLY			GLY
	69									THR	THR	THR			THR	THR	THR					THR	THR			THR
	70									ASP	LYS	HIS			ASP	ASP	ASP					ASX	GLU			ASP
FR3	71									PHE		PHE			PHE	PHE	PHE					PHE	PHE			PHE
	72									ILE		THR			THR	THR	ALA					THR	THR			THR
	73									LEU		LEU			LEU	LEU	LEU					PHE	LEU			LEU
	74									THR		THR			THR	THR	SER					THR	THR			THR
	75									ILE		ILE			ILE	ILE	ILE					ILE	ILE			ILE
	76									SER					SER	SER	SER					SER	SER			SER
	77									SER		SER			SER	SER	SER					SER	SER			SER
	78									LEU		LEU			LEU	LEU	LEU					VAL	LEU			LEU
	79									GLN		GLN			GLX	GLN	GLN					GLX	GLN			GLN
	80									PRO		PRO			PRO	PRO	PRO					PRO	PRO			PRO
	81									GLU		ALA			ASX	ASP	GLU					GLX	GLU			GLU
	82									ASP		ASP			ASX	ASP	ASP					ASX	ASP			ASP
	83									PHE		PHE			PHE	PHE	PHE					PHE	PHE			PHE
	84									ALA		ALA			ALA	ALA	ALA					ALA	ALA			ALA
	85									THR		THR			THR	THR	THR					THR	THR			THR
	86									TYR		TYR			TYR	TYR	TYR					TYR	TYR			TYR
	87									TYR		TYR			TYR	TYR	TYR					TYR	TYR			TYR
	88									CYS		CYS			CYS	CYS	CYS					CYS	CYS			CYS
	89									GLN		GLN			GLN	GLN	GLN					GLN	GLN			GLN
	90									GLN		GLN			GLN	GLN	GLN					GLX	GLN			GLN
	91									TYR	PHE	TYR			TYR	SER	TYR					TYR	LEU			PHE
	92									ASN	ASP	ASX			ASN	TYR	TYR					LEU	ASN			ASN
	93									SER	ASP	HIS			THR	THR	ASN					ASP	SER			SER
	94									TYR	LEU	PHE			PHE	ASN	LEU					LEU	TYR			TYR
	95									PRO	PRO	PRO			---	PRO	PRO					PRO	PRO			PRO
	95A									---	---	---			---	GLU	---					---	---			---
CDR3	95B									---	---	---			---	---	---					---	---			---
	95C									---	---	---			---	---	---					---	---			---
	95D									---	---	---			---	---	---					---	---			---
	95E									---	---	---			---	---	---					---	---			---
	95F									---	---	---			---	---	---					---	---			---
	96									TYR	TYR	LEU			PHE	VAL	TYR					ARG	---			---
	97									THR	THR	THR			THR	THR	THR					THR	---			---
	98									PHE	PHE	PHE			PHE	PHE	PHE					PHE	---			---
	99									GLY	GLY	GLY			GLY	GLY	GLY					GLY	---			---
	100									GLN	PRO	GLY			PRO	GLY	GLN					GLN	---			---
	101									GLY	GLY	GLY			GLY	GLY	GLY					GLY	---			---
FR4	102									THR	THR	THR			THR	THR	THR					THR	---			---
	103									LYS	LYS	GLU			LYS	THR	LYS					LYS	---			---
	104									#	VAL	VAL			VAL	VAL	LEU					VAL	---			---
	105									#	GLU	GLU			ASP	ASP	GLU					ASP	---			---
	106									ILE	LEU	VAL			ILE	ILE	ILE					LEU	---			---
	106A									---	---	---			---	---	---					---	---			---
	107									LYS	LYS	LYS			LYS	LYS	LYS					LYS	---			---
	108									ARG					ARG	ARG	ARG					ARG	---			---
	109														THR		THR					THR	---			---

HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

		73 NI	74 PW #	75 AMYLOID X	76 ALE	77 SHE	78 ADA	79 KUE	80 GO	81 BOL	82 RI #	83 Ve 'CL	84 OCO	85 V13 'CL	86 V18A 'CL	87 V19A 'CL	88 V19B 'CL	89 V18B 'CL	90 HF6-21/28	91 SAC	92* WAG	93 HBJ 1	94 AMYLOID 547	95 WEB	96 HOE
	0	---	---	---	---	---	---	---	---	---	pca	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1	ASP	ASP	ASP	ASX	ASP	ASP	ASP	ASP	ASP	ASP	ala	ASX	val	ASP	ala	ala	ala	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	ILE	ILE	ILE	ILE	ILE	pro	gln	ILE	gln	val	ILE	ILE	ILE	ILE	ILE	ILE
	3	GLN	his	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLN	arg	GLX	trp	val	val	asp	val	val	GLN	GLN	leu	GLX	GLN	GLN
	4	MET	MET	MET	MET	leu	val	MET	MET	ile	MET	MET	MET	MET	MET	leu	MET	leu	MET	MET	MET	MET	MET	MET	MET
	5	THR	THR	THR	THR	THR	THR	THR	THR	met	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLX	GLX	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	thr	thr	thr	thr	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	ala	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	glu	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9	SER	SER	SER	SER	thr	SER	SER	SER	SER	SER	SER	SER	SER	SER	ala	ala	SER	leu	SER	SER	thr	SER	SER	SER
FR 1	10	SER	SER	SER		SER	SER	thr	phe	SER	thr	SER	leu	leu	SER	SER	SER	pro	SER	SER	SER	SER	SER	SER	thr
	11	LEU	LEU	LEU		LEU	LEU	gln	val	val	LEU	phe	LEU	LEU	thr	val	val	val	LEU	LEU	LEU	LEU	LEU	val	LEU
	12	SER	SER	SER	SER	SER	SER	pro	SER	SER	SER	SER	val	SER	SER	SER	glu	SER	pro	SER	SER	SER	SER	SER	SER
	13	ALA	ALA	ALA	ALA	ALA	val	ALA	ALA	ALA	ALA	ALA	ser	ALA	ALA	ALA	ALA	ALA	val	ALA	ALA	ALA	ALA	ALA	ALA
	14	thr	SER	SER	SER	SER	phe	SER	SER	SER	SER	SER	pro	SER	ala	ala	ala	pro	thr	SER	SER	SER	SER	SER	SER
	15	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	thr	VAL	thr	VAL	VAL	VAL	VAL	leu	VAL	VAL	VAL	VAL	VAL	VAL
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY			
	17	ASP	ASP	ASP	ASP	ASX	ASP	ASP	ASX	ASX	ASP	ASP	ASX	ASP	gly	gly	gly	gly	gly	ASP	ASP	ASP			
	18	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	gly	ARG	leu	ARG	thr	thr	thr	thr	pro	---					
	19	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ile	VAL	ala	---					
	20	THR	THR	ile	THR	THR	THR	THR	ILE	THR	THR	THR	THR	THR	THR	THR	THR	THR	ser	---					
	21	leu	val	ILE	leu	phe	ILE	ILE	THR	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	---					
	22	leu	arg		THR	THR	THR	THR	THR	THR	ser	THR	THR	ser	asn	asn	asn	asn	ser	---					
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	---					
	24	GLU	ARG	GLX	ARG	GLX	GLX	ARG	ARG	ARG	ARG	ARG	GLX	ARG	GLN	GLN	GLN	GLN	ARG	---					
	25	ALA	ALA	ALA		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	MET	SER	ALA	ALA	ALA	SER	---					
	26	SER	SER			SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	---					
	27	GLN	GLX	GLX		GLX	GLX	GLN		GLX	GLX	GLN	GLX	GLN	GLN	GLU	GLU	GLN	GLN	---					
	27A	SER	---	---		---	---	---		---	---	---	---	---	ASN	---	---	SER	SER	---					
	27B	VAL	---	---		---	---	---		---	---	---	---	---	VAL	---	---	VAL	LEU	---					
CDR 1	27C	LEU	---	---		---	---	---		---	---	---	---	---	---	---	---	---	VAL	---					
	27D	GLU	---	---		---	---	---		---	---	---	---	---	---	---	---	---	TRP	---					
	27E	---	---	---		---	---	---		---	---	---	---	---	---	---	---	---	SER	---					
	27F	---	---	---		---	---	---		---	---	---	---	---	---	---	---	---	---	---					
	28	SER	SER	ASX		ASX	ASX	SER		GLY	SER	GLY	ASX	GLY	TYR	SER	SER	TYR	ASP	---					
	29	GLY	ILE	ILE		ILE	ILE	ILE		ILE	ILE	ILE	ILE	ILE	SER	ILE	ILE	ASP	GLY	---					
	30	ASN	GLY			SER		ASN			SER	SER	SER	SER	ASN	SER	SER	ASN	ARG	---					
	31	THR		PRO		ASX	ASX	ILE				SER	ASX	SER	ASN	SER	SER	ASN	SER	---					
	32	PHE	TYR	TYR		TYR	TYR	TRP				TYR	TYR	SER	TYR	TYR	TRP	TRP	TYR	---					
	33	LEU	SER	LEU		LEU	LEU	LEU				LEU		LEU	LEU	LEU	LEU	LEU	LEU	---					
	34	ALA	ASX			ASX	ASX	ALA				ALA		ALA	SER	ASN	ALA	SER	GLU	---					
	35	TRP	TRP			TRP	TRP	TRP				TRP		TRP	TRP	TRP	TRP	TRP	TRP	---					
	36	TYR		TYR		TYR	TYR	TYR				TYR		TYR	PHE	TYR	TYR	TYR	TYR	---					
	37	GLN	GLN			HIS	GLX	GLN				GLN		GLN	GLN	GLN	GLN	GLN	GLN	---					
	38	GLN	GLN			GLX	TYR	GLN				GLN		GLN	GLN	GLN	GLN	GLN	GLN	---					
	39	LYS	LYS			LYS	LYS	LYS				LYS		LYS	LYS	LYS	LYS	LYS	LYS	---					
	40	PRO				PRO	PRO	PRO				PRO		PRO	PRO	LEU	PRO	PRO	PRO	---					
FR 2	41	LYS						GLU				GLY		GLY	GLY	GLY	GLY	GLY		---					
	42	LYS						LYS				LYS		LYS	GLN	GLN	GLN	GLN		---					
	43	ALA						ALA				ALA		ALA	PRO	PRO	PRO	PRO		---					
	44	PRO						PRO				PRO		PRO	PRO	PRO	PRO	PRO		---					
	45	LYS						LYS				LYS		GLU	LYS	LYS	LYS	LYS		---					
	46	LEU						LEU				LEU		LEU	LEU	LEU	LEU	LEU		---					
	47	LEU						LEU				LEU		LEU	LEU	LEU	LEU	LEU		---					
	48	ILE						ILE				ILE		ILE	ILE	ILE	ILE	ILE		---					
	49	TYR						TYR				TYR		TYR	TYR	TYR	TYR	TYR		---					
	50	ASP						LYS				ALA		ALA	GLY	TYR	GLU	ASP		LYS					
	51	ALA						ALA				ALA		ALA	ALA	ALA	ALA	ALA		SER					
CDR 2	52	SER						SER				SER		SER	SER	SER	SER	SER		---					
	53	ASN						THR				THR		THR	LYS	THR	LYS	LYS		---					
	54	LEU						LEU				LEU		LEU	LEU	LEU	LEU	LEU		---					
	55	GLU						GLU				GLN		GLN	ALA	ALA	ALA	ALA		---					
	56	THR						THR				SER		SER	SER	SER	SER	SER		---					
	57	GLY						GLY				GLY		GLY	GLY	GLY	GLY	GLY		---					
	58	VAL						VAL				VAL		VAL	VAL	VAL	VAL	VAL		---					
	59	PRO						PRO				PRO		PRO	PRO	PRO	PRO	PRO		---					
	60	SER						SER				SER		SER	SER	SER	SER	SER		---					
	61	ARG						ARG				ARG		ARG	ARG	ARG	ARG	ARG		---					
	62	PHE						PHE				PHE		PHE	PHE	PHE	PHE	PHE		---					
	63	SER						SER				SER		SER	SER	LYS	SER	SER		---					
	64	GLY						GLY				GLY		GLY	GLY	GLY	GLY	GLY		---					
	65	SER						SER				SER		SER	SER	SER	SER	SER		---					
	66	GLY						GLY				GLY		GLY	GLY	GLY	GLY	GLY		---					
	67	SER						SER				SER		SER	SER	SER	SER	SER		---					
	68	GLY						GLY				GLY		GLY	GLY	GLY	GLY	GLY		---					
	69	THR						THR				THR		THR	LYS	THR	THR	THR		---					
	70	ASP						GLN				ASP		ASP	GLN	GLU	GLN	GLN		---					
	71	PHE						PHE				PHE		PHE	PHE	TYR	PHE	PHE		---					
FR 3	72	THR						THR				THR		THR	THR	THR	THR	THR		---					
	73	PHE						LEU				LEU		LEU	LEU	LEU	LEU	LEU		---					
	74	THR						THR				THR		THR	THR	THR	THR	THR		---					
	75	ILE						ILE				ILE		ILE	ILE	ILE	ILE	ILE		---					
	76	SER						ASN				SER		SER	SER	SER	SER	SER		---					
	77	GLY						SER				CYS		CYS	GLY	GLY	GLY	GLY		---					
	78	LEU						LEU				LEU		LEU	VAL	VAL	VAL	VAL		---					
	79	GLX						GLN				GLN		GLN	GLN	GLN	GLN	GLN		---					
	80	PRO						PRO				SER		SER	CYS	CYS	CYS	CYS		---					
	81	GLX						ASP				GLU		GLU	ASP	ASP	ASP	ASP		---					
	82	ASX						ASP				ASP		ASP	ASP	ASP	ASP	ASP		---					
	83	PHE						PHE				PHE		PHE	ALA	ALA	ALA	ALA		---					
	84	ALA						ALA				ALA		ALA	ALA	ALA	ALA	ALA		---					
	85	VAL						THR				THR		THR	THR	THR	THR	THR		---					
	86	TYR						TYR				TYR		TYR	TYR	TYR	TYR	TYR		---					
	87	TYR						TYR				TYR		TYR	TYR	TYR	TYR	TYR		---					
	88	CYS						CYS				CYS		CYS	CYS	CYS	CYS	CYS		CYS					
	89	GLN						GLN				GLN		GLN	ALA	GLN	GLN	GLN		GLX					
	90	GLX						GLN				GLN		GLN	GLY	HIS	GLY	GLY		GLX					
	91	TYR						TYR				TYR		TYR	TYR	GLY	GLY	SER		GLX					
	92	ASP						SER				TYR		TYR	TYR	TYR	TYR	TYR		ASX					
	93	THR						ARG				SER		SER	TYR	ILE	TYR	TYR		ALA					
	94	LEU						TYR				TYR		PHE	SER	TYR	ASN	SER		ALA					
CDR 3	95	PRO						PRO				PRO		PRO	GLY	SER	SER	SER		THR					
	95A	---						---				---		---	SER	SER	GLY	GLY		---					
	95B	---						---				---		---	GLY	GLY	TRP	TRP		---					
	95C	---						---				---		---	THR	ASP	TYR	TYR		---					
	95D	---						---				---		---	ASP					---					
	95E	---						---				---		---						---					
	95F	---						---				---		---						---					
	96	SER						TYR				---		---						ILE					
	97	THR						THR				---		---						PRO					
	98	PHE						PHE				---		---						ILE					
	99	GLY						GLY				---		---						GLY					
	100	VAL						GLN				---		---						GLY					
	101	GLY						GLY				---		---						GLY					
FR 4	102	SER						THR				---		---						THR					
	103	LYS						LYS				---		---						LYS					
	104	VAL						LEU				---		---						VAL					
	105	GLU						ASP				---		---						ASX					
	106	SER						ILE				---		---						VAL					
	106A	---						---				---		---						---					
	107	LYS						LYS				---		---						LYS					
	108	ARG						ARG				---		---						ARG					
	109	THR						THR				---		---						THR					

HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

		97 LOD	98 HBJ 10	99 BEN	100 GR	101 MAA	102 MUK	103 AMYLOID 594	104* MAR	105 AMYLOID	106 BJ	107 HBJ 6	108 PEN	109 AMYLOID MS #	110 CL*	111 GM131 CL #	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID
	0	---	---	---	---	---	---	---	---	---	---	---	---	---	---		1	1	1(PCA)
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASX	ASP	ASP	ASP	---		109	3 : 4	103(ASP) : 99(ASP)
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE	ILE	#	---		107	4	101(ILE)
	3	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	glu		GLN	GLN	GLN	---		108	8	97(GLN) : 93(GLN)
	4		MET	MET	MET	leu	MET	MET	leu	MET	MET	MET	MET	MET	---		108	4	93(MET)
	5	THR	THR	THR	THR	THR	THR	THR	THR	pro	THR	THR		THR	---		108	3	106(THR)
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN			---		107	1 : 2	107(GLN) : 100(GLN)
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER					---		105	3	100(SER)
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO					---		105	3	103(PRO)
	9	SER	SER	SER	SER	SER	SER	SER	SER	SER					---		105	4	99(SER)
FR1	10	thr	SER	SER	SER	thr	SER	SER	SER	SER					---		104	5	81(SER)
	11		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU					---		103	5	91(LEU)
	12	SER	SER	SER	SER	SER	SER								---		102	4	98(SER)
	13	ALA	ALA	ALA	val	ALA									---		101	4	91(ALA)
	14	-	SER												---		97	7	86(SER)
	15	VAL													---		97	3	93(VAL)
	16														---		93	2	92(GLY)
	17														---		93	3 : 4	87(ASP) : 79(ASP)
	18										ARG				---		90	6	82(ARG)
	19										VAL				---		91	3	88(VAL)
	20										THR				---		91	4	87(THR)
	21										ILE				---		88	4	84(ILE)
	22										THR				---		88	7	75(THR)
	23										CYS				---		83	1	83(CYS)
	24										GLN				---		75	5	43(ARG)
	25										ALA				---		75	4	71(ALA)
	26										SER				---		72	4	67(SER)
	27										GLN				---		72	4	66(GLN) : 53(GLN)
	27A										---				---		4	2	3(SER)
	27B										---				---		4	2	3(VAL)
CDR1	27C										---				---		2	2	1(+)
	27D										---				---		2	2	1(+)
	27E										---				---		1	1	1(SER)
	27F										---				---				
	28										ASP				---		72	8	25(ASP) : 22(SER)
	29										ILE				---		71	5	61(ILE)
	30										ASN				---		68	10 : 11	35(SER)
	31										LYS				---		66	10	24(SER)
	32														---		66	7	33(TYR)
	33														---		64	4	60(LEU)
	34														---		60	7 : 8	24(ASN) : 22(ALA)
	35														---		63	1	63(TRP)
	36														---		61	2	57(TYR)
	37														---		60	4	56(GLN) : 49(GLN)
	38														---		58	4	55(GLN) : 50(GLN)
	39														---		55	4	50(LYS)
	40														---		57	4	54(PRO)
FR2	41														---		44	3	40(GLY)
	42														---		46	5	35(LYS)
	43														---		47	2	42(ALA)
	44														---		47	1	47(PRO)
	45														---		47	6	41(LYS)
	46														---		46	7	33(LEU)
	47														---		45	2	44(LEU)
	48														---		43	2	42(ILE)
	49														---		45	4	42(TYR)
	50														---		45	7 : 8	15(+)
	51														---		45	5	39(ALA)
CDR2	52														---		44	4	41(SER)
	53														---		43	5 : 6	18(SER)
	54														---		44	2	43(LEU)
	55														---		44	7	20(GLU)
	56														---		42	7	27(SER)
	57														---		43	1	43(GLY)
	58														---		43	2	42(VAL)
	59														---		42	4	39(PRO)
	60														---		42	1	42(SER)
	61														---		43	3	41(ARG)
	62														---		43	3	41(PHE)
	63														---		43	7	36(SER)
	64														---		43	1	43(GLY)
	65														---		42	4	38(SER)
	66														---		43	3	41(GLY)
	67														---		41	3	38(SER)
	68														---		41	3	38(GLY)
	69														---		41	3	38(THR)
	70														---		41	5 : 6	25(ASP) : 23(ASP)
FR3	71														---		40	4	36(PHE)
	72														---		40	4	37(THR)
	73														---		40	3	31(LEU)
	74														---		40	4	37(THR)
	75														---		40	3	38(ILE)
	76														---		39	2	37(SER)
	77														---		40	5	27(SER)
	78														---	LEU	40	2	35(LEU)
	79														---	GLN	40	2 : 3	39(GLN) : 35(GLN)
	80														---	PRO	40	3	33(PRO)
	81														---	GLU	40	3 : 5	29(GLU) : 26(GLU)
	82														---	ASP	40	1 : 2	40(ASP) : 37(ASP)
	83														---	PHE	40	4	28(PHE)
	84														---	ALA	40	2	39(ALA)
	85														---	THR	40	4	37(THR)
	86										TYR				---	TYR	42	2	41(TYR)
	87										TYR				---	TYR	41	2	40(TYR)
	88										CYS				---	CYS	42	1	42(CYS)
	89										GLN				---	GLN	43	3 : 4	40(GLN) : 37(GLN)
	90										GLN				---	GLN	43	3 : 4	39(GLN) : 34(GLN)
	91										TYR				---	HIS	45	10 : 11	24(TYR)
	92										GLU				ASP	ASP	46	8	15(ASN) : 13(+)
	93										ASN				ILE	HIS	46	9	20(SER)
	94										LEU				PHE	LEU	46	10	12(LEU)
	95										PRO				PRO	PRO	45	5	35(PRO)
	95A										---				---	---	5	3	2(+)
CDR3	95B										---				---	---	4	2	2(+)
	95C										---				---	---	4	3	2(TYR)
	95D										---				---	---	1	1	1(ASP)
	95E										---				---	---			
	95F										---				---	---			
	96										TYR				GLY	LEU	32	12	9(TYR)
	97														THR	THR	31	4	27(THR)
	98														PHE	PHE	31	3	29(PHE)
	99														GLY	GLY	31	1	31(GLY)
	100														GLN	GLY	31	4 : 5	18(GLN) : 17(GLN)
	101														GLY	GLY	31	1	31(GLY)
FR4	102														THR	THR	31	2	30(THR)
	103														LYS	THR	31	4	23(LYS)
	104														VAL	VAL	30	2	23(VAL)
	105														GLU	GLU	30	3 : 4	20(GLU) : 19(GLU)
	106														ILE	MET	31	7	15(ILE)
	106A														---	---			
	107														LYS	LYS	31	2	29(LYS)
	108														ARG	ARG	24	2	22(ARG)
	109														THR	THR	20	1	20(THR)

HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

VARIABILITY

	0	
	1	3.2 : 4.4
	2	4.2
	3	8.9 : 9.3
	4	4.6
	5	3.1
	6	1. : 2.1
	7	3.2
	8	3.1
	9	4.2
FR1	10	6.4
	11	5.7
	12	4.2
	13	4.4
	14	7.9
	15	3.1
	16	2.
	17	3.2 : 4.7
	18	6.6
	19	3.1
	20	4.2
	21	4.2
	22	8.2
	23	1.
	24	8.7
	25	4.2
	26	4.3
	27	4.4 : 5.4
	27A	
	27B	
CDR1	27C	
	27D	
	27E	
	27F	
	28	23. : 26.
	29	5.8
	30	19. : 21.
	31	28.
	32	14.
	33	4.3
	34	18. : 22.
	35	1.
	36	2.1
	37	4.3 : 4.9
	38	4.2 : 4.6
	39	4.4
	40	4.2
FR2	41	3.3
	42	6.6
	43	2.2
	44	1.
	45	6.9
	46	9.8
	47	2.
	48	2.
	49	4.3
	50	21. : 24.
	51	5.8
	52	4.3
CDR2	53	12. : 14.
	54	2.
	55	15.
	56	11.
	57	1.
	58	2.
	59	4.3
	60	1.
	61	3.1
	62	3.1
	63	8.4
	64	1.
	65	4.4
	66	3.1
	67	3.2
	68	3.2
	69	3.2
	70	8.2 : 11.
	71	4.4
FR3	72	4.3
	73	3.9
	74	4.3
	75	3.2
	76	2.1
	77	7.4
	78	2.3
	79	2.1 : 3.4
	80	3.6
	81	4.1 : 7.7
	82	1. : 2.2
	83	5.7
	84	2.1
	85	4.3
	86	2.
	87	2.1
	88	1.
	89	3.2 : 4.6
	90	3.3 : 5.1
	91	19. : 21.
	92	25. : 28.
	93	21.
	94	38.
	95	6.4
	95A	
	95B	
CDR3	95C	
	95D	
	95E	
	95F	
	96	43.
	97	4.6
	98	3.2
	99	1.
	100	6.9 : 9.1
	101	1.
	102	2.1
FR4	103	5.4
	104	2.6
	105	4.5 : 6.3
	106	14.
	106A	
	107	2.1
	108	2.2
	109	1.

ANTIBODY SPECIFICITIES: HUMAN KAPPA LIGHT CHAINS SUBGROUP I

8) **WEA:** ANTI-3,4-PYRUVYLATED GALACTOSE MONOCLONAL
25) **LOW:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
39) **LAY:** ANTI-HUMAN GAMMA G1 AND G3 GLOBULINS; PO IDIOTYPE
53) **HEI:** COLD AGGLUTININ WITH ANTI-GD (MEMBRANE-GLYCOLIPID-DEPENDENT) ACTIVITY
66) **DAV:** ANTI-HUMAN GAMMA G GLOBULIN
67) **FIN:** ANTI-HUMAN GAMMA G GLOBULIN
92) **WAG:** ANTI-DINITROPHENYL
104) **MAR:** ANTI-LIPOPROTEIN LIPASE

ALLOTYPE: HUMAN KAPPA LIGHT CHAINS SUBGROUP I

79) **KUE:** INV(2)

CLASS: HUMAN KAPPA LIGHT CHAINS SUBGROUP I

8) **WEA:** IGM-KAPPA
33) **F-GUI:** IGG3-KAPPA
55) **S-GUI:** IGG3-KAPPA
74) **PW:** IGG1-KAPPA
82) **RI:** IGG1-KAPPA

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP I

1) **ROY:** HILSCHMANN,N. & CRAIG,L.C. (1965) PROC.NAT.ACAD.SCI.USA,53,1403-1409; HILSCHMANN,N. (1967) Z.PHYSIOL.CHEM.,348,1077-1080; HILSCHMANN,N.,BARNIKOL,H.U.,HESS,M.,LANGER,B.,PONSTINGL,H.,STEINMETZ-KAYNE,M.,SUTER,L. & WATANABE,S. (1969) PROC. 5TH FEBS SYMP., 15,57-74 (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED AND CORRECTED RESIDUES 65 AND 67 AS GIVEN IN THE TABLE)
2) **AU:** SCHIECHL,H. & HILSCHMANN,N. (1971) Z.PHYSIOL.CHEM.,352,111-115; (1972) Z.PHYSIOL.CHEM.,353,345-370. (CHECKED BY AUTHOR)
3) **REI:** PALM,W. & HILSCHMANN,N. (1973) Z.PHYSIOL.CHEM.,354,1651-1654; (1975) Z.PHYSIOL.CHEM.,356,167-191. (CHECKED BY AUTHOR)
4) **HAU:** WATANABE,S. & HILSCHMANN,N. (1970) Z.PHYSIOL.CHEM.,351,1291-1295. (CHECKED BY AUTHOR)
5) **HK101'CL:** BENTLEY,D.L. & RABBITTS,T.H. (1980) NATURE,288,730-733. (CHECKED BY AUTHOR 11/30/82)
6) **SCW:** EULITZ,M.,GOTZE,D. & HILSCHMANN,N. (1972) Z.PHYSIOL.CHEM.,353,487-491; EULITZ,M. & HILSCHMANN,N. (1974) Z.PHYSIOL.CHEM.,355,842-866. (CHECKED BY AUTHOR)
7) **AG:** TITANI,K.,SHINODA,T. & PUTNAM,F.W. (1969) J.BIOL.CHEM.,244,3550-3560. (CHECKED BY AUTHOR 06/15/83)
8) **WEA:** GONI,F. & FRANGIONE,B. (1983) PROC.NAT.ACAD.SCI.USA,80,4837-4841. (CHECKED BY AUTHOR 03/23/84)
9) **HK137'CL:** BENTLEY,D.L. & RABBITTS,T.H. (1983) CELL,32,181-189.
10) **HK134'CL:** BENTLEY,D.L. & RABBITTS,T.H. (1983) CELL,32,181-189.
11) **DAUDI'CL:** KLOBECK,H.G.,COMBRIATO,G. & ZACHAU,H.G. (1984) NUC.ACIDS RES.,12,18,6995-7006.
12) **WALKER'CL:** KLOBECK,H.G.,COMBRIATO,G. & ZACHAU,H.G. (1984) NUC.ACIDS RES.,12,18,6995-7006. (CHECKED BY AUTHOR 08/22/85 WHO CORRECTED RESIDUE 34)
13) **HF3-16/6:** ATKINSON,P.M.,LAMPMAN,G.W.,FURIE,B.C.,NAPARSTEK,Y.,SCHWARTZ,R.S.,STOLLAR,B.D. & FURIE,B. (1985) J.CLIN.INVEST.,75,1138-1143. (CHECKED BY AUTHOR 08/21/85)
14) **HF2-1/13B:** ATKINSON,P.M.,LAMPMAN,G.W.,FURIE,B.C.,NAPARSTEK,Y.,SCHWARTZ,R.S.,STOLLAR,B.D. & FURIE,B. (1985) J.CLIN.INVEST.,75,1138-1143. (CHECKED BY AUTHOR 08/21/85)
15) **HF2-16/2:** ATKINSON,P.M.,LAMPMAN,G.W.,FURIE,B.C.,NAPARSTEK,Y.,SCHWARTZ,R.S.,STOLLAR,B.D. & FURIE,B. (1985) J.CLIN.INVEST.,75,1138-1143. (CHECKED BY AUTHOR 08/21/85)
16) **HF2-1/17:** ATKINSON,P.M.,LAMPMAN,G.W.,FURIE,B.C.,NAPARSTEK,Y.,SCHWARTZ,R.S.,STOLLAR,B.D. & FURIE,B. (1985) J.CLIN.INVEST.,75,1138-1143. (CHECKED BY AUTHOR 08/21/85)
17) **BJ26:** ALESCIO-ZONTA,L. & BAGLIONI,C. (1970) EUR.J.BIOCHEM.,15,450-463. (CHECKED BY AUTHOR)
18) **RFZ:** SMITHIES,O.,GIBSON,D.,FANNING,E.M.,GOODFLIESH,R.M.,GILMAN,J.G. & BALLANTYNE,D.L. (1971) BIOCHEMISTRY,10,4912-4921. (CHECKED BY AUTHOR)
19) **PSM:** SEON,B.K. (1982) MOL.IMMUNOL.,19,83-86. (CHECKED BY AUTHOR 05/23/83)
20) **HOM:** CAVVIDOU,G.,KLEIN,M.,HORNE,C.,HOFMANN,T. & DORRINGTON,K.J. (1981) MOL.IMMUNOL.,18,793-805.
21) **ESM IGG:** KUAN,T.K.,TUNG,E.,WANG,I.Y. & WANG,A.C. (1981) IMMUNOL.,44,265-271. (CHECKED BY AUTHOR 05/26/83)
22) **ESM IGM:** KUAN,T.K.,TUNG,E.,WANG,I.Y. & WANG,A.C. (1981) IMMUNOL.,44,265-271. (CHECKED BY AUTHOR 05/26/83)
23) **WAT:** STEVENS,F.J.,WESTHOLM,F.A.,PANAGIOTOPOULOS,N.,SCHIFFER,M.,POPP,R.A. & SOLOMON,A. (1981) J.MOL.BIOL.,147,185-193. (CHECKED BY AUTHOR 05/26/1983)
24) **AMYLOID VIII-B:** GLENNER,G.G.,TERRY,W.,HERADA,M.,ISERSKY,C. & PAGE,D. (1971) SCIENCE,172,1150-1151. (CHECKED BY AUTHOR 09/22/78)
25) **LOW:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR WHO CORRECTED RESIDUE 16 AS GIVEN IN TABLE)
26) **DIE:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)
27) **CAR A:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)
28) **TEI:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)
29) **BJ48:** ALESCIO-ZONTA,L. & BAGLIONI,C. (1970) EUR.J.BIOCHEM.,15,450-463. (CHECKED BY AUTHOR)
30) **CON:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)
31) **TRA:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)
32) **AMYLOID LEP:** LIAN,J.B.,SKINNER,M.,BENSON,M.D. & COHEN,A.S. (1977) BIOCHIM.BIOPHYS.ACTA,491,167-176.
33) **F-GUI:** WANG,A.C.,FUDENBERG,H.H. & CREYSSEL,R. (1982) ACTA HAEMAT.,68,187-195. (CHECKED BY AUTHOR 05/26/83)
34) **OU(IOC):** KOHLER,H.,SHIMIZU,A.,PAUL,C. & PUTNAM,F.W. (1970) SCIENCE,169,56-59. (KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951.) (CHECKED BY AUTHOR 06/15/83)
35) **DEE:** MILSTEIN,C. & DEVERSON,E.V. (1971) BIOCHEM.J.,123,945-958. (CHECKED BY AUTHOR)
36) **GAL(I):** LAURE,C.J.,WATANABE,S. & HILSCHMANN,N. (1973) Z.PHYSIOL.CHEM.,354,1503-1504. (CHECKED BY AUTHOR)
37) **JOH:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)
38) **KER:** MILSTEIN,C. (1966) BIOCHEM.J.,101,352-368. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED)
39) **LAY:** KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951. (CHECKED BY AUTHOR); KLAPPER,D.G. & CAPRA,J.D. (1976) ANN.IMMUNOL.(INST.PASTEUR),127C,261-271. (CHECKED BY AUTHOR 08/01/79)
40) **BRA:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)
41) **WES:** KRATZIN,H.,YANG,C.Y.,KRUSCHE,J.U. & HILSCHMANN,N. (1980) Z.PHYSIOL.CHEM.,361,1591-1598.
42) **Vb'CL:** PECH,M.,JAENICHEN,H.-R.,POHLENZ,H.-D.,NEUMAIER,P.S.,KLOBECK,H.-G. & ZACHAU,H.G. (1984) J.MOL.BIOL.,176,189-204. (CHECKED BY AUTHOR 12/14/84)
43) **Vb''CL:** PECH,M.,JAENICHEN,H.-R.,POHLENZ,H.-D.,NEUMAIER,P.S.,KLOBECK,H.-G. & ZACHAU,H.G. (1984) J.MOL.BIOL.,176,189-204. (CHECKED BY AUTHOR 12/14/84)
44) **HK102'CL:** BENTLEY,D.L. & RABBITTS,T.H. (1980) NATURE,288,730-733. (CHECKED BY AUTHOR 11/30/82)
45) **EU:** GOTTLIEB,P.D.,CUNNINGHAM,B.A.,RUTISHAUSER,U. & EDELMAN,G.M. (1970) BIOCHEMISTRY,9,3155-3161. (CHECKED BY AUTHOR)
46) **DEN:** YANG,C.Y.,PAULY,E.,KRATZIN,H. & HILSCHMANN,N. (1981) Z.PHYSIOL.CHEM.,362,1131-1146.
47) **PAU:** DAYHOFF,M.O. (1972) ATLAS OF PROTEIN SEQUENCE & STRUCTURE,5,D-245. SUBMITTED BY SMITHIES,O.,GIBSON,D.M. AND FANNING,E.M. (CHECKED BY AUTHOR)
48) **HBJ4:** SMITH,G.P.,HOOD,L. & FITCH,W.M. (1971) ANN.REV.BIOCHEM.,40,969-1012.
49) **FRA:** MEINKE,G.C.,SIGRIST,P.H. & SPIEGELBERG,H.L. (1974) IMMUNOCHEM.,11,457-460. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED); MEINKE,G.C. & SPIEGELBERG,H.L. (1976) IMMUNOCHEM.,13,915-919. (CHECKED BY AUTHOR 10/17/77)
50) **GR':** FAIR,D.S.,SLEDGE,C.,KRUEGER,R.G.,MANN,K.G. & HOOD,L.E. (1975) BIOCHEMISTRY,14,5561-5568.
51) **PAUL:** SMITH,G.P.,HOOD,L. & FITCH,W.M. (1971) ANN.REV.BIOCHEM.,40,969-1012.
52) **MON:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)
53) **HEI:** RIESEN,W.F.,MAJANIEMI,I.,HUSER,H.,BRAUN,D.G. & ROELCKE,D. (1978) SCAND.J.IMMUNOL.,8,145-148. (CHECKED BY AUTHOR 10/10/79)
54) **POT:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR WHO CORRECTED RESIDUE 9 AS GIVEN IN TABLE)
55) **S-GUI:** WANG,A.C.,FUDENBERG,H.H. & CREYSSEL,R. (1982) ACTA HAEMAT.,68,187-195. (CHECKED BY AUTHOR 05/26/83)
56) **AMYLOID BAN:** DWULET,F.E.,O'CONNOR,T.P. & BENSON,M.D. (1986) MOL.IMMUNOL.,23,73-78.
57) **BJ19:** ALESCIO-ZONTA,L. & BAGLIONI,C. (1970) EUR.J.BIOCHEM.,15,450-463. (CHECKED BY AUTHOR)
58) **BEL:** MILSTEIN,C. (1969) PROC. 5TH FEBS SYMP.,15,43-56. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED AND CORRECTED RESIDUES 1,3,6,27,79 AND 82 AS GIVEN IN TABLE)
59) **JBL:** SEON,B.K. (1982) MOL.IMMUNOL.,19,83-86. (CHECKED BY AUTHOR 05/23/83)
60) **PAP:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)
61) **CAR:** MILSTEIN,C.P. & DEVERSON,E.V. (1974) EUR.J.BIOCHEM.,49,377-391. (CHECKED BY AUTHOR)
62) **MEV:** EULITZ,M. & LINKE,R.P. (1982) Z.PHYSIOL.CHEM.,363,1347-1358. (CHECKED BY AUTHOR 10/10/83)

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

63) **BI:** BRAUN,H.,LEIBOLD,W.,BARNIKOL,H.U. & HILSCHMANN,N. (1971) Z.PHYSIOL.CHEM.,352,647-651; (1972) Z.PHYSIOL.CHEM.,353,1284-1306. (CHECKED BY AUTHOR WHO PROVIDED AN ADDITIONAL RESIDUE TO THOSE PUBLISHED AND CORRECTED RESIDUE 72 AS GIVEN IN TABLE)

64) **AMYLOID ES305:** WESTERMARK,P.,SLETTEN,K. & NATVIG,J.B. (1981) ACTA PATH.MICROBIOL.SCAND.,C89,199-203. (CHECKED BY AUTHOR 11/09/81)

65) **CRA:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

66) **DAV:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)

67) **FIN:** CAPRA,J.D. & KUNKEL,H.G. (1970) PROC.NAT.ACAD.SCI.USA,67,87-92. (CHECKED BY AUTHOR)

68) **KA:** SHINODA,T. (1975) J.BIOCHEM.,77,1277-1296. (CHECKED BY AUTHOR)

69) **Vd'CL:** PECH,M.,JAENICHEN,H.-R.,POHLENZ,H.-D.,NEUMAIER,P.S.,KLOBECK,H.-G. & ZACHAU,H.G. (1984) J.MOL.BIOL.,176,189-204. (CHECKED BY AUTHOR 12/14/84)

70) **LUX:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

71) **NE:** MATTHEWS,J.B. & JEFFERIS,R. (1977) IMMUNOCHEM.,14,793-797. (CHECKED BY AUTHOR 06/10/79)

72) **Va''CL:** PECH,M.,JAENICHEN,H.-R.,POHLENZ,H.-D.,NEUMAIER,P.S.,KLOBECK,H.-G. & ZACHAU,H.G. (1984) J.MOL.BIOL.,176,189-204. (CHECKED BY AUTHOR 12/14/84)

73) **NI:** SHINODA,T. (1973) J.BIOCHEM.,73,433-446. (CHECKED BY AUTHOR)

74) **FW:** PICK,A.I.,WANG,A.C.,FROHLICHMAN,R. & FUDENBERG,H.H. (1982) ACTA HAEMAT.,68,207-214. (CHECKED BY AUTHOR 05/26/83)

75) **AMYLOID X:** GLENNER,G.G.,TERRY,W.,HERADA,M.,ISERSKY,C. & PAGE,D. (1971) SCIENCE,172,1150-1151. (CHECKED BY AUTHOR 09/22/78)

76) **ALE:** MILSTEIN,C.,MILSTEIN,C.P.& FEINSTEIN,A. (1969) NATURE,221,151-154. (CHECKED BY AUTHOR)

77) **SHE:** MEINKE,G.C. & SPIEGELBERG,H.L. (1976) IMMUNOCHEM.,13,915-919. (CHECKED BY AUTHOR 10/17/77)

78) **ADA:** MEINKE,G.C. & SPIEGELBERG,H.L. (1976) IMMUNOCHEM.,13,915-919. (CHECKED BY AUTHOR 10/17/77)

79) **KUE:** EULITZ,M.,KLEY,H.P. & ZEITLER,H.J. (1979) Z.PHYSIOL.CHEM.,360,725-734. (CHECKED BY AUTHOR 07/17/79)

80) **GO:** WANG,A.C.,FUDENBERG,H.H. & CREYSSEL,R. (1974) EUR.J.IMMUNOL.,4,446-448. (CHECKED BY AUTHOR)

81) **BOL:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)

82) **RI:** PICK,A.I.,WANG,A.C.,FROHLICHMAN,R. & FUDENBERG,H.H. (1982) ACTA HAEMAT.,68,207-214. (CHECKED BY AUTHOR 05/26/83)

83) **Ve'CL:** PECH,M.,JAENICHEN,H.-R.,POHLENZ,H.-D.,NEUMAIER,P.S.,KLOBECK,H.-G. & ZACHAU,H.G. (1984) J.MOL.BIOL.,176,189-204. (CHECKED BY AUTHOR 12/14/84)

84) **OCO:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)

85) **V13'CL:** JAENICHEN,H.-R.,PECH,M.,LINDENMAIER,W.,WILDGRUBER,N. & ZACHAU,H.G. (1984) NUC.ACIDS RES.,12,5249-5263. (CHECKED BY AUTHOR 12/14/84)

86) **V18A'CL:** HEIDMANN,O. & ROUGEON,F. (1984) NATURE,311,74-76.

87) **V19A'CL:** HEIDMANN,O. & ROUGEON,F. (1984) NATURE,311,74-76.

88) **V19B'CL:** HEIDMANN,O. & ROUGEON,F. (1984) NATURE,311,74-76.

89) **V18B'CL:** HEIDMANN,O. & ROUGEON,F. (1984) NATURE,311,74-76.

90) **HF6-21/28:** ATKINSON,P.M.,LAMPMAN,G.W.,FURIE,B.C.,NAPARSTEK,Y.,SCHWARTZ,R.S.,STOLLAR,B.D. & FURIE,B. (1985) J.CLIN.INVEST.,75,1138-1143. (CHECKED BY AUTHOR 08/21/85)

91) **SAC:** SMITHIES,O.,GIBSON,O.M.,FANNING,E.M.,PERCY,M.E.,PARR,D.M. & CONNELL,G.E. (1971) SCIENCE,172,574-577. (CHECKED BY AUTHOR)

92) **WAG:** KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951. (CHECKED BY AUTHOR)

93) **HBJ1:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

94) **AMYLOID 547:** WESTERMARK,P.,SLETTEN,K. & NATVIG,J.B. (1981) ACTA PATH.MICROBIOL.SCAND.,C89,199-203. (CHECKED BY AUTHOR 11/09/81)

95) **WEB:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

96) **HOE:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

97) **LOD:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

98) **HBJ10:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

99) **BEN:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

100) **GR:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

101) **MAA:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

102) **MUK:** LITMAN,G.W.,GERBER-JENSON,B.,LITMAN,R.,MIDDAUGH,C.R. & SCHEFFEL,C. (1980) MOL.IMMUNOL.,17,337-344.

103) **AMYLOID 594:** WESTERMARK,P.,SLETTEN,K. & NATVIG,J.B. (1981) ACTA PATH.MICROBIOL.SCAND.,C89,199-203. (CHECKED BY AUTHOR 11/09/81)

104) **MAR:** KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951. (CHECKED BY AUTHOR)

105) **AMYLOID:** COHEN,A.S.,SHIRAHAMA,T.,SKINNER,M.,BENSON,M.D. & CATHCART,E.S. (1973) PROTIDES BIOL.FLUIDS,20,73-80.

106) **BJ:** MILSTEIN,C. (1966) BIOCHEM.J.,101,352-368. (CHECKED BY AUTHOR)

107) **HBJ6:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

108) **PEN:** MOULIN,A. & FOUGEREAU,M. (1973) NATURE NEW BIOLOGY,246,176-178.

109) **AMYLOID MS:** PICK,A.I.,SCHREIBMAN,S.,LAVIE,G. & FROHLICHMAN,R. (1973) PROTIDES BIOL.FLUIDS,20,63-72.

110) **CL*:** SOLOMON,A.,MCLAUGHLIN,C.L. & CAPRA,J.D. (1975) J.CLINICAL INVESTIGATION,55,579-586. (CHECKED BY AUTHOR)

111) **GM131'CL:** MORIN,J.W.,BLACK,A.,WU,M. & BEYCHOK,S. (1985) PROC.NAT.ACAD.SCI.USA,82,7025-7029.

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP I

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1:
- SET 1: ROY[1],AU[2],REI[3],HAU[4],HK101'CL[5],SCW[6],AG[7],WEA[8],HK137'CL[9],HK134'CL[10],DAUDI'CL[11],WALKER'CL[12], HF3-16/6[13],HF2-1/13B[14],HF2-18/2[15],HF2-1/17[16],BJ26[17],RFZ[18],PSM[19],HOM[20],ESM IGG[21],ESM IGM[22],WAT[23], AMYLOID VIII-B[24],LOW[25],DIE[26],CAR A[27],TEI[28],BJ48[29],CON[30],TRA[31],F-GUI[33],OU(IOC)[34],DEE[35]. (34 IDENTICAL)
- SET 2: WES[41],Vb'CL[42],Vb''CL[43]. (3 IDENTICAL)
- SET 3: HK102'CL[44],EU[45],DEN[46],PAU[47],HBJ4[48],FRA[49],GR'[50],PAUL[51],MON[52]. (9 IDENTICAL)
- SET 4: AMYLOID BAN[56],BJ19[57],BEL[58]. (3 IDENTICAL)
- SET 5: DAV(66),FIN[67]. (2 IDENTICAL)
- SET 6: Vd'CL[69],LUX[70]. (2 IDENTICAL)

FR2:
- SET 1: ROY[1],AU[2],WALKER'CL[12],Vb'CL[42],Vb''CL[43],HK102'CL[44],KA[68],Vd'CL[69],Va''CL[72],Ve'CL[83]. (10 IDENTICAL)
- SET 2: HK101'CL[5],HK134'CL[10]. (2 IDENTICAL)
- SET 3: HK137'CL[9],AMYLOID BAN[56]. (2 IDENTICAL)
- SET 4: V18A'CL[86]. (IDENTICAL TO 7 MOUSE V-KAPPA-III: PC1229(NZB)[1],PC2880(NZB)[2],PC7132(NZB)[3],MOPC70[5],PC2413(NZB)[11], 50S10.1[27],V-21B18KB'CL[46]; AND 5 RABBIT V-KAPPA: K9-335[1],K9-338[2],K29-213[3],V20'CL[36],K16-167[64].)
- SET 5: V19B'CL[88],V18B'CL[89]. (2 IDENTICAL HUMAN V-KAPPA-I; ALSO 4 HUMAN V-KAPPA-IV: VJI'CL[1],VKAPPA IV GERMLINE'CL[2], PB17IV'CL[3],LEN[4]; 1 MOUSE V-KAPPA-I: MCPC603[47]; 30 MOUSE V-KAPPA-III: MPC11'CL[6],TEPC111[7],PC3741(NZB)[8], TEPC124[9],MOPC321[12],PC7043(NZB)[13],PC7183(NZB)[14],PC6308(NZB)[15],PC6684(NZB)[17],PC7940(NZB)[18],PC7175(NZB)[19], PC2485(NZB)[20],PC4039(NZB)[21],PC7210(NZB)[23],H36-15[26],2242[29],V-21E1.5KB'CL[30],V-21C9.5KB'CL[31], PC7461(NZB)[33],PC2960(NZB)[34],97.C(A.BY)[35],10.A(A.TH)[39],H36-5[48],40.C(A.TH)[52],MOPC63[54],ABPC22[55], PC9245(NZB)[56],PC4050(NZB)[57],V-21B16KB'CL[58],11949[62]; 1 MOUSE V-KAPPA-VI: BFPC61A'CL[64]; AND 15 RABBIT V-KAPPA: K9-335-I[19],3368[20],BS-5[38],BS-1[39],K49-501[45],3547[47],K4820[57],K30-267[61],311[65],4422[66],17D9'CL[68], 4192[71],4363[85],120[103],K-25[112].)

FR3:
- SET 1: HAU[4],HK101'CL[5],HK137'CL[9],HK134'CL[10],Vb'CL[42],Vb''CL[43],Va''CL[72]. (7 IDENTICAL)
- SET 2: Ve'CL[83],V13'CL[85]. (2 IDENTICAL)
- SET 3: V19B'CL[88],V18B'CL[89]. (2 IDENTICAL)

FR4:
- SET 1: AU[2],GAL(I)[36],CL*[110]. (3 IDENTICAL HUMAN V-KAPPA-I; ALSO 2 HUMAN V-KAPPA-II: GM 607 'CL[5],RPM1-6410'CL[16]; 7 HUMAN V-KAPPA-III: WOL[2],PAY[7],PIE[11],GLO[15],CUR[20],REE[57],VKAPPA3'CL[82]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
- SET 2: HAU[4]. (IDENTICAL TO 1 HUMAN V-KAPPA-III: POM[48].)
- SET 3: AG[7],DEN[46],BI[63]. (3 IDENTICAL HUMAN V-KAPPA-I; ALSO 2 HUMAN V-KAPPA-II: NIM[3],FR[14]; 6 HUMAN V-KAPPA-III: NEU[5], GOT[6],GAR'[10],FLO[12],FR4[21],IARC/BL41'CL[28]; AND 1 HUMAN V-KAPPA-IV: LEN[4].)
- SET 4: WEA[8],BJ48[29],LAY[39],EU[45]. (4 IDENTICAL)
- SET 5: WALKER'CL[12],OU(IOC)[34]. (2 IDENTICAL HUMAN V-KAPPA-I; ALSO 1 HUMAN V-KAPPA-II: TEW[1].)
- SET 6: WES[41],MEV[62]. (2 IDENTICAL)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1:
- SET 1: AU[2],NE[71],SHE[77]. (3 IDENTICAL)
- SET 2: WEA[8],GAL(I)[36]. (2 IDENTICAL)
- SET 3: HK134'CL[10],Vb'CL[42],Vb''CL[43]. (3 IDENTICAL)
- SET 4: HF3-16/6[13],HF2-1/13B[14],HF2-18/2[15],HF2-1/17[16]. (4 IDENTICAL)
- SET 5: Vd'CL[69],Ve'CL[83]. (2 IDENTICAL)

CDR2:
- SET 1: HK101'CL[5],HK137'CL[9],HK134'CL[10],WALKER'CL[12],Vb'CL[42],Vb''CL[43]. (6 IDENTICAL)
- SET 2: AG[7],NI[73]. (2 IDENTICAL)
- SET 3: HK102'CL[44],Va''CL[72]. (2 IDENTICAL)
- SET 4: Vd'CL[69],Ve'CL[83],V13'CL[85]. (3 IDENTICAL)
- SET 5: V18A'CL[86]. (IDENTICAL TO 1 RABBIT V-KAPPA: 4153-II[24].)
- SET 6: V19A'CL[87]. (IDENTICAL TO 1 RABBIT V-KAPPA: AH80-5[4].)

CDR3:
- SET 1: HK101'CL[5],HK134'CL[10]. (2 IDENTICAL)
- SET 2: LAY[39]. (IDENTICAL TO 1 HUMAN V-KAPPA-III: POM[48].)
- SET 3: Vb'CL[42],Vb''CL[43]. (2 IDENTICAL)

IDENTICAL SETS OF J-MINIGENES:
- SET 1: AU[2]. (IDENTICAL TO 1 HUMAN V-KAPPA-II: RPM1-6410'CL[16]; 2 HUMAN V-KAPPA-III: PIE[11],VKAPPA3'CL[82]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
- SET 2: AG[7]. (IDENTICAL TO 1 HUMAN V-KAPPA-III: GOT[6].)
- SET 3: WALKER'CL[12]. (IDENTICAL TO 1 HUMAN V-KAPPA-II: TEW[1].)
- SET 4: DEN[46],BI[63]. (2 IDENTICAL HUMAN V-KAPPA-I; ALSO 1 HUMAN V-KAPPA-II: FR[14]; AND 3 HUMAN V-KAPPA-III: GAR'[10],FLO[12], IARC/BL41'CL[28].)

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP I (cont'd)

GENERAL NOTES:

SEE SIGNAL PEPTIDE TABLE IF # OCCURS AT POSITION 0.

SPECIFIC NOTES:

5) **HK101'CL:** THE SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN FOETAL LIVER DNA.

7) **AG:** THE AMINO ACID RESIDUES AT POSITIONS 39 AND 41 WERE REPORTED BY THE AUTHORS AS GLY AND LYS RESPECTIVELY; HOWEVER, THE PROOF WAS NOT ABSOLUTE. THUS, THEY ARE OMITTED.

9) **HK137'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN FETAL DNA.

10) **HK134'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN FETAL DNA.

17) **BJ26:** ACID RESIDUES AT POSITIONS 39 AND 41 OF BJ26 WERE REPORTED BY THE AUTHORS AS GLY AND LYS RESPECTIVELY. SINCE THIS PROTEIN WAS SEQUENCED BEFORE THE SEQUENCES OF MANY OTHER PROTEINS WERE KNOWN AT THESE TWO POSITIONS, WE HAVE OMITTED THEM.

33) **F-GUI:** THE SEQUENCES OF F-GUI AND S-GUI WERE FROM THE SAME PATIENT.

44) **HK102'CL:** THE SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN FOETAL LIVER DNA.

55) **S-GUI:** THE SEQUENCES OF F-GUI AND S-GUI WERE FROM THE SAME PATIENT.

56) **AMYLOID BAN:** AMINO ACID RESIDUES FOUND AT POSITIONS 104 AND 105 ARE VAL,LEU AND GLN,GLU RESPECTIVELY.

57) **BJ19:** THE AMINO ACID RESIDUES AT POSITIONS 39 AND 41 WERE REPORTED BY THE AUTHORS AS GLY AND LYS RESPECTIVELY. SINCE THIS PROTEIN WAS SEQUENCED BEFORE THE SEQUENCES OF MANY OTHER PROTEINS WERE KNOWN AT THESE TWO POSITIONS, WE HAVE OMITTED THEM.

59) **JBL:** THE AMINO ACID RESIDUE FOUND AT POSITION 34 WAS ALA OR SER.

64) **AMYLOID ES305:** THE AMINO ACID RESIDUES AT POSITIONS 21 AND 29 WERE ILE OR LEU.

74) **PW:** THE SEQUENCE WAS FROM A PATIENT WITH TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER.

82) **RI:** THE SEQUENCE WAS FROM A PATIENT WITH TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER.

109) **AMYLOID MS:** THE AMINO ACID RESIDUE AT POSITION 2 MS WAS ILE OR LEU.

111) **GM131'CL:** FROM AN EPSTEIN-BARR VIRUS-TRANSFORMED HUMAN LYMPHOID CELL LINE

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
27C	(LEU,VAL)
27D	(TRP,GLU)
50	(ALA,ASP)
92	(TYR,ASP,ASN)
95A	(SER,GLY)
95B	(TRP,GLY)

HUMAN KAPPA LIGHT CHAINS SUBGROUP II

		INVARIANT RESIDUES	1 TEW	2 MIL	3 NIM	4 CUM	5 GM 607 'CL	6 BAT	7 BATES	8* ROB	9 SLO	10* WILS	11 GLI	12 AMYLOID TEW #	13 RAI	14* FR #	15 YOS	16 RPM1-6410 'CL #	17 MAN	18 KIR	19 HYL	20 MAG	21 TVE	22 EID	23 GAL (II)
	0		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP
	2	ILE(.97)	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3	VAL(.97)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	4		MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET		MET	MET	MET	MET	MET	MET
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR		THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN		GLN	GLN	GLN	GLN	GLN	
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER	SER	SER	
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO	PRO	PRO	PRO	PRO	
	9	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
FR 1	10	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12	PRO(.96)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	13	VAL(.96)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	gly	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	14	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR							
	15		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	leu	PRO						
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLU	GLY	GLY	GLY	GLY						
	17		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	gln	GLU						
	18	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO						
	19	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA						
	20	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER						
	21	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE						
	22		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	gln	SER	SER	SER						
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS						
	24	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG		ARG	ARG		ARG	ARG						ARG
	25		SER	SER	SER	SER	SER	SER	SER	ALA	SER	SER	SER	SER		SER		SER							
	26	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER		SER							
	27		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLX		GLN		GLN							
	27A		SER	ASN	SER	SER	SER	SER		ARG	SER	SER	SER			SER		SER							
	27B	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	---	LEU	LEU	LEU			LEU		LEU							
CDR 1	27C		LEU	LEU	LEU	LEU	LEU	LEU	LEU	---	ARG	LEU	LEU			VAL		VAL							
	27D		HIS	GLX	TRP	ASP	HIS	HIS	HIS	---	HIS					TYR		TYR							
	27E		SER	---	SER	SER	SER	SER		---						ARG		SER							
	27F		---	---	---	GLY	---	---	---	---	ASX					---		---							
	26		ASP	SER	ASP	ASP	ASN	ASX	ASX	VAL						ASX		ASP							
	29		GLY	ASX	GLY	GLY	GLY	GLY	GLY	LEU						GLY		GLY							
	30		PHE	GLY	TYR	ASN	TYR	ASX	ASX							ASX		ASN							
	31		ASP	ASX	LYS	THR	ASN	ASX	ASX							THR		THR							
	32	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR							TYR		TYR							
	33	LEU	LEU	LEU	LEU	LEU	LEU	LEU								LEU		LEU							
	34		ASN	ASP	ASN	ASN	ASP	ASX								ASX		ASN							
	35	TRP	TRP	TRP	TRP	TRP	TRP	TRP								TRP		TRP							
	36		TYR	TYR	TYR	TYR	TYR	TYR								TYR		PHE							
	37		LEU	LEU	LEU	LEU	LEU	LEU								LEU		GLN							
	38		GLN	GLX	GLN	GLN	GLN	GLX								GLN		GLN							
	39		LYS	LYS	LYS	LYS	LYS	LYS								LYS		ARG							
	40		PRO	PRO	PRO	ALA	PRO	PRO								PRO		PRO							
FR 2	41	GLY	GLY	GLY	GLY	GLY	GLY	GLY								GLY		GLY							
	42		GLN	GLX	GLN	GLN	GLN	GLX								GLN		GLN							
	43	SER		SER	SER	SER	SER									SER		SER							
	44	PRO		PRO	PRO	PRO	PRO	PRO								PRO		PRO							
	45			GLX	GLN	GLN	GLN	GLX								GLU		ARG							
	46		LEU	LEU	LEU	LEU	LEU									LEU		ARG							
	47	LEU	LEU	LEU	LEU	LEU	LEU									LEU		LEU							
	48	ILE	ILE	ILE	ILE	ILE	ILE									ILE		ILE							
	49	TYR		TYR	TYR	TYR	TYR									TYR		TYR							
	50			LEU	LEU	THR	LEU									LEU		LYS							
	51			GLY	GLY	LEU	GLY									SER		VAL							
CDR 2	52	SER	SER	SER	SER	SER	SER									SER		SER							
	53		ASN	ASN	ASN	TYR	ASN									TYR		ASN							
	54	ARG	ARG	ARG	ARG	ARG	ARG									ARG		ARG							
	55		ALA	ALA	ALA	ALA	ALA									ASP		ASP							
	56	SER	SER	SER	SER	SER	SER									SER		SER							
	57	GLY	GLY	GLY	GLY	GLY	GLY									GLY		GLY							
	58	VAL	VAL	VAL	VAL	VAL	VAL									VAL		VAL							
	59	PRO	PRO	PRO	PRO	PRO	PRO									PRO		PRO							
	60		ASP	ASN	ASP	ASP	ASP									ASP		ASP							
	61	ARG	ARG	ARG	ARG	ARG	ARG									ARG		ARG							
	62	PHE	PHE	PHE	PHE	PHE	PHE								PHE	PHE		PHE							
	63	SER	SER	SER	SER	SER	SER								SER	SER		SER							
	64		GLY	GLY	GLY	GLY	GLY								GLY	ASP		GLY							
	65	SER	SER	SER	SER	SER	SER								SER	SER		SER							
	66	GLY	GLY	GLY	GLY	GLY	GLY								GLY	GLY		GLY							
	67	SER	SER	SER	SER	SER	SER								SER	SER		SER							
	68		GLY	GLY	ASP	GLY	GLY								GLY	GLY		GLY							
	69	THR	THR	THR	THR	THR	THR									THR		THR							
	70		ASP	ASX	ASP	ASP	ASP									ASP		ASP							
FR 3	71	PHE	PHE	PHE	PHE	PHE	PHE								PHE	PHE		PHE							
	72	THR	THR	THR	THR	THR	THR								THR	THR		THR							
	73	LEU	LEU	LEU	LEU	LEU	LEU								LEU	LEU		LEU							
	74		LYS	LYS	ILE	LYS	LYS								ASX	LYS		LYS							
	75	ILE	ILE	ILE	ILE	ILE	ILE								ILE	ILE		ILE							
	76		SER	SER	SER	SER	SER								SER	THR		SER							
	77	ARG	ARG	ARG	ARG	ARG	ARG								ARG	ARG		ARG							
	78	VAL	VAL	VAL	VAL	VAL	VAL									VAL		VAL	VAL						
	79		GLU	GLX	GLU	GLN	GLU									GLN		GLU	GLX						
	60		ALA	ALA	PRO	ALA	ALA									ALA		ALA	ALA						
	81		GLU	GLX	GLU	GLU	GLU									GLU		GLU	GLX						
	82		ASP	ASX	ASP	ASP	ASP									ASP		ASP	ASX						
	83	VAL	VAL	VAL	VAL	VAL	VAL									VAL		VAL	VAL						
	84	GLY	GLY	GLY	GLY	GLY	GLY									GLY		GLY	GLY						
	85	VAL	VAL	VAL	VAL	VAL	VAL									VAL		VAL	VAL						
	86	TYR	TYR	TYR	TYR	TYR	TYR									TYR		TYR	TYR						
	87	TYR	TYR	TYR	TYR	TYR	TYR									TYR		TYR	TYR						
	88	CYS	CYS	CYS	CYS	CYS	CYS									CYS		CYS	CYS						
	89	MET	MET	MET	MET	MET	MET									MET		MET							
	90		GLX	GLN	GLN	GLN	GLN									GLN		GLN							
	91		ALA	ALA	ALA	ARG	ALA									ALA		GLY							
	92		LEU	LEU	LEU	LEU	LEU									THR		THR							
	93		GLN	GLN	GLN	GLU	GLN									GLX		HIS							
	94		ALA	THR	SER	ILE	THR									SER		TRP							
	95		PRO	PRO	PRO	PRO	PRO									PRO		SER							
CDR 3	95A		---	---	---	---	---									---		---							
	95B		---	---	---	---	---									---		---							
	95C		---	---	---	---	---									---		---							
	95D		---	---	---	---	---									---		---							
	95E		---	---	---	---	---									---		---							
	95F		---	---	---	---	---									---		---							
	96		ILE	LEU	PRO	TYR	GLN									TYR		TRP							
	97	THR	THR	THR	THR	THR	THR									THR		THR							
	98	PHE	PHE	PHE	PHE	PHE	PHE									PHE		PHE							
	99	GLY	GLY	GLY	GLY	GLY	GLY									GLY		GLY							
	100		GLN	GLY	GLN	GLN	GLN									GLN		GLN							
	101	GLY	GLY	GLY	GLY	GLY	GLY									GLY		GLY							
FR 4	102	THR	THR	THR	THR	THR	THR									THR		THR							
	103		ARG	ASN	LYS	LYS	LYS									LYS		LYS							
	104		LEU	VAL	LEU	LEU	VAL									LEU		VAL	VAL						
	105		GLU	GLU	GLU	GLU	GLU									GLX		GLU	GLU						
	106	ILE	ILE	ILE	ILE	ILE	ILE									ILE		ILE	ILE						
	106A		---	---	---	---	---									---		---	---						
	107		LYS	LYS	LYS	ARG	LYS									LYS		LYS	LYS						
	108	ARG	ARG	ARG	ARG	ARG	ARG									ARG		ARG							
	109	THR		THR	THR	THR										THR									

HUMAN KAPPA LIGHT CHAINS SUBGROUP II (cont'd)

		24* GIL	25 MEH	26 SC	27* TH	28 SYV	29 LUT	30 ROB 2	31 RAI 2	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0	---	---	---	---	---	---	---	---	31	1	31(ASP)	1.
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	30	2	29(ILE)	2.1
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	30	2	29(VAL)	2.1
	3	VAL	VAL	VAL	VAL	VAL	VAL	VAL	met	30	3	28(MET)	3.2
	4	MET	MET	MET	MET	MET	MET	leu	thr				
	5	THR	THR	THR	THR	THR	THR			28	1	28(THR)	1.
	6	GLN	GLN	GLN	GLN	GLN	GLN			27	1	27(GLN)	1.
	7	SER	SER	SER	SER					25	1	25(SER)	1.
	8	PRO	PRO		PRO					24	1	24(PRO)	1.
	9	LEU	LEU							25	1	25(LEU)	1.
	10	SER								24	1	24(SER)	1.
FR1	11	LEU								24	1	24(LEU)	1.
	12	ser								24	2	23(PRO)	2.1
	13									23	2	22(VAL)	2.1
	14									17	1	17(THR)	1.
	15									17	2	16(PRO)	2.1
	16									17	1	17(GLY)	1.
	17									17	2	16(GLU)	2.1
	18									17	1	17(PRO)	1.
	19									17	1	17(ALA)	1.
	20									17	1	17(SER)	1.
	21									17	1	17(ILE)	1.
	22									17	2	16(SER)	2.1
	23									17	1	17(CYS)	1.
	24									16	1	16(ARG)	1.
	25									14	2	13(SER)	2.2
	26									14	1	14(SER)	1.
	27									14	1 : 2	14(GLN) : 12(GLN)	1. : 2.3
	27A									12	3	10(SER)	
	27B									12	1	12(LEU)	
CDR1	27C									12	3	9(LEU)	
	27D									10	5	5(HIS)	
	27E									7	2	6(SER)	
	27F									2	2	1(+)	
	28									10	4	7(ASP) : 4(+)	5.7 : 10.
	29									10	3	8(GLY)	3.8
	30									9	4 : 5	5(ASN) : 3(ASP)	7.2 : 15.
	31									9	4	4(ASN) : 3(+)	9. : 12.
	32									9	1	9(TYR)	1.
	33									8	1	8(LEU)	1.
	34									8	2	6(ASN) : 4(+)	2.7 : 4.
	35									8	1	8(TRP)	1.
	36									8	2	7(TYR)	2.3
	37									8	2	7(LEU)	2.3
	38									8	1 : 2	8(GLN) : 6(GLN)	1. : 2.7
	39									8	2	7(LYS)	2.3
	40									8	2	7(PRO)	2.3
FR2	41									8	1	8(GLY)	1.
	42									8	1 : 2	8(GLN) : 6(GLN)	1. : 2.7
	43									6	1	6(SER)	1.
	44									7	1	7(PRO)	1.
	45									7	3	5(GLN) : 3(+)	4.2 : 7.
	46									7	2	6(LEU)	2.3
	47									7	1	7(LEU)	1.
	48									7	1	7(ILE)	1.
	49									6	1	6(TYR)	1.
	50									6	3	4(LEU)	4.5
	51									6	4	3(GLY)	8.
CDR2	52									7	1	7(SER)	1.
	53									7	2	5(ASN)	2.8
	54									7	1	7(ARG)	1.
	55									7	2	5(ALA)	2.8
	56									7	1	7(SER)	1.
	57									7	1	7(GLY)	1.
	58									7	1	7(VAL)	1.
	59									7	1	7(PRO)	1.
	60									7	2	6(ASP)	2.3
	61									7	1	7(ARG)	1.
	62									8	1	8(PHE)	1.
	63									8	1	8(SER)	1.
	64									8	2	7(GLY)	2.3
	65									8	1	8(SER)	1.
	66									8	1	8(GLY)	1.
	67									8	1	8(SER)	1.
	68									8	2	7(GLY)	2.3
	69									7	1	7(THR)	1.
	70									7	1 : 2	7(ASP) : 6(ASP)	1. : 2.3
FR3	71									8	1	8(PHE)	1.
	72									8	1	8(THR)	1.
	73									8	1	8(LEU)	1.
	74									8	3	6(LYS)	4.
	75									8	1	8(ILE)	1.
	76									8	2	7(SER)	2.3
	77									8	1	8(ARG)	1.
	78									8	1	8(VAL)	1.
	79									8	2	6(GLU) : 4(+)	2.7 : 4.
	80									8	2	7(ALA)	2.3
	81									8	1 : 2	8(GLU) : 6(GLU)	1. : 2.7
	82									8	1 : 2	8(ASP) : 6(ASP)	1. : 2.7
	83									8	1	8(VAL)	1.
	84									8	1	8(GLY)	1.
	85									8	1	8(VAL)	1.
	86									8	1	8(TYR)	1.
	87									8	1	8(TYR)	1.
	88									8	1	8(CYS)	1.
	89									7	1	7(MET)	1.
	90									7	1 : 2	7(GLN) : 6(GLN)	1. : 2.3
	91									7	3	5(ALA)	4.2
	92									7	2	5(LEU)	2.8
	93									7	3	5(GLN) : 4(GLN)	4.2 : 5.3
	94									7	5	2(+)	18.
	95									7	2	6(PRO)	2.3
CDR3	95A												
	95B												
	95C												
	95D												
	95E												
	95F												
	96									7	6	2(TYR)	21.
	97									7	1	7(THR)	1.
	98									7	1	7(PHE)	1.
	99									7	1	7(GLY)	1.
	100									7	2	6(GLN)	2.3
	101									7	1	7(GLY)	1.
FR4	102									7	1	7(THR)	1.
	103									7	3	5(LYS)	4.2
	104									8	2	4(+)	4.
	105									8	1 : 2	8(GLU) : 7(GLU)	1. : 2.3
	106									8	1	8(ILE)	1.
	106A												
	107									8	2	7(LYS)	2.3
	108									7	1	7(ARG)	1.
	109									4	1	4(THR)	1.

ANTIBODY SPECIFICITIES: HUMAN KAPPA LIGHT CHAINS SUBGROUP II

8) **ROB:** COLD AGGLUTININ WITH ANTI-PR1D ACTIVITY
10) **WILS:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
14) **FR:** ANTI-PHOSPHOCHOLINE(BINDING CONSTANT=6.4X10EXP4)
24) **GIL:** ANTI-IGG
27) **TH:** COLD AGGLUTININ WITH ANTI-PR2 ACTIVITY (RBC MEMBRANE ANTIGEN ON HUMAN, RAT AND GUINEA PIG ERYTHROCYTES INACTIVATED BY PROTEOLYTIC ENZYMES AND NEURAMINIDASE)

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP II

1) **TEW:** PUTNAM,F.W.,WHITLEY,E.J.,JR., PAUL,C.& DAVIDSON,J.N. (1973) BIOCHEMISTRY,12,3763-3780. (CHECKED BY AUTHOR 06/15/83)
2) **MIL:** DREYER,W.J.,GRAY,W.R. & HOOD,L. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,353-367.
3) **NIM:** EULITZ,M. & KLEY,H.-P. (1977) IMMUNOCHEM.,14,289-297. (CHECKED BY AUTHOR 10/18/77)
4) **CUM:** HILSCHMANN,N. & CRAIG,L.C. (1965) PROC.NAT.ACAD.SCI.USA,53,1403-1409; HILSCHMANN,N. (1967) Z.PHYSIOL.CHEM.,348,1718-1722; HILSCHMANN,N. (1969) NATURE.,56,195-205. (CHECKED BY AUTHOR)
5) **GM 607'CL:** KLOBECK,H.G.,SOLOMON,A. & ZACHAU,H.G. (1984) NATURE,309,73-76.
6) **BAT:** DAYHOFF,M.O. (1972) ATLAS OF PROTEIN SEQUENCE & STRUCTURE,5,D-246. SUBMITTED BY SMITHIES,O.,GIBSON,D.M. AND FANNING,E.M. (CHECKED BY AUTHOR)
7) **BATES:** SMITH,G.P.,HOOD,L. & FITCH,W.M. (1971) ANN.REV.BIOCHEM.,40,969-1012.
8) **ROB:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)
9) **SLO:** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-66. (CHECKED BY AUTHOR 03/18/81)
10) **WILS:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)
11) **GLI:** FRANGIONE,B.,FRANKLIN,E.C. & PRELLI,F. (1976) SCAND.J.IMMUNOL.,5,623-627. (CHECKED BY AUTHOR 10/17/77)
12) **AMYLOID TEW:** TERRY,W.D.,PAGE,D.L.,KIMURA,S.,ISOBE,T.,OSSERMAN,E.F. & GLENNER,G.G. (1973) J.CLIN.INVEST.,52,1276-1281. (CHECKED BY AUTHOR 03/02/84)
13) **RAI:** MILSTEIN,C.P. & MILSTEIN,C. (1971) BIOCHEM.J.,121,211-215. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED)
14) **FR:** RIESEN,W.,RUDIKOFF,S.,ORIOL,R. & POTTER,M. (1975) BIOCHEMISTRY,14,1052-1057; RIESEN,W.F.,BRAUN,D.G. & JATON,J.C. (1976) PROC.NAT.ACAD.SCI USA,73,2096-2100; RIESEN,W.F. & JATON,J.C. (1976) BIOCHEMISTRY,15,3829-3833 (CHECKED BY AUTHOR 12/05/77)
15) **YOS:** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)
16) **RPM1-6410'CL:** HIETER,P.A.,MAX,E.E.,SEIDMAN,J.G.,MAIZEL,J.V.,JR. & LEDER,P. (1980) CELL,22,197-207; KLOBECK,H.G.,MEINDL,A.,COMBRIATO,G., SOLOMON,A. & ZACHAU,H.G. (1985) NUC.ACIDS RES.,13,6499-6513.
17) **MAN:** MILSTEIN,C. (1969) PROC. 5TH FEBS SYMP.,15,43-56. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED)
18) **KIR:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
19) **HYL:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
20) **MAG:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
21) **TVE:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
22) **EID:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
23) **GAL(II):** MILSTEIN,C.,JARVIS,J.M. & MILSTEIN,C.P. (1969) J.MOL.BIOL.,46,599-602. (CHECKED BY AUTHOR)
24) **GIL:** ABRAHAM,G.N.,BROWN,P.,JOHNSTON,S.L.,NELLIS,L.,MARKS,S. & WELCH,E.H. (1978) IMMUNOLOGY,35,447-453. (CHECKED BY AUTHOR 07/23/79)
25) **MEH:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
26) **SC:** SEON,B.K.,YAGI,Y. & PRESSMAN,D. (1973) J.IMMUNOL.,110,345-349. (CHECKED BY AUTHOR)
27) **TH:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)
28) **SYV:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
29) **LUT:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,215-218. (CHECKED BY AUTHOR 12/05/77)
30) **ROB2:** MOULIN,A. & FOUGEREAU,M. (1973) NATURE NEW BIOLOGY,246,176-178.
31) **RAI2:** MOULIN,A. & FOUGEREAU,M. (1973) NATURE NEW BIOLOGY,246,176-178.

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP II

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: TEW[1],MIL[2],NIM[3],CUM[4],GM 607 'CL[5],BAT[6],BATES[7],ROB[8],SLO[9],WILS[10],GLI[11],AMYLOID TEW[12],RAI[13]. (13 IDENTICAL)

FR2: SET 1: MIL[2],NIM[3],GM 607 'CL[5]. (3 IDENTICAL HUMAN V-KAPPA-II; ALSO 2 MOUSE V-KAPPA-II: VKAPPA 24B'CL[63],2S1.3[67].)
SET 2: MIL[2],FR[14]. (2 IDENTICAL)

FR3: SET 1: TEW[1],GM 607 'CL[5],RPM1-6410'CL[16]. (3 IDENTICAL)

FR4: SET 1: GM 607 'CL[5],RPM1-6410'CL[16]. (2 IDENTICAL HUMAN V-KAPPA-II; ALSO 3 HUMAN V-KAPPA-I: AU[2],GAL(I)[36],CL'[110]; 7 HUMAN V-KAPPA-III: WOL[2],PAY[7],PIE[11],GLO[15],CUR[20],REE[57],VKAPPA3'CL[82]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
SET 2: NIM[3],FR[14]. (2 IDENTICAL HUMAN V-KAPPA-II; ALSO 3 HUMAN V-KAPPA-I: AG[7],DEN[46],BI[63]; 6 HUMAN V-KAPPA-III: NEU[5], GOT[6],GAR'[10],FLO[12],FR4[21],IARC/BL41'CL[28]; AND 1 HUMAN V-KAPPA-IV: LEN[4].)
SET 3: TEW[1]. (IDENTICAL TO 2 HUMAN V-KAPPA-I: WALKER'CL[12],OU(IOC)[34].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1:

CDR2: SET 1: MIL[2],NIM[3],GM 607 'CL[5]. (3 IDENTICAL)

CDR3:

IDENTICAL SETS OF J-MINIGENES:

SET 1: RPM1-6410'CL[16]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: AU[2]; 2 HUMAN V-KAPPA-III: PIE[11],VKAPPA3'CL[82]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
SET 2: TEW[1]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: WALKER'CL[12].)
SET 3: FR[14]. (IDENTICAL TO 2 HUMAN V-KAPPA-I: DEN[46],BI[63]; AND 3 HUMAN V-KAPPA-III: GAR'[10],FLO[12],IARC/BL41'CL[28].)

SPECIFIC NOTES:

12) **AMYLOID TEW:** IT HAS THE SAME SEQUENCE AS THAT OF TEW SO FAR AS THE SEQUENCED POSITIONS ARE CONCERNED.
14) **FR:** AN IDIOTYPIC ANTIBODY TO FR NOT INHIBITABLE BY PHOSPHORYLCHOLINE REACTED BETTER WITH THE FR HEAVY CHAIN THAN WITH THE LIGHT CHAIN. THE CROSS-REACTION WITH MOPC167 WAS 10,000 TIMES WEAKER. (RIESEN,W.F. (1979) EUR.J.IMMUNOL.,9,421-425.)
16) **RPM1-6410'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN ADULT DNA.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
27F	(GLY,ASN) : (GLY,ASP)
28	(ASP,ASN)
31	(THR,ASP)
34	(ASP,ASN)
45	(GLU,GLN)
79	(GLU,GLN)
94	(THR,SER)
104	(LEU,VAL)

HUMAN KAPPA LIGHT CHAINS SUBGROUP III

		INVARIANT RESIDUES	1 TI	2 WOL	3 SIE	4 NG9 CL #	5 NEU	6 GOT	7 PAY	8 SON	9 WEI	10 GAR	11 PIE	12 FLO	13 LOP	14 SCA	15 GLO	16 SAL	17 WIL	18 MA	19 NIC	20 CUR	21 FR4	22 DRE	23 PER	24 CAM
	0		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLX	GLU	GLU	GLU	GLU
	2		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3	VAL(.96)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	4		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLX	GLX	GLN
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
FR1	10		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	11	LEU(.99)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	14	SER(.97)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	15	PRO(.98)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLX	GLX	GLX	GLU
	18		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	19		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	20		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	21	LEU(.95)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	22	SER(.97)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS
	24		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	25	ALA(.98)	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	26		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	GLY	SER	SER	SER	SER	SER	SER	SER	SER
	27		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLX	GLN
	27A		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	GLY	SER	SER	SER	SER	SER	SER	SER	SER		SER
	27B		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---
CDR1	27C		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---
	27D		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---
	27E		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---
	27F		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---
	28		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ILE	VAL	SER	VAL	VAL	VAL	VAL	VAL	VAL		VAL
	29		SER	SER	SER	SER	SER	ARG	SER	SER	SER	SER	SER	SER	SER	SER	SER	VAL	SER	SER	SER	SER	ARG	SER		SER
	30		ASN	SER	ASN	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	ASN			SER	ASN	SER		SER
	31		SER	GLY	SER	SER	ARG	SER	SER	SER	SER	SER	SER	SER	ASN	ASN	SER	SER	SER			SER	ASN	SER		SER
	32		PHE	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	MET			TYR	TYR	TYR		TYR
	33		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	VAL	LEU			LEU	LEU	LEU		LEU
	34		ALA	GLY	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA			ALA	ALA	ALA		ALA
	35	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP		TRP	TRP	TRP			TRP	TRP	TRP		TRP
	36	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR			TYR	TYR			TYR
	37		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN			GLN	GLN			GLN
	38		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN				GLN	GLN			GLN
	39		LYS	LYS	LYS	LYS	LYS	LYS	ARG	LYS	LYS	LYS	LYS	LYS	LYS		LYS	LYS				LYS	ARG			
	40		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO				PRO	PRO			
FR2	41	GLY(.96)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY					GLY	GLY			
	42		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN					GLN	GLN			
	43		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA		ALA					ALA	ALA			
	44		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO					PRO	PRO			
	45		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG		ARG					ARG	LYS			
	46	LEU(.96)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU					LEU				
	47	LEU(.96)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU					LEU				
	48		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE	ILE	ILE			ILE					ILE				
	49		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR	TYR	TYR			TYR					TYR				
	50		VAL	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY				
	51		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA		ALA	ALA	ALA			ALA					ALA				
CDR2	52		SER	SER	SER	THR	SER	SER	SER	SER		SER	SER	SER			SER					SER				
	53		SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER					SER				
	54	ARG(.95)	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG		ARG	ARG	ARG			ARG					ARG				
	55		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA		ALA	ALA	ALA			ALA					ALA	ALA			
	56		THR	THR	THR	THR	THR	THR	THR	THR		THR	THR	THR			THR					THR	THR			
	57	GLY(.96)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	58		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE	ILE	ILE			ILE					ILE	ILE			
	59	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO	PRO	PRO			PRO					PRO	PRO			
	60		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASN		ASP	ASP	ASP			ASP					ASP	ASP			
	61	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG		ARG	ARG	ARG			ARG					ARG	ARG			
	62	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE			PHE	PHE	PHE			PHE					PHE	PHE			
	63		SER	SER	SER	SER	THR	SER	SER	SER		SER	SER	SER			SER					SER	SER			
	64	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	65	SER(.95)	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER					SER	SER			
	66		GLY	GLY	GLY	ALA	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	67	SER(.95)	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER					SER	SER			
	68	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	69	THR(.95)	THR	THR	THR	THR	THR	THR	THR	THR		THR	THR	THR			THR					THR	THR			
	70		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP		ASP	ASP	ASP			ASP					ASP	ASP			
FR3	71	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE		PHE	PHE	PHE			PHE					PHE	PHE			
	72	THR	THR	THR	THR	THR	THR	THR	THR			THR	THR	THR			THR					THR	THR			
	73	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU			LEU	LEU	LEU			LEU					LEU	LEU			
	74	THR(.95)	THR	THR	THR	THR	THR	THR	THR	THR		THR	THR	THR			THR					THR	THR			
	75	ILE(.95)	ILE	ILE	ILE	ILE	VAL	ILE	ILE	ILE		ILE	ILE	ILE			ILE					ILE	ILE			
	76		SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER					SER	SER			
	77		GLY	GLY	GLY	ARG	ARG	ARG	ARG	ARG		ARG	ARG	ARG			ARG					ARG	ARG			
	78		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU	LEU	LEU			LEU					LEU	LEU			
	79		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU		GLU	GLU	GLU			GLU					GLU	GLU			
	80		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO	PRO	PRO			PRO					PRO	PRO			
	81	GLU(.95)	GLU	GLU	ASP	GLU	GLU	GLU	GLU	GLU		GLU	GLU	GLU			GLU					GLU	GLU			
	82	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP		ASP	ASP	ASP			ASP					ASP	ASP			
	83		PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE		PHE	PHE	PHE			PHE					PHE	PHE			
	84	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA		ALA	ALA	ALA			ALA					ALA	ALA			
	85	VAL(.95)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		VAL	VAL	VAL			VAL					VAL	VAL			
	86	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR	TYR	TYR			TYR					TYR	TYR			
	87		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR	TYR	TYR			TYR					TYR	PHE			
	88	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		CYS	CYS	CYS			CYS					CYS	CYS			
	89	GLN(.95)	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN		GLN	GLN	GLN			GLN					GLN	GLN			
	90	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN		GLN	GLN	GLN			GLN					GLN	GLN			
	91		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR	TYR	TYR			TYR					TYR	TYR			
	92		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	93		SER	SER	SER	ASN	ALA	SER	SER	SER		SER	SER	SER			SER					SER	GLY			
	94		SER	LEU	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER					SER	SER			
	95		PRO	GLY	PRO	GLN	PRO	PRO	PRO	PRO		PRO	PRO	PRO			PRO					PRO	PRO			
	95A		---	---	---	---	---	---	---	PRO		---	---	---			---					---	---			
CDR3	95B		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	95C		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	95D		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	95E		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	95F		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	96		SER	ARG	GLN	---	CYS	ARG	LEU	TYR		TYR	TRP	TYR			LEU					ARG	GLN			
	97	THR(.95)	THR	THR	THR	---	THR	THR	THR	THR		THR	THR	THR			THR					THR	PRO			
	98	PHE	PHE	PHE	PHE	---	PHE	PHE	PHE	PHE		PHE	PHE	PHE			PHE					PHE	PHE			
	99	GLY	GLY	GLY	GLY	---	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
	100		GLN	GLN	GLN	---	GLN	GLN	GLN	GLY		GLN	GLN	GLN			GLN					GLN	GLN			
	101	GLY	GLY	GLY	GLY	---	GLY	GLY	GLY	GLY		GLY	GLY	GLY			GLY					GLY	GLY			
FR4	102		THR	THR	SER	---	THR	THR	THR	THR		THR	THR	THR			THR					THR	THR			
	103		LYS	LYS	LYS	---	LYS	LYS	LYS	LYS		LYS	LYS	LYS			LYS					LYS	LYS			
	104		VAL	VAL	VAL	---	LEU	LEU	VAL	VAL		LEU	VAL	LEU			VAL					VAL	LEU			
	105		GLU	GLU	GLU	---	GLU	GLU	GLU	GLU		GLU	GLU	GLU			GLU					GLU	GLU			
	106		LEU	ILE	ILE	---	ILE	ILE	ILE	ILE		ILE	ILE	ILE			ILE					ILE	ILE			
	106A		---	---	---	---	---	---	---	---		---	---	---			---					---	---			
	107	LYS(.95)	LYS	LYS	LYS	---	LYS	LYS	LYS	LYS		LYS	LYS	LYS			LYS					LYS	LYS			
	108	ARG	ARG	ARG	ARG	---	ARG	ARG	ARG	ARG		ARG	ARG	ARG			ARG					ARG				
	109	THR	THR				THR	THR	THR	THR		THR	THR	THR			THR					THR				

HUMAN KAPPA LIGHT CHAINS SUBGROUP III (cont'd)

		25* STE	26* GJ	27* TAK	28 IARC/ BL41 CL	29 RAD	30 DIL	31 CAS	32 MCE' #	33 KEA	34 SMI	35* AJ	36 BRO IGG	37 NIG	38 IKE	39 TIL	40 AMYLOID KSA	41 POL	42* CLA #	43* SHE' #	44 JH #	45 WIN	46 LEA	47 ARP	48* POM	49 VAND
	0	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	lys	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp	lys	GLU	GLU	GLU
	2	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE
	3	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ILE	VAL	VAL	VAL	VAL
	4	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	met	LEU	met	met	met	LEU	LEU	LEU	met	met
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	glu	GLN	GLN	GLN	GLN	glu	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	ala	ala	asp	GLY	GLY	pro	ala	GLY	ala	#	#	ala	ala	GLY	val	VAL	ala
FR1	10	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13	LEU	LEU	LEU	LEU	LEU	LEU	LEU	phe	LEU	LEU	LEU	LEU	LEU	LEU	LEU	val	LEU	val	val	LEU	LEU	LEU	val	val	val
	14	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	15	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLX	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17	GLU	GLU	GLX	GLU	asp	asp	asp	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLX	GLU	GLU	GLU
	18	ARG	ARG	ARG	ser	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	19	ALA	val	val	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	val	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	20	ala	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	ala	THR	THR	THR	THR	THR	THR	THR	THR	ile	THR	THR
	21	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	22	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	23		CYS	CYS	CYS	CYS	CYS		CYS	CYS		CYS			CYS	CYS	CYS	CYS	CYS	CYS			CYS	CYS	CYS	CYS
	24		ARG	ARG	ARG	ARG	ARG		ARG	ARG		ARG	ARG		ARG	ARG	ARG	ARG	ARG		THR		ARG	ARG	ARG	ARG
	25		ALA	ALA	ALA	ALA	ALA		ALA	ALA		ALA	ALA		ALA	ALA	ALA	ALA	ALA		ALA		ALA	ALA	ALA	ALA
	26		SER	SER	SER	SER	SER		SER	GLY		SER	SER		SER	SER	SER	SER					SER	GLN	GLN	SER
	27			GLX	GLN	GLN	GLN		GLN	SER		GLN	GLN		GLN	GLN	GLX	GLX					GLX	GLN	GLN	GLN
	27A			SER	---	VAL	SER		---	---		SER	SER		SER	---	THR	---					---	---	SER	---
	27B			---	---	---	---		---	---		---	---		---	---	---	---					---	---	---	---
CDR1	27C			---	---	---	---		---	---		---	---		---	---	---	---					---	---	---	---
	27D			---	---	---	---		---	---		---	---		---	---	---	---					---	---	---	---
	27E			---	---	---	---		---	---		---	---		---	---	---	---					---	---	---	---
	27F			---	---	---	---		---	---		---	---		---	---	---	---					---	---	---	---
	28			VAL	SER	SER	LEU		SER	ASX		VAL	VAL		VAL	SER	LEU	SER					SER	HIS	ILE	ASX
	29			SER	VAL	SER	ASX			VAL		SER	ARG		SER	VAL		VAL					VAL	VAL	SER	ILE
	30				SER	ASN	SER			ALA			SER		ASN	SER		ARG					SER	ILE	ASN	GLY
	31			SER	SER	SER	LYS			LYS			SER		SER	SER							LEU	ALA	SER	SER
	32			TYR	ASN	TYR	SER			SER			TYR		TYR	TYR		TYR					TYR	GLY	TYR	ASN
	33			LEU	LEU	LEU	LEU			LEU			LEU		LEU	LEU		LEU					LEU	TYR	LEU	LEU
	34			ALA	ALA	ALA	SER			ALA			ASP		ALA	ALA		ALA					ALA	ALA	ALA	ALA
	35				TRP	TRP	TRP			TRP			TRP		TRP	TRP								TRP	TRP	TRP
	36				TYR	TYR	TYR			TYR			TYR		TYR	TYR	TYR							TYR	TYR	TYR
	37				GLN	GLN	GLX			GLX			GLN		GLN	GLN	GLN							GLN	GLN	GLX
	38				GLN	GLN	GLX			GLX			GLN		GLN		GLN							GLN	GLN	GLX
	39				LYS	LYS	LYS			LYS			LYS		ARG		SER							LYS	LYS	LYS
	40				ARG	PRO	PRO			PRO			PRO		PRO		PRO							PRO	PRO	PRO
FR2	41				GLY	GLY	GLY										GLY								SER	GLY
	42				GLN	GLN	GLX										GLN								GLY	ARG
	43				SER	ALA	THR										ALA								SER	ALA
	44				PRO	PRO	PRO										PRO								PRO	PRO
	45				ARG	ARG	ARG										ARG								ARG	ARG
	46				LEU		LEU										LEU								LEU	LEU
	47				LEU		LEU										LEU								LEU	
	48				ILE		ILE										ILE								ILE	
	49				ARG		TYR										TYR								TYR	
	50				ASP												GLY								GLY	
	51				ALA												THR								ALA	
	52				SER												SER								SER	
CDR2	53				SER												THR								THR	
	54				ARG												ARG								ARG	
	55				ALA	ALA											ALA								ALA	
	56				ASN	THR											THR								THR	
	57				GLY	GLY											GLY								GLY	
	58				ILE	THR											ILE								ILE	
	59				PRO	PRO											PRO								PRO	
	60				ASP	VAL											ALA								ALA	
	61				ARG	ARG											ARG								ARG	
	62				PHE	PHE											PHE								PHE	
	63				SER	SER											SER								SER	
	64				GLY	GLY											GLY								GLY	
	65				SER	SER																			SER	
	66				GLY	GLU																			GLY	
	67				SER	SER																			SER	
	68				GLY	GLY																			GLY	
	69				THR	THR																			THR	
	70				ASP	ASP																			GLU	
	71				PHE	PHE																			PHE	
FR3	72				THR	THR																			THR	
	73				LEU	LEU																			LEU	
	74				ILE	THR																			THR	
	75				ILE	ILE																			ILE	
	76				SER	SER																			SER	
	77				ARG	ARG																			SER	
	78				LEU	LEU																			LEU	
	79				GLU	GLU																			GLN	
	80				PRO	PRO																			SER	
	81				GLU	GLU																			GLU	
	82				ASP	ASP																			ASP	
	83				PHE	PHE																			PHE	
	84				ALA	ALA																			ALA	
	85				VAL	VAL																			VAL	
	86				TYR	TYR																			TYR	
	87				TYR	TYR																			TYR	
	88				CYS	CYS																			CYS	
	89				GLN	GLN																			GLN	
	90				GLN	GLN																			GLN	
	91				TYR	TYR																			TYR	
	92				SER	GLU																			ASN	
	93				THR	THR																			ASN	
	94				SER	SER																			TRP	
	95				PRO	PRO																			PRO	
	95A				---	---																			---	
CDR3	95B				---	---																			---	
	95C				---	---																			---	
	95D				---	---																			---	
	95E				---	---																			---	
	95F				---	---																			---	
	96				TYR	THR																			PRO	
	97				THR	THR																			THR	
	98				PHE	PHE																			PHE	
	99				GLY	GLY																			GLY	
	100				GLN	GLN																			GLN	
	101				GLY	GLY																			GLY	
	102				THR	THR																			THR	
FR4	103				LYS	ARG																			ARG	
	104				LEU	LEU																			VAL	
	105				GLU	ASP																			GLU	
	106				ILE	ILE																			ILE	
	106A				---	---																			---	
	107				LYS	LYS																			LYS	
	108				ARG																				ARG	
	109																									

HUMAN KAPPA LIGHT CHAINS SUBGROUP III (cont'd)

		50 AMYLOID SO124	51 DOV	52 SHM	53 GRA	54* GOE II	55 LOW*	56 VER	57 REE	58 WE #	59 HOW	60 HS4	61 HBJ 5	62* TEH	63* CRA (III)	64* PLA	65* PIN	66 MCE	67 HAC	68 K- EV15 CL	69 BER	70* BOR	71* DRI	72* WAL	73* GOL	74* GAG
	0	---	---	---	---	---	---	---	---	asp	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1	GLU	GLU	GLU	GLU	asp	GLU	thr	leu	ILE	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	thr	GLU	GLU	GLU	GLU	GLU	GLU
	2	ILE	ILE	ILE	met	ILE	ILE	VAL	VAL	gln	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	thr	ILE	ILE	ILE	ILE	ILE	ILE
	3	VAL	VAL	VAL	VAL	VAL	VAL	LEU	LEU	met	LEU	LEU	VAL	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	4	met	met	met	met	LEU	met	LEU	LEU	met	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLX	THR	THR	THR	THR
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	GLN	GLN	GLN	GLN
	9	ala	ala	ala	ala	ala	ala	GLY	ala	ser	GLY	GLY	asx	GLY	GLY	GLY	GLY	GLY	GLY	ala	GLY	ala	ASN	ASN	ASN	SER
FR1	10	THR	THR	THR	THR	ser	gly	THR	THR	ser	THR	THR	THR	THR	THR	THR	THR	THR	THR	phe	THR	THR				
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	met						
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER						
	13	val	val	val	met	val	val	LEU	val	ala	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		ala						
	14	SER	SER	SER	SER	thr	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER			thr						
	15	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	val	PRO	PRO	PRO	PRO	PRO	PRO	PRO			PRO						
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	PRO	PRO	PRO							GLY						
	17	GLU	GLU	GLU	GLU	GLU	gly	GLU	GLU	asp	GLY	GLY	GLX							asp						
	18	ARG	ser	gly	ARG	ARG	thr	val	glu		GLU	GLU								lys						
	19	val	ALA	ALA	ALA	ALA	ALA	val	val	val										val						
	20	THR	THR	THR	THR	ser	THR	THR	THR	#										asn						
	21	LEU	LEU	LEU	LEU	LEU	LEU	ile	LEU	ile										ile						
	22	SER	SER	SER	SER	SER	SER	tyr	SER	thr										SER						
	23	CYS	CYS	CYS		CYS	CYS	CYS	CYS											CYS						
	24	ARG	ARG	ARG			SER	LYS	ARG											LYS						
	25	ALA	ALA	ALA			ALA	SER	ALA	ALA										ALA						
	26		SER	SER			GLY		SER	SER										SER						
	27		GLU	GLU			GLN		GLU	GLN										GLN						
	27A		---	---			---	---	---	---										---						
	27B		---	---			---	---	---	---										---						
CDR1	27C		---	---			---	---	---	---										---						
	27D		---	---			---	---	---	---										---						
	27E		---	---			---	---	---	---										---						
	27F		---	---			---	---	---	---										---						
	28		SER	THR			SER	LEU	SER	THR										ASP						
	29		VAL	VAL			VAL	SER	LEU	#										ILE						
	30		SER	ALA			ASP		SER	GLY										ASP						
	31		THR	LYS			GLX		ASP											ASP						
	32		ASX	SER			THR		ASN											ASP						
	33		LEU	LEU			VAL	LEU	VAL	#										MET						
	34		ALA	ALA			ALA	ALA	ALA											ASN						
	35		TRP	TRP			TRP	TRP	TRP											TRP						
	36		TYR	TYR			TYR	TYR	TYR											TYR						
	37		GLX	GLX			GLX	GLN	GLN											GLN						
	38		GLX	GLX			GLX	GLN	HIS											GLN						
	39		LYS				LYS		LYS											LYS						
	40		PRO				PRO		PRO											PRO						
FR2	41								GLY											GLY						
	42								GLN											GLU						
	43								ALA											ALA						
	44							LEU	PRO											ALA						
	45							ARG	ARG											ILE						
	46							LEU	LEU											PHE						
	47							LEU	LEU											ILE						
	48							ILE	LEU											ILE						
	49							TYR	TYR											GLN						
	50							GLY	ALA											GLU						
	51							VAL	THR											ALA						
CDR2	52							SER	SER											THR						
	53							THR	THR											THR						
	54							ARG	ARG											LEU						
	55							ALA	PRO											VAL						
	56							ALA	THR											PRO						
	57							GLY	ASP											GLY						
	58							ILE	ILE											ILE						
	59							PRO	PRO											PRO						
	60							ASP	ALA											PRO						
	61							ARG	ARG											ARG						
	62							PHE	PHE											PHE						
	63							THR	SER											SER						
	64							GLY	GLY											GLY						
	65							ARG	SER											SER						
	66							ALA	MET											GLY						
	67							SER	SER											TYR						
	68							GLY	GLY											GLY						
	69							THR	THR											THR						
	70							ASP	GLU											ASP						
FR3	71							PHE	PHE											PHE						
	72							THR	THR											THR						
	73							LEU	LEU											LEU						
	74							THR	THR											THR						
	75							ILE	ILE											ILE						
	76							SER	PHE											ASN						
	77							ASP	ARG											ASN						
	78							LEU	VAL											ILE						
	79							GLU	GLU											GLU						
	80							PRO	SER											SER						
	81							GLU	GLU											GLU						
	82							ASP	ASP											ASP						
	83							PHE	SER											ALA						
	84							ALA	ALA											ALA						
	85							VAL	VAL											TYR						
	86							TYR	TYR											TYR						
	87							TYR	TYR											PHE						
	88							CYS	CYS											CYS						
	89							GLN	GLN											LEU						
	90							GLN	GLN											GLN						
	91							TYR	HIS											HIS						
	92							ASP	GLU											ASP						
	93							THR	---											ASN						
	94							SER	---											PHE						
CDR3	95							PRO	---											PRO						
	95A							---	---											---						
	95B							---	---											---						
	95C							---	---											---						
	95D							---	---											---						
	95E							---	---											---						
	95F							---	---											---						
	96							LEU	---											---						
	97							THR	THR											---						
	98							PHE	PHE											---						
	99							GLY	GLY											---						
	100							GLY	GLN											---						
	101							GLY	GLY											---						
FR4	102							THR	THR											---						
	103							LYS	LYS											---						
	104							LEU	VAL											---						
	105							ASP	GLU											---						
	106							VAL	ILE											---						
	106A							---	---											---						
	107							ARG	LYS											---						
	108								ARG											---						
	109																			---						

HUMAN KAPPA LIGHT CHAINS SUBGROUP III (cont'd)

		75 DOB	76 HS6	77 HBJ 12	78 BUR (K)	79 LEG	80 B6	81 AMYLOID WR #	82 VKAPPA3 CL #	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0	---	---	---	---	---							
	1	GLU	GLU	GLU	GLU	GLU				79	3 : 4	74(GLU) : 73(GLU)	3.2 : 4.3
	2	ILE	ILE	ILE	ILE	ILE				79	5	74(ILE)	5.3
	3	ile	VAL	VAL	VAL	VAL				79	4	76(VAL)	4.2
	4	met	LEU	val	LEU	LEU				79	3	65(LEU)	3.6
	5	THR	THR	THR						77	1	77(THR)	1.
	6	GLN	GLN	GLN						77	2	75(GLN) : 69(GLN)	2.1 : 2.2
	7	SER								75	1	75(SER)	1.
	8	PRO								74	1	74(PRO)	1.
	9	ala								69	6 : 7	46(GLY)	9. : 11.
FR1	10									70	4	66(THR)	4.2
FR1	11									68	2	67(LEU)	2.
FR1	12									67	1	67(SER)	1.
FR1	13									67	5	52(LEU)	6.4
FR1	14									66	2	64(SER)	2.1
FR1	15									66	2	65(PRO)	2.
FR1	16									62	1	62(GLY)	1.
FR1	17									62	3 : 4	56(GLU) : 50(GLU)	3.3 : 5.
FR1	18						ARG			58	7	51(ARG)	8.
FR1	19						ALA			60	2	52(ALA)	2.3
FR1	20						ala			59	5	53(THR)	5.6
FR1	21						LEU			60	2	57(LEU)	2.1
FR1	22						SER			60	3	58(SER)	3.1
FR1	23						CYS			50	1	50(CYS)	1.
	24						ARG			51	4	47(ARG)	4.3
	25						ALA			52	2	51(ALA)	2.
	26						SER			49	2	46(SER)	2.1
	27						GLN			47	3	43(GLN) : 37(GLN)	3.3 : 3.8
	27A						SER			32	4	29(SER)	
	27B						---						
CDR1	27C						---						
CDR1	27D						---						
CDR1	27E						---						
CDR1	27F						---						
CDR1	28						LEU			47	7 : 8	25(VAL)	13. : 15.
	29						SER			44	6	27(SER)	9.8
	30						GLY			40	7	24(SER)	12.
	31						ASN			39	10	24(SER)	16.
	32						TYR			40	8	28(TYR)	11.
	33						LEU			41	4	36(LEU)	4.6
	34						ALA			41	5	37(ALA)	5.5
	35						TRP	TRP		38	1	38(TRP)	1.
	36						TYR	TYR		39	1	39(TYR)	1.
	37						GLN	GLN		39	1 : 2	39(GLN) : 33(GLN)	1. : 2.4
	38						GLN	GLN		37	2 : 3	36(GLN) : 30(GLN)	2.1 : 3.7
	39						LYS	LYS		33	3	29(LYS)	3.4
	40						PRO	PHE		34	3	32(PRO)	3.2
FR2	41						GLY	GLY		27	2	26(GLY)	2.1
FR2	42						GLN	GLN		27	4	24(GLN) : 23(GLN)	4.5 : 4.7
FR2	43						ALA	ALA		26	3	23(ALA)	3.4
	44						PRO	PRO		27	3	25(PRO)	3.2
	45						ARG			26	3	24(ARG)	3.3
	46						LEU	LEU		24	2	23(LEU)	2.1
	47						LEU	LEU		23	2	22(LEU)	2.1
	48						MET	ILE		22	3	20(ILE)	3.3
	49						TYR	PHE		22	4	19(TYR)	4.6
	50						GLY	ASP		21	5	16(GLY)	6.6
	51						VAL			20	3	16(ALA)	3.8
CDR2	52						SER			20	2	18(SER)	2.2
CDR2	53						SER	SER		21	2	16(SER)	2.6
CDR2	54						ARG	#		20	2	19(ARG)	2.1
CDR2	55						ALA	ALA		23	3	21(ALA)	3.3
CDR2	56						THR			22	4	19(THR)	4.6
	57						GLY	GLY		23	2	22(GLY)	2.1
	58						ILE	VAL		23	3	21(ILE)	3.3
	59						PRO		PRO	23	1	23(PRO)	1.
	60						ASP		ASP	23	5	17(ASP)	6.8
	61						ARG		ARG	23	1	23(ARG)	1.
	62						PHE		PHE	23	1	23(PHE)	1.
	63						SER		SER	23	2	21(SER)	2.2
	64						GLY		GLY	23	1	23(GLY)	1.
	65						SER		SER	22	2	21(SER)	2.1
	66						GLY		ALA	22	4	17(GLY)	5.2
	67						SER		SER	22	2	21(SER)	2.1
	68						GLY		GLY	22	1	22(GLY)	1.
	69						ALA		THR	22	2	21(THR)	2.1
	70								ASP	21	2	19(ASP)	2.2
FR3	71								PHE	21	1	21(PHE)	1.
FR3	72								THR	21	1	21(THR)	1.
FR3	73								LEU	21	1	21(LEU)	1.
	74								THR	21	2	20(THR)	2.1
	75								ILE	21	2	20(ILE)	2.1
	76								SER	21	3	19(SER)	3.3
	77						ARG		ARG	22	5	16(ARG)	6.9
	78						LEU		LEU	22	3	20(LEU)	3.3
	79						GLX		GLU	22	2	21(GLU) : 20(GLU)	2.1 : 2.2
	80						PRO		PRO	22	2	19(PRO)	2.3
	81						GLU		GLU	22	2	21(GLU)	2.1
	82						ASP		ASP	22	1	22(ASP)	1.
	83						PHE		PHE	22	3	20(PHE)	3.3
	84						ALA		ALA	22	1	22(ALA)	1.
	85						VAL		VAL	22	2	21(VAL)	2.1
	86						TYR		TYR	22	1	22(TYR)	1.
	87						TYR		TYR	22	2	20(TYR)	2.2
	88						CYS		CYS	22	1	22(CYS)	1.
	89						GLN		GLN	22	2	21(GLN)	2.1
	90						GLN		GLN	22	1	22(GLN)	1.
	91						TYR		TYR	22	2	20(TYR)	2.2
	92						GLY		GLY	22	5	16(GLY)	6.9
	93						SER		ASN	21	5	12(SER)	8.8
	94						SER		SER	21	4	18(SER)	4.7
	95						PRO		GLN	21	3	18(PRO)	3.5
CDR3	95A						---		---	1	1	1(PRO)	
CDR3	95B						---		---				
CDR3	95C						---		---				
CDR3	95D						---		---				
CDR3	95E						---		---				
CDR3	95F						---		---				
CDR3	96						PHE		TRP	19	10	4(TYR)	48
CDR3	97						THR		THR	20	2	19(THR)	2.1
	98						PHE		PHE	20	1	20(PHE)	1.
	99						GLY		GLY	20	1	20(GLY)	1.
	100						GLN		GLN	20	2	18(GLN)	2.2
	101						GLY		GLY	20	1	20(GLY)	1.
FR4	102						SER		THR	20	2	18(THR)	2.2
FR4	103						LYS		LYS	20	2	18(LYS)	2.2
FR4	104						LEU		VAL	20	2	11(VAL)	3.6
FR4	105						GLU		GLU	20	2	18(GLU)	2.2
FR4	106						ILE		ILE	20	3	18(ILE)	3.3
FR4	106A						---		---				
FR4	107						LYS		LYS	20	2	19(LYS)	2.1
	108								ARG	16	1	16(ARG)	1.
	109									10	1	10(THR)	1.

ANTIBODY SPECIFICITIES: HUMAN KAPPA LIGHT CHAINS SUBGROUP III

2) **WOL:** ANTI-HUMAN GAMMA G GLOBULIN; WA IDIOTYPE
3) **SIE:** ANTI-HUMAN GAMMA G GLOBULIN; WA IDIOTYPE
5) **NEU:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE (KUNKEL,H.G.,WINCHESTER,R.J.,JOSLIN,F.G. & CAPRA,J.D. (1974) J.EXP.MED.,139,128)
6) **GOT:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
7) **PAY:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
8) **SON:** CRYOGLOBULIN WITH ANTI-LOW-DENSITY LIPOPROTEIN ACTIVITY; B IDIOTYPE
9) **WEI':** CRYOGLOBULIN WITH ANTI-LOW-DENSITY LIPOPROTEIN ACTIVITY; B IDIOTYPE
10) **GAR':** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
11) **PIE:** AUTOANTIBODY WHICH BINDS SPECIFICALLY TO INTERMEDIATE FILAMENTS
12) **FLO:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
13) **LOP:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
14) **SCA:** CRYOGLOBULIN WITH ANTI-LOW-DENSITY LIPOPROTEIN ACTIVITY; B IDIOTYPE
15) **GLO:** ANTI-HUMAN GAMMA G GLOBULIN; WA IDIOTYPE; CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
18) **MA:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY (GROUP 1)
19) **NIC:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP SMALL I ACTIVITY
20) **CUR:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
22) **DRE:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
23) **PER:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
25) **STE:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
26) **GJ:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY (ATYPICAL)
27) **TAK:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
35) **AJ:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
42) **CLA:** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
43) **SHE':** CRYOGLOBULIN WITH ANTI-IGG ACTIVITY; B IDIOTYPE
48) **POM:** ANTI-HUMAN GAMMA G1 GLOBULIN; PO IDIOTYPE
54) **GOEII:** ANTI-MEASLES VIRUS (WOODFOLK STRAIN); ANTI-SUBACUTE SCLEROSING PANENCEPHALITIS VIRUS (LEC STRAIN)
62) **TEH:** ANTI-HUMAN GAMMA G GLOBULIN
63) **CRA(III):** ANTI-HUMAN GAMMA G GLOBULIN
64) **PLA:** ANTI-HUMAN GAMMA G GLOBULIN
65) **PIN:** ANTI-HUMAN GAMMA G GLOBULIN
70) **BOR:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
71) **DRI:** ANTI-HUMAN GAMMA G GLOBULIN
72) **WAL:** ANTI-HUMAN GAMMA G GLOBULIN
73) **GOL:** ANTI-HUMAN GAMMA G GLOBULIN
74) **GAG:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY

CLASS: HUMAN KAPPA LIGHT CHAINS SUBGROUP III

5) **NEU:** IGM-KAPPA
6) **GOT:** IGM-KAPPA
7) **PAY:** IGM-KAPPA
8) **SON:** IGM-KAPPA
9) **WEI':** IGM-KAPPA
10) **GAR':** IGM-KAPPA
11) **PIE:** IGM-KAPPA
12) **FLO:** IGM-KAPPA
13) **LOP:** IGM-KAPPA
14) **SCA:** IGM-KAPPA
15) **GLO:** IGM-KAPPA
20) **CUR:** IGM-KAPPA
42) **CLA:** IGM-KAPPA
43) **SHE':** IGM-KAPPA

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP III

1) **TI:** SUTER,L.,BARNIKOL,H.U.,WATANABE,S. & HILSCHMANN,N. (1969) Z.PHYSIOL.CHEM.,350,275-278; (1972) Z.PHYSIOL.CHEM.,353,189-208. (CHECKED BY AUTHOR)
2) **WOL:** ANDREWS,D.W. & CAPRA,J.D. (1981) PROC.NAT.ACAD.SCI.USA,78,3799-3803. (CHECKED BY AUTHOR 08/25/81); ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5816-5822.
3) **SIE:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR); ANDREWS,D.W. & CAPRA,J.D. (1981) PROC.NAT.ACAD.SCI.USA,78,3799-3803. (CHECKED BY AUTHOR 08/25/81 WHO SUGGESTED THAT THE SEQUENCE DETERMINED IN 1975 WAS INCORRECT AND SHOULD BE DELETED); ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5816-5822.
4) **NG9'CL:** BENTLEY,D.L. (1984) NATURE,307,77-80.
5) **NEU:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
6) **GOT:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); PONS-ESTEL,B.,GONI,F.,SOLOMON,A. & FRANGIONE,B. (1984) J.EXP.MED.,160,893-904; GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
7) **PAY:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
8) **SON:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); PONS-ESTEL,B.,GONI,F.,SOLOMON,A. & FRANGIONE,B. (1984) J.EXP.MED.,160,893-904.
9) **WEI':** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84)
10) **GAR':** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); PONS-ESTEL,B.,GONI,F.,SOLOMON,A. & FRANGIONE,B. (1984) J.EXP.MED.,160,893-904; GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
11) **PIE:** PONS-ESTEL,B.,GONI,F.,SOLOMON,A. & FRANGIONE,B. (1984) J.EXP.MED.,160,893-904. (CHECKED BY AUTHOR 05/16/86)
12) **FLO:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
13) **LOP:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84)
14) **SCA:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84)
15) **GLO:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR); LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
16) **SAL:** CAPRA,J.D.,KEHOE,J.M.,WINCHESTER,R.J. & KUNKEL,H.G. (1971) ANN.N.Y.ACAD.SCI.,190,371-381. (CHECKED BY AUTHOR)
17) **WIL:** CAPRA,J.D.,KEHOE,J.M.,WINCHESTER,R.J. & KUNKEL,H.G. (1971) ANN.N.Y.ACAD.SCI.,190,371-381. (CHECKED BY AUTHOR)
18) **MA:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)
19) **NIC:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)
20) **CUR:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84); GONI,F.,CHEN,P.P.,PONS-ESTEL,B.,CARSON,D.A. & FRANGIONE,B. (1985) J.IMMUNOL.,135,4073-4079.
21) **FR4:** MILSTEIN,C. (1969) FEBS LETTERS,2,301-304. (CHECKED BY AUTHOR WHO PROVIDED ADDITIONAL RESIDUES TO THOSE PUBLISHED)
22) **DRE:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)
23) **PER:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)
24) **CAM:** HOPPER,J.E.,NOYES,C.,HSU,R.,HEINRIKSON,R. & GALLAGHER,W. (1979) J.IMMUNOL.,122,2007-2010. (CHECKED BY AUTHOR 01/26/83)
25) **STE:** EDMAN,P. & COOPER,A.G. (1968) FEBS LETTERS,2,33-35. (CHECKED BY AUTHOR)
26) **GJ:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)
27) **TAK:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)
28) **IARC/BL41'CL:** KLOBECK,H.G.,MEINDL,A.,COMBRIATO,G.,SOLOMON,A. & ZACHAU,H.G. (1985) NUC.ACIDS RES.,13,6499-6513.
29) **RAD:** MILSTEIN,C. (1969) FEBS LETTERS,2,301-304. (CHECKED BY AUTHOR)
30) **DIL:** DAYHOFF,M.O. (1972) ATLAS OF PROTEIN SEQUENCE & STRUCTURE,5,D-250. SUBMITTED BY SMITHIES,O.,GIBSON,D.M. AND FANNING,E.M. (CHECKED BY AUTHOR 07/24/79)

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP III (cont'd)

31) **CAS:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

32) **MCE':** MIDDAUGH,C.R.,KEHOE,J.M.,PRYSTOWSKY,M.B.,GERBER-JENSON,B.,JENSON,J.C. & LITMAN,G.W. (1978) IMMUNOCHEM.,15,171-187. (CHECKED BY AUTHOR 10/22/80)

33) **KEA:** WANG,A.C. & FUDENBERG,H.H. (1975) IMMUNOL.COMMUN.,4,483-497. (CHECKED BY AUTHOR 09/23/77); WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG, H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)

34) **SMI:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

35) **AJ:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

36) **BRO'IGG:** HOPPER,J.E.,NOYES,C.,HEINRIKSON,R. & KESSEL,J.W. (1976) J.IMMUNOL.,116,743-746. (CHECKED BY AUTHOR 01/26/83)

37) **NIG:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

38) **IKE:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR)

39) **TIL:** PINK,J.R.L.,WANG,A.C. & FUDENBERG,H.H. (1971) ANN.REV.MED.,22,145-170. (CHECKED BY AUTHOR)

40) **AMYLOID KSA:** SLETTEN,K.,WESTERMARK,P.,PITKANEN,P.,THYRESSON,N. & OLSTAD,O.K. (1983) SCAND.J.IMMUNOL.,18,557-560. (CHECKED BY AUTHOR 04/26/84)

41) **POL:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)

42) **CLA:** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84)

43) **SHE':** LEDFORD,D.K.,GONI,F.,PIZZOLATO,M.,FRANKLIN,E.C.,SOLOMON,A. & FRANGIONE,B. (1983) J.IMMUNOL.,131,1322-1325. (CHECKED BY AUTHOR 03/23/84)

44) **JH:** JEMMERSON,R.,KAPLAN,B.,DENTON,M.D.,ANDERAS,P.,ANDERSON,B. & MARGOLIASH,E. (1979) BIOCHEMISTRY,18,4676-4683.

45) **WIN:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

46) **LEA:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)

47) **ARP:** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)

48) **POM:** KLAPPER,D.G. & CAPRA,J.D. (1976) ANN.IMMUNOL.(INST.PASTEUR),127C,261-271. (CHECKED BY AUTHOR 08/01/79)

49) **VAND:** SEON,B.K.,GAILANI,S.,HENDERSON,E.S. & PRESSMAN,D. (1977) IMMUNOCHEM.,14,567-572. (CHECKED BY AUTHOR 08/28/78)

50) **AMYLOID SO124:** SLETTEN,K.,WESTERMARK,P.,PITKANEN,P.,THYRESSON,N. & OLSTAD,O.K. (1983) SCAND.J.IMMUNOL.,18,557-560. (CHECKED BY AUTHOR 04/26/84)

51) **DOV:** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)

52) **SHM:** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)

53) **GRA:** NIALL,H.D. & EDMAN,P. (1967) NATURE,216,262-263. (CHECKED BY AUTHOR 07/25/79)

54) **GOEII:** STROSBERG,A.D.,KARCHER,D. & LOWENTHAL,A. (1975) J.IMMUNOL.,115,157-160. (CHECKED BY AUTHOR)

55) **LOW':** WANG,A.C.,TUNG,E.,WANG,I.,FUDENBERG,H.H.,PICK,A.I. & FROEHLICHMAN,R. (1980) CANCER IMMUNOL.IMMUNOTHER.,9,81-86. (CHECKED BY AUTHOR 03/18/81)

56) **VER:** CHERSI,A. & NATALI,P.G. (1978) IMMUNOCHEMISTRY,15,585-589. (CHECKED BY AUTHOR 09/13/79)

57) **REE:** PRELLI,F.,TUMMOLO,D.,SOLOMON,A. & FRANGIONE,B. (1986) J.IMMUNOL., IN PRESS.

58) **WE:** DWORSKY,E.,SLETTEN,K.,HARBOE,M. & WETTELAND,P. (1980) SCAND.J.IMMUNOL.,12,281-287. (CHECKED BY AUTHOR 02/28/1984)

59) **HOW:** KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951. (CHECKED BY AUTHOR)

60) **HS4:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

61) **HBJ5:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

62) **TEH:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

63) **CRA(III):** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

64) **PLA:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

65) **PIN:** JOHNSTON,S.L.,ABRAHAM,G.N. & WELCH,E.H. (1975) BIOCHEM.BIOPHYS.RES.COMMUN.,66,842-847. (CHECKED BY AUTHOR 10/17/77)

66) **MCE:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

67) **HAC:** HOOD,L. & TALMAGE,D.W. (1970) SCIENCE,168,325-334.

68) **K- EV15'CL:** STAVNEZER,J.,KEKISH,O.,BATTER,D.,GRENIER,J.,BALAZS,I.,HENDERSON,E. & ZEGERS,B.J.M. (1985) NUC.ACIDS RES.,13,3495-3514.

69) **BER:** WANG,A.C.,WELLS,J.V.,FUDENBERG,H.H. & GERGELY,J. (1974) IMMUNOCHEM.,11,341-345. (CHECKED BY AUTHOR)

70) **BOR:** GERGELY,J.,WANG,A.C. & FUDENBERG,H.H. (1973) VOX SANG.,24,432-440. (CHECKED BY AUTHOR)

71) **DRI:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR)

72) **WAL:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR)

73) **GOL:** CAPRA,J.D. (1975) ADV.IMMUNOLOGY,20,1-40. (CHECKED BY AUTHOR)

74) **GAG:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)

75) **DOB:** HOOD,L. & TALMAGE,D.W. (1970) SCIENCE,168,325-334.

76) **HS6:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

77) **HBJ12:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

78) **BUR(K):** MOULIN,A. & FOUGEREAU,M. (1973) NATURE NEW BIOLOGY,246,176-178. (CHECKED BY AUTHOR)

79) **LEG:** MOULIN,A. & FOUGEREAU,M. (1973) NATURE NEW BIOLOGY,246,176-178. (CHECKED BY AUTHOR)

80) **B6:** MILSTEIN,C. (1969) FEBS LETTERS,2,301-304. (CHECKED BY AUTHOR)

81) **AMYLOID WR:** WESTERMARK,P.,SLETTEN,K.,PITKANEN,P.,NATVIG,J.B. & LINDHOLM,C.E. (1982) MOL.IMMUNOL.,19,447-450. (CHECKED BY AUTHOR 06/01/83)

82) **VKAPPA3'CL:** BENTLEY,D.L. & RABBITTS,T.H. (1981) CELL,24,613-623. (CHECKED BY AUTHOR 12/07/81)

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP III

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1:
SET 1: TI[1],WOL[2],SIE[3],NG9'CL[4],NEU[5],GOT[6],PAY[7],SON[8],WEI'[9],GAR'[10],PIE[11],FLO[12],LOP[13],SCA[14],GLO[15],SAL[16], WIL[17],MA[18],NIC[19],CUR[20],FR4[21],DRE[22],PER[23],CAM[24]. (24 IDENTICAL)
SET 2: GJ[26],TAK[27]. (2 IDENTICAL)
SET 3: RAD[29],DIL[30],CAS[31]. (3 IDENTICAL)
SET 4: KEA[33],SMI[34]. (2 IDENTICAL HUMAN V-KAPPA-III; ALSO 1 MOUSE V-KAPPA-V: Vg'CL[122].)
SET 5: DRE[22],PER[23],BRO'IGG[36]. (3 IDENTICAL)
SET 6: CLA[42],SHE'[43]. (2 IDENTICAL)

FR2:
SET 1: TI[1],WOL[2],SIE[3],NG9'CL[4],NEU[5],GOT[6],SON[8],GAR'[10],PIE[11],FLO[12],GLO[15],CUR[20]. (12 IDENTICAL HUMAN V-KAPPA-III; ALSO 1 MOUSE V-KAPPA-IV: Vh'CL[12]; AND 1 MOUSE V-KAPPA-V: Vg'CL[122].)

FR3:
SET 1: TI[1],WOL[2]. (2 IDENTICAL)
SET 2: GOT[6],PAY[7],GAR'[10],PIE[11],FLO[12],GLO[15],CUR[20]. (7 IDENTICAL)

FR4:
SET 1: WOL[2],PAY[7],PIE[11],GLO[15],CUR[20],REE[57],VKAPPA3'CL[82]. (7 IDENTICAL HUMAN V-KAPPA-III; ALSO 3 HUMAN V-KAPPA-I: AU[2],GAL(I)[36],CL'[110]; 2 HUMAN V-KAPPA-II: GM 607 'CL[5],RPM1-6410'CL[16]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
SET 2: POM[48]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: HAU[4].)
SET 3: NEU[5],GOT[6],GAR'[10],FLO[12],FR4[21],IARC/BL41'CL[28]. (6 IDENTICAL HUMAN V-KAPPA-III; ALSO 3 HUMAN V-KAPPA-I: AG[7], DEN[46],BI[63]; 2 HUMAN V-KAPPA-II: NIM[3],FR[14]; AND 1 HUMAN V-KAPPA-IV: LEN[4].)
SET 4: SON[8]. (IDENTICAL TO 1 HUMAN V-KAPPA-IV: VJI'CL[1].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1:
SET 1: SIE[3],IKE[38]. (2 IDENTICAL)
SET 2: NG9'CL[4],PAY[7],SON[8],WEI'[9],GAR'[10],PIE[11],FLO[12],GLO[15],CUR[20],DRE[22],CAM[24]. (11 IDENTICAL)
SET 3: TIL[39]. (IDENTICAL TO 1 MOUSE V-KAPPA-V: Vg'CL[122].)

CDR2:
SET 1: WOL[2],SIE[3],NEU[5],GOT[6],PAY[7],SON[8],GAR'[10],PIE[11],FLO[12],GLO[15],CUR[20]. (11 IDENTICAL)
SET 2: POM[48]. (IDENTICAL TO 1 MOUSE V-KAPPA-IV: Vh'CL[12].)

CDR3:
SET 1: POM[48]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: LAY[39].)
SET 2: GOT[6],CUR[20]. (2 IDENTICAL)
SET 3: PAY[7],GLO[15]. (2 IDENTICAL)
SET 4: GAR'[10],FLO[12]. (2 IDENTICAL)

IDENTICAL SETS OF J-MINIGENES:

SET 1: PIE[11],VKAPPA3'CL[82]. (2 IDENTICAL HUMAN V-KAPPA-III; ALSO 1 HUMAN V-KAPPA-I: AU[2]; 1 HUMAN V-KAPPA-II: RPM1-6410'CL[16]; AND 1 HUMAN V-KAPPA-IV: PB17IV'CL[3].)
SET 2: GOT[6]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: AG[7].)
SET 3: GAR'[10],FLO[12],IARC/BL41'CL[28]. (3 IDENTICAL HUMAN V-KAPPA-III; ALSO 2 HUMAN V-KAPPA-I: DEN[46],BI[63]; AND 1 HUMAN V-KAPPA-II: FR[14].)
SET 4: WOL[2],CUR[20]. (2 IDENTICAL)
SET 5: PAY[7],GLO[15]. (2 IDENTICAL)

SPECIFIC NOTES:

4) **NG9'CL:** THE AMINO ACID SEQUENCE IS TRANSLATED FROM THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN CDNA.

32) **MCE':** IT IS A CRYOIMMUNOGLOBULIN. THE AUTHORS ORIGINALLY DESIGNATED IT AS MCE, BUT IN ORDER TO DIFFERENTIATE IT FROM ANOTHER MCE SEQUENCED BY CAPRA ET AL., IT IS DENOTED AS MCE'.

42) **CLA:** THE AMINO ACID RESIDUES FOUND AT POSITION 9 WERE GLY AND ALA.

43) **SHE':** THE AMINO ACID RESIDUES FOUND AT POSITION 9 WERE GLY AND ALA.

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP III (cont'd)

44) **JH:** THE NAME WAS GIVEN TO US BY THE AUTHORS. IT IS NOT INCLUDED IN THE PAPER.

58) **WE:** AT POSITIONS 20,29 AND 33 OF AMINO ACID SEQUENCE WERE FOUND BOTH LEU AND ILE. IN THE SAME SEQUENCE TWO RESIDUES WERE FOUND IN POSITIONS 1,3,4,9,10,15,17,19,20,21,22 AND 29. THE SECOND RESIDUES WERE GLU,VAL,LEU,GLY,THR,PRO,GLU,ALA,THR,LEU,SER AND VAL, RESPECTIVELY. A DETERMINATION WAS NOT MADE IN THE ARTICLE AS TO WHETHER THE SEQUENCE BELONGED TO SUBGROUP I OR TO SUBGROUP III.

81) **AMYLOID WR:** AMINO ACID RESIDUES FOUND AT POSITION 54 ARE LEU AND ALA.

82) **VKAPPA3'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF CDNA FROM A MOUSE-HUMAN HYBRID CELL LINE.

HUMAN KAPPA LIGHT CHAINS SUBGROUP IV

		INVARIANT RESIDUES	1 VJI 'CL	2 VKAPPA IV GERMLINE 'CL	3* PB17IV 'CL	4 LEN	5* R.K.	6* L TH.	7* TUR	8 AH	9 DA	10 DA-H	11 DA-N	12 JAH	13 SCH	14 JUV	15 AMYLOID GAB	# OF SEQUENCES	# OF AMINO ACIDS
	0		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		
	1	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	15	1
	2		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	leu	ILE	15	2
	3	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	15	1
	4		MET	MET	MET	MET	MET	leu	MET	MET	MET	MET	leu	MET	MET	MET	MET	15	2
	5		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	gln	THR	THR	THR	THR	15	2
	6	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	15	1
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		14	1
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	15	1
	9		ASP	ASP	ASP	asn	ASX	ASX	ser	glx	ASP	ASP	ASP	ASP	ala	asn	ASX	15	5
FR1	10		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	thr	thr			13	2
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		14	1
	12	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	LEU	ALA	ALA	ALA	ALA	ALA		14	1
	13	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		14	1
	14	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER					11	1
	15		LEU	LEU	LEU	LEU	LEU	LEU	LEU	pro	pro	pro	LEU					11	2
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY					11	1
	17		GLU	GLU	GLU	GLU	GLX	GLX	GLU	asp	asp	asp	asp					11	2 : 3
	18		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	gln	gln	leu					11	3
	19	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA				ALA	12	1
	20	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR				THR	12	1
	21		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	val	val				ILE	12	3
	22		ASN	ASN	ASN	ASN	ASX	ASX	ser	ASX	ser	ser	ser				asp	12	3
	23	CYS	CYS	CYS	CYS	CYS			CYS	CYS	CYS	CYS	CYS				CYS	10	1
	24		LYS	LYS	LYS	LYS			ARG	ARG	GLN	GLN	GLN				LYS	10	3
	25		SER	SER	SER	SER			SER	ARG	ALA	ALA	ALA					9	3
	26		SER	SER	SER	SER			SER	ALA			SER					7	2
	27		GLN	GLN	GLN	GLN			GLN	GLX			GLN					7	1 : 2
	27A		SER	SER	SER	SER			SER	ARG			---					6	2
	27B		VAL	VAL	ILE	VAL			VAL	VAL			VAL					7	2
CDR1	27C	LEU	LEU	LEU	LEU	LEU			LEU				LEU					6	1
	27D	TYR	TYR	TYR	TYR	TYR							TYR					5	1
	27E		SER	SER	SER	SER				TYR								5	2
	27F	SER	SER	SER	SER	SER												4	1
	28		ASN	ASN	ASP	ASN							ASP					5	2
	29		ASN	ASN	ASN	SER												4	2
	30	LYS	LYS	LYS	LYS	LYS							LYS					5	1
	31	ASN	ASN	ASN	ASN	ASN												4	1
	32	TYR	TYR	TYR	TYR	TYR												4	1
	33	LEU	LEU	LEU	LEU	LEU												4	1
	34	ALA	ALA	ALA	ALA	ALA												4	1
	35	TRP	TRP	TRP	TRP	TRP												4	1
	36	TYR	TYR	TYR	TYR	TYR												4	1
	37	GLN	GLN	GLN	GLN	GLN												4	1
	38	GLN	GLN	GLN	GLN	GLN												4	1
	39	LYS	LYS	LYS	LYS	LYS												5	1
	40	PRO	PRO	PRO	PRO	PRO					PRO							5	1
	41	GLY	GLY	GLY	GLY	GLY					GLY							5	1
FR2	42	GLN	GLN	GLN	GLN	GLN					GLN							5	2
	43		PRO	PRO	PRO	PRO					ALA							5	1
	44	PRO	PRO	PRO	PRO	PRO					PRO							5	1
	45	LYS	LYS	LYS	LYS	LYS					LYS							5	1
	46	LEU	LEU	LEU	LEU	LEU					LEU							5	1
	47	LEU	LEU	LEU	LEU	LEU					LEU							5	1
	48	ILE	ILE	ILE	ILE	ILE					ILE							5	1
	49	TYR	TYR	TYR	TYR	TYR					TYR							5	1
	50	TRP	TRP	TRP	TRP	TRP					TRP							5	2
	51		ALA	ALA	ALA	ALA					GLY							5	2
CDR2	52		SER	SER	SER	SER					ARG							4	1
	53	THR	THR	THR	THR	THR												4	1
	54	ARG	ARG	ARG	ARG	ARG												4	1
	55	GLU	GLU	GLU	GLU	GLU												4	1
	56	SER	SER	SER	SER	SER												4	1
	57	GLY	GLY	GLY	GLY	GLY												4	1
	58	VAL	VAL	VAL	VAL	VAL												4	1
	59	PRO	PRO	PRO	PRO	PRO												4	1
	60	ASP	ASP	ASP	ASP	ASP												4	1
	61	ARG	ARG	ARG	ARG	ARG												4	1
	62	PHE	PHE	PHE	PHE	PHE												5	1
	63	SER	SER	SER	SER	SER					SER							5	1
	64	GLY	GLY	GLY	GLY	GLY					GLY							5	1
	65	SER	SER	SER	SER	SER					SER							5	1
	66	GLY	GLY	GLY	GLY	GLY					GLY							5	1
	67	SER	SER	SER	SER	SER					SER							5	2
	68		GLY	GLY	GLY	GLY					LYS							4	1
	69	THR	THR	THR	THR	THR												4	1
	70	ASP	ASP	ASP	ASP	ASP												4	1
	71	PHE	PHE	PHE	PHE	PHE												4	1
FR3	72	THR	THR	THR	THR	THR												4	1
	73	LEU	LEU	LEU	LEU	LEU												4	1
	74	THR	THR	THR	THR	THR												4	1
	75	ILE	ILE	ILE	ILE	ILE												4	1
	76	SER	SER	SER	SER	SER												4	1
	77	SER	SER	SER	SER	SER												4	1
	78	LEU	LEU	LEU	LEU	LEU												4	1
	79	GLN	GLN	GLN	GLN	GLN												4	1
	80	ALA	ALA	ALA	ALA	ALA												4	1
	81	GLU	GLU	GLU	GLU	GLU												4	1
	82	ASP	ASP	ASP	ASP	ASP												4	1
	83	VAL	VAL	VAL	VAL	VAL												4	1
	84	ALA	ALA	ALA	ALA	ALA												4	1
	85	VAL	VAL	VAL	VAL	VAL												4	1
	86	TYR	TYR	TYR	TYR	TYR												4	1
	87	TYR	TYR	TYR	TYR	TYR												4	1
	88	CYS	CYS	CYS	CYS	CYS												4	1
	89	GLN	GLN	GLN	GLN	GLN												4	1
	90	GLN	GLN	GLN	GLN	GLN												4	1
	91	TYR	TYR	TYR	TYR	TYR												4	2
	92		ASP	TYR	TYR	TYR												4	3
	93		THR	SER	ASN	SER												4	3
	94		ILE	THR	LEU	THR												4	1
CDR3	95	PRO	PRO	PRO	PRO	PRO													
	95A		---	---	---	---													
	95B		---	---	---	---													
	95C		---	---	---	---													
	95D		---	---	---	---													
	95E		---	---	---	---													
	95F		---	---	---	---													
	96		---	---	TRP	TYR												2	2
	97		THR	---	THR	SER												3	2
	98	PHE	PHE	---	PHE	PHE												3	1
	99	GLY	GLY	---	GLY	GLY												3	1
	100		GLY	---	GLN	GLN												3	2
	101	GLY	GLY	---	GLY	GLY												3	1
	102	THR	THR	---	THR	THR												3	1
FR4	103	LYS	LYS	---	LYS	LYS												3	1
	104		VAL	---	VAL	LEU						LEU						4	2
	105	GLU	GLU	---	GLU	GLU						GLU						4	1
	106	ILE	ILE	---	ILE	ILE						ILE						4	1
	106A		---	---	---	---						---							
	107		LYS	---	LYS	LYS						ARG						4	2
	108	ARG	ARG	---	ARG	ARG												3	1
	109			---		THR												1	1

HUMAN KAPPA LIGHT CHAINS SUBGROUP IV (cont'd)

		OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0		
	1	15(ASP)	1.
	2	14(ILE)	2.1
	3	15(VAL)	1.
	4	13(MET)	2.3
	5	14(THR)	2.1
	6	15(GLN)	1.
	7	14(SER)	1.
	8	15(PRO)	1.
	9	10(ASP) : 7(ASP)	7.5 : 11.
FR1	10	11(SER)	2.4
FR1	11	14(LEU)	1.
FR1	12	14(ALA)	1.
FR1	13	14(VAL)	1.
FR1	14	11(SER)	1.
	15	8(LEU)	2.8
	16	11(GLY)	1.
	17	7(GLU) : 5(GLU)	3.1 : 6.6
	18	8(ARG)	4.1
	19	12(ALA)	1.
	20	12(THR)	1.
	21	9(ILE)	4.
	22	7(ASN) : 4(+)	5.1 : 9.
	23	10(CYS)	1.
	24	5(LYS)	6.
	25	5(SER)	5.4
	26	6(SER)	2.3
	27	7(GLN) : 6(GLN)	1. : 2.3
	27A	5(SER)	
	27B	6(VAL)	
CDR1	27C	6(LEU)	
CDR1	27D	5(TYR)	
CDR1	27E	4(SER)	
CDR1	27F	4(SER)	
CDR1	28	3(ASN)	3.3
	29	3(ASN)	2.7
	30	5(LYS)	1.
	31	4(ASN)	1.
	32	4(TYR)	1.
	33	4(LEU)	1.
	34	4(ALA)	1.
	35	4(TRP)	1.
	36	4(TYR)	1.
	37	4(GLN)	1.
	38	4(GLN)	1.
	39	4(LYS)	1.
	40	5(PRO)	1.
FR2	41	5(GLY)	1.
FR2	42	5(GLN)	1.
FR2	43	4(PRO)	2.5
	44	5(PRO)	1.
	45	5(LYS)	1.
	46	5(LEU)	1.
	47	5(LEU)	1.
	48	5(ILE)	1.
	49	5(TYR)	1.
	50	5(TRP)	1.
CDR2	51	4(ALA)	2.5
CDR2	52	4(SER)	2.5
CDR2	53	4(THR)	1.
	54	4(ARG)	1.
	55	4(GLU)	1.
	56	4(SER)	1.
	57	4(GLY)	1.
	58	4(VAL)	1.
	59	4(PRO)	1.
	60	4(ASP)	1.
	61	4(ARG)	1.
	62	4(PHE)	1.
	63	5(SER)	1.
	64	5(GLY)	1.
	65	5(SER)	1.
	66	5(GLY)	1.
	67	5(SER)	1.
	68	4(GLY)	2.5
	69	4(THR)	1.
	70	4(ASP)	1.
FR3	71	4(PHE)	1.
FR3	72	4(THR)	1.
FR3	73	4(LEU)	1.
	74	4(THR)	1.
	75	4(ILE)	1.
	76	4(SER)	1.
	77	4(SER)	1.
	78	4(LEU)	1.
	79	4(GLN)	1.
	80	4(ALA)	1.
	81	4(GLU)	1.
	82	4(ASP)	1.
	83	4(VAL)	1.
	84	4(ALA)	1.
	85	4(VAL)	1.
	86	4(TYR)	1.
	87	4(TYR)	1.
	88	4(CYS)	1.
	89	4(GLN)	1.
	90	4(GLN)	1.
	91	4(TYR)	1.
	92	3(TYR)	2.7
	93	2(SER)	6.
	94	2(THR)	6.
CDR3	95	4(PRO)	1.
CDR3	95A		
CDR3	95B		
CDR3	95C		
	95D		
	95E		
	95F		
	96	1(+)	4.
	97	2(THR)	3.
	98	3(PHE)	1.
	99	3(GLY)	1.
	100	2(GLN)	3.
	101	3(GLY)	1.
FR4	102	3(THR)	1.
FR4	103	3(LYS)	1.
FR4	104	2(+)	4.
FR4	105	4(GLU)	1.
FR4	106	4(ILE)	1.
	106A		
	107	3(LYS)	2.7
	108	3(ARG)	1.
	109	1(THR)	

ANTIBODY SPECIFICITIES: HUMAN KAPPA LIGHT CHAINS SUBGROUP IV

3) **PB17IV'CL:** ANTI-STREPTOCOCCUS GROUP A CARBOHYDRATE WITH SPECIFICITY FOR N-ACETYL GLUCOSAMINE
5) **R.K.:** COLD AGGLUTININ WITH ANTI-PR1H ACTIVITY (RBC MEMBRANE ANTIGEN ON HUMAN ERYTHROCYTES INACTIVATED BY PROTEOLYTIC ENZYMES AND NEURAMINIDASE)
6) **L.TH.:** COLD AGGLUTININ WITH ANTI-PR2 ACTIVITY (RBC MEMBRANE ANTIGEN ON HUMAN, RAT AND GUINEA PIG ERYTHROCYTES INACTIVATED BY PROTEOLYTIC ENZYMES AND NEURAMINIDASE)
7) **TUR:** COLD AGGLUTININ WITH ANTI-PR ACTIVITY

REFERENCE: HUMAN KAPPA LIGHT CHAINS SUBGROUP IV

1) **VJI'CL:** KLOBECK,H.G.,BORNKAMMM,G.W.,COMBRIATO,G.,MOCIKAT,R.,POHLENZ,H.D. & ZACHAU,H.G. (1985) NUC.ACIDS RES.,13,6515-6529. (CHECKED BY AUTHOR 02/25/86)
2) **VKAPPA IV GERMLINE'CL:** KLOBECK,H.G.,BORNKAMMM,G.W.,COMBRIATO,G.,MOCIKAT,R.,POHLENZ,H.D. & ZACHAU,H.G. (1985) NUC.ACIDS RES.,13, 6515-6529.
3) **PB17IV'CL:** MARSH,P.,MILLS,F. & GOULD,H. (1985) NUC.ACIDS RES.,13,6531-6544. (CHECKED BY AUTHOR 03/19/86 WHO CORRECTED A MISPRINT IN THE ORIGINAL PAPER FOR RESIDUE 50)
4) **LEN:** SCHNEIDER,M. & HILSCHMANN,N. (1974) Z.PHYSIOL.CHEM.,355,1164-1168. (CHECKED BY AUTHOR)
5) **R.K.:** WANG,A.C.,FUDENBERG,H.H.,WELLS,J.V. & ROELCKE,D. (1973) NATURE NEW BIOLOGY,243,126-128. (CHECKED BY AUTHOR)
6) **L.TH.:** WANG,A.C.,FUDENBERG,H.H.,WELLS,J.V. & ROELCKE,D. (1973) NATURE NEW BIOLOGY,243,126-128. (CHECKED BY AUTHOR)
7) **TUR:** CAPRA,J.D.,KEHOE,J.M.,WILLIAMS,R.C.,JR.,FEIZI,T. & KUNKEL,H.G. (1972) PROC.NAT.ACAD.SCI.USA,69,40-43. (CHECKED BY AUTHOR)
8) **AH:** PICK,A.I.,WANG,A.C.,FROHLICHMAN,R. & FUDENBERG,H.H. (1982) ACTA HAEMAT.,68,207-214. (CHECKED BY AUTHOR 05/26/83)
9) **DA:** WANG,A.C.,ZHANG,H.S.,BONEWALD,L.,TUNG,E.,BOUVET,J.P. & LIACOPOULOS,P. (1985) MIAMI WINTER SYMP.,17,335-336. (CHECKED BY AUTHOR 02/25/86 WHO CORRECTED RESIDUES AS SHOWN)
10) **DA-H:** BOUVET,J.P.,LIACOPOULOS,P.,PILLOT,J.,BANDA,R.,TUNG,E. & WANG,A.C. (1980) J.IMMUNOL.,125,213-220. (CHECKED BY AUTHOR 08/04/80); BOUVET,J.P.,LIACOPOULOS,P.,PILLOT,J.,BANDA,R.,TUNG,E. & WANG,A.C. (1982) J.IMMUNOL.,129,1519-1524.
11) **DA-N:** BOUVET,J.P.,LIACOPOULOS,P.,PILLOT,J.,BANDA,R.,TUNG,E. & WANG,A.C. (1980) J.IMMUNOL.,125,213-220. (CHECKED BY AUTHOR 08/04/80); BOUVET,J.P.,LIACOPOULOS,P.,PILLOT,J.,BANDA,R.,TUNG,E. & WANG,A.C. (1982) J.IMMUNOL.,129,1519-1524.
12) **JAH:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,219-222. (CHECKED BY AUTHOR 12/05/77)
13) **SCH:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,219-222. (CHECKED BY AUTHOR 12/05/77)
14) **JUV:** SLETTEN,K.,HANNESTAD,K. & HARBOE,M. (1974) SCAND.J.IMMUNOL.,3,219-222. (CHECKED BY AUTHOR 12/05/77)
15) **AMYLOID GAB:** PRAS,M.,FRANGIONE,B. & FRANKLIN,E.C. (1980) IN AMYLOID AND AMYLOIDOSIS,G.G.GLENNER,P.P.E COSTA & F.DE FREITAS EDS., EXCERPTA MEDICA AMSTERDAM OXFORD-PRINCETON,249-252. (CHECKED BY AUTHOR 11/18/81)

NOTES: HUMAN KAPPA LIGHT CHAINS SUBGROUP IV

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: VJI'CL[1],VKAPPA IV GERMLINE'CL[2],PB17IV'CL[3],R.K.[5]. (4 IDENTICAL)
SET 2: LEN[4],R.K.[5]. (2 IDENTICAL)
SET 3: DA[9],DA-H[10]. (2 IDENTICAL)

FR2: SET 1: VJI'CL[1],VKAPPA IV GERMLINE'CL[2],PB17IV'CL[3],LEN[4]. (4 IDENTICAL HUMAN V-KAPPA-IV; ALSO 2 HUMAN V-KAPPA-I: V19B'CL[88], V18B'CL[89]; 1 MOUSE V-KAPPA-I: MCPC603[47]; 30 MOUSE V-KAPPA-III: MPC11'CL[6],TEPC111[7],PC3741(NZB)[8],TEPC124[9], MOPC321[12],PC7043(NZB)[13],PC7183(NZB)[14],PC6308(NZB)[15],PC6684(NZB)[17],PC7940(NZB)[18],PC7175(NZB)[19], PC2485(NZB)[20],PC4039(NZB)[21],PC7210(NZB)[23],H36-15[26],2242[29],V-21E1.5KB'CL[30],V-21C9.5KB'CL[31], PC7461(NZB)[33],PC2960(NZB)[34],97.C(A.BY)[35],10.A(A.TH)[39],H36-5[48],40.C(A.TH)[52],MOPC63[54],ABPC22[55], PC9245(NZB)[56],PC4050(NZB)[57],V-21S16KB'CL[58],11949[62]; 1 MOUSE V-KAPPA-VI: BFPC61A'CL[64]; AND 15 RABBIT V-KAPPA: K9-335-I[19],3368[20],BS-5[38],BS-1[39],K49-501[45],3547[47],K4820[57],K30-267[61],311[65],4422[66],17D9'CL[68], 4192[71],4363[85],120[103],K-25[112].)

FR3: SET 1: VJI'CL[1],VKAPPA IV GERMLINE'CL[2],PB17IV'CL[3],LEN[4]. (4 IDENTICAL)

FR4: SET 1: PB17IV'CL[3]. (IDENTICAL TO 3 HUMAN V-KAPPA-I: AU[2],GAL(I)[36],CL*[110]; 2 HUMAN V-KAPPA-II: GM 607 'CL[5], RPM1-6410'CL[16]; AND 7 HUMAN V-KAPPA-III: WOL[2],PAY[7],PIE[11],GLO[15],CUR[20],REE[57],VKAPPA3'CL[82].)
SET 2: LEN[4]. (IDENTICAL TO 3 HUMAN V-KAPPA-I: AG[7],DEN[46],BI[63]; 2 HUMAN V-KAPPA-II: NIM[3],FR[14]; AND 6 HUMAN V-KAPPA-III: NEU[5],GOT[6],GAR'[10],FLO[12],FR4[21],IARC/BL41'CL[28].)
SET 3: VJI'CL[1]. (IDENTICAL TO 1 HUMAN V-KAPPA-III: SON[8].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1: SET 1: VJI'CL[1],VKAPPA IV GERMLINE'CL[2]. (2 IDENTICAL)

CDR2: SET 1: VJI'CL[1],VKAPPA IV GERMLINE'CL[2],PB17IV'CL[3],LEN[4]. (4 IDENTICAL HUMAN V-KAPPA-IV; ALSO 1 MOUSE V-KAPPA-VI: KPNI6 'CL[70].)

CDR3:

IDENTICAL SETS OF J-MINIGENES:

SET 1: PB17IV'CL[3]. (IDENTICAL TO 1 HUMAN V-KAPPA-I: AU[2]; 1 HUMAN V-KAPPA-II: RPM1-6410'CL[16]; AND 2 HUMAN V-KAPPA-III: PIE[11],VKAPPA3'CL[82].)

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
22	(SER,ASP,ASN)
96	(TRP,TYR)
104	(LEU,VAL)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP I

		INVARIANT RESIDUES	1 NEWM	2 HA	3 LR	4 NIG -64	5 NEW	6 BL2 CL	7 WAH	8 NIG -77	9 VOR	10 RHE	11 LOC	12 OKA	13 AMYLOID EPS	14 HBJ 7	15 COX	16 KOH	17 HS 92	18 HS 78	19 NIG -51	20 HS 94	21 HBJ 11	22 BJ 98	23 MZ
	0		---	---	---	---	---	---	---	---	---	---	---	---		---	---	---	---	---	---	---	---	---	
	1	PCA(.95)	PCA	PCA	PCA	PCA	PCA	gln	PCA	PCA	PCA	PCA	PCA	PCA		PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA		
	2	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER	SER	SER	SER	SER	SER		
	3	VAL(.95)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ala	VAL	VAL	VAL		
	4	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		
	5	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	
	6	GLN(.95)	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN		GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN		
	7	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		
	9	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		
FR1	10		---	---	---	---	---	---	---	---	---	---	---	---		---	---	---	---	---	---	---	---		
	11		VAL	VAL	VAL	VAL	VAL	VAL	ala	ala	ala	ala	ala	ala	leu	ala	ala	ala	VAL	VAL	ala	VAL	ala		
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	ala	SER	SER	
	13		GLY	GLY	GLY	ala	ala	ala	GLY	GLY	GLY	GLY	GLY	GLY	ala	GLY	GLY	thr	GLY	GLY	GLY	ala	GLY	ala	
	14		ALA	thr	ALA	ALA	ALA	ALA	thr	thr	thr	thr	thr	thr	ALA	thr	thr	thr	ALA	ALA	val	ALA	thr	ALA	
	15	PRO(.95)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	ser	PRO	PRO	PRO	PRO	PRO	PRO		
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		
	17		GLN	GLN	glu	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN	GLN	GLN		
	18		ARG	ARG	ARG	glu	lys	lys	ARG	ARG	ARG	ARG	ARG	ARG	ARG	gly	ARG	ser	ARG	thr	ser	ARG	ARG		
	19	VAL(.95)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		VAL	VAL			VAL	ala
	20		THR	THR	glu	THR	THR	THR	THR	THR	THR	THR	THR	THR	ser	THR	THR	THR		THR	ile			THR	ile
	21	ILE(.95)	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE			ILE			ser	ILE
	22	SER(.95)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER			SER			ile	SER
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS				CYS			CYS	CYS
	24		THR	SER	SER	SER	SER	SER	PHE	SER	SER	THR	SER	SER	SER	SER	SER				SER				SER
	25	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY				GLY				GLY
	26		SER	GLY		SER	GLY	SER	SER	SER	GLY	SER	SER	SER		SER	SER				SER				SER
	27		SER	SER		SER	SER	SER	SER	THR	ASN	ALA	SER	GLY	SER		SER				SER				SER
	27A		---	---		---	---	---	---	---	---	---	---	---	---		---				---				---
	27B		---	---		---	---	---	---	---	---	---	---	---	---		---				---				---
CDR1	27C		---	---		---	---	---	---	---	---	---	---	---	---		---				---				---
	27D		SER	SER		SER	THR	SER	SER	SER	PHE	THR	SER	SER	---		SER				SER				SER
	27E		ASN	ASN		ASN	ASN	ASN	ASN	ASN	ASP	ASP	ASN	ASN	SER		ASN				ASN				ASN
	27F		ILE	GLY		---	---	---	---	---	---	---	ILE	---	ASN		---				---				---
	28		GLY	THR		ILE	ILE	ILE	ILE	ILE	ILE	ILE	GLY	ILE	ILE		LEU				ILE				MET
	29		ALA	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLU	GLY	GLY		GLY				GLY				
	30		GLY	ASN		ASP	ASN	ASN	ARG	SER	ARG	SER	THR	SER	LYS		SER				ARG				
	31		ASN	ASN		ASN	ASN	ASP	TYR	ASN	ASN	ASN	ASN	HIS	ASN		ASN				ASN				
	32		HIS	TYR		PHE	TYR	TYR	TYR	THR	SER	SER	SER	THR	TYR		GLN				THR				
	33	VAL	VAL	VAL		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		VAL				VAL				
	34		LYS	TYR		SER	SER	SER	TYR	THR	ASN	ILE	SER	ASN	ASP		ASN				ASN				
	35	TRP	TRP	TRP		TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP		TRP				TRP				
	36		TYR	TYR		TYR	HIS	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR				TYR				
	37		GLN	GLN		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	HIS	GLN		ARG				GLN				
	38		GLN	GLN		GLN	HIS	GLN	GLN	HIS	VAL	GLN	HIS	GLN	GLN		HIS				GLN				
	39		LEU	LEU		LEU	LEU	VAL	LEU	LEU	HIS	VAL	LEU	PHE	LEU		LEU				VAL				
	40	PRO	PRO	PRO		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO				PRO				
FR2	41	GLY	GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
	42		THR	THR		THR	THR	THR	THR	THR	THR	LYS	THR	THR	THR		THR				ALA				
	43		ALA	ALA		ALA	ALA	ALA	THR	ALA	ALA	ALA	ALA	ALA	ALA		ALA				ALA				
	44	PRO	PRO	PRO		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO				PRO				
	45		LYS	LYS		LYS	LYS	LYS	LYS	LYS	ARG	LYS	LYS	LYS	LYS		LYS				LYS				
	46	LEU	LEU	LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU				LEU				
	47		LEU	LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		VAL				LEU				
	48		ILE	ILE		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE				VAL				
	49		PHE	TYR		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	PHE		TYR				TYR				
	50		HIS	ARG		ASP	GLU	ASP	LYS	SER	SER	TYR	GLU	ARG	ASN		SER				SER				
	51		ASN	ASP		ASN	ASP	ASN	ASP	ASN	SER	ASN	ASP	ASN	ASN		ASP				ASN				
CDR2	52		ASN	ASP		ASN	ASN	ASN	ASN	ASP	ASP	ASP	ASN	ASP	ASN		SER				ASN				
	53		ALA	LYS		LYS	LYS	LYS	GLN	GLN	GLN	LEU	SER	GLN	LYS		GLN				GLN				
	54		ARG	ARG		ARG	ARG	ARG	ARG	ARG	ARG	LEU	ARG	ARG	ARG		ARG				TRP				
	55		---	PRO		PRO	PRO	PRO	PRO	PRO	SER	PRO	ALA	PRO			PRO				PRO				
	56	SER	---	SER		SER	SER	SER	SER	SER	SER	SER	SER	SER			SER				SER				
	57	GLY	---	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY			GLY				GLY				
	58		---	VAL		ILE	ILE	ILE	VAL	VAL	VAL	VAL	VAL	VAL			VAL				VAL				
	59		---	PRO		PRO	PRO	PRO	PRO	PRO	PRO	SER	SER	PRO			PRO				PRO				
	60		---	ASP		ASP	ASP	ASP	ASP	HIS	ASP	ASP	ASP	ASP			ASP				ASP				
	61	ARG	---	ARG		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG		ARG				ARG				
	62		PHE	PHE		PHE	ILE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE		ILE				PHE				
	63	SER	SER	SER		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER				SER				
	64		VAL	GLY		GLY	ALA	GLY	GLY	GLY	GLY	ALA	ALA	GLY	GLY		ALA				GLY				
	65	SER	SER	SER		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER				SER				
	66	LYS	LYS	LYS		LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS		LYS				LYS				
	67	SER	SER	SER		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER				SER				
	68	GLY	GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
	69		SER	THR		THR	THR	THR	THR	ALA	THR	THR	THR	THR	THR		THR				THR				
	70	SER	SER	SER		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER				SER				
FR3	71	ALA	ALA	ALA		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA		ALA				ALA				
	72		THR	SER		THR	THR	THR	SER	SER	SER	SER	SER	SER	THR		SER				SER				
	73	LEU	LEU	LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU				LEU				
	74		ALA	ALA		GLY	ALA	GLY	ALA	ALA	ALA	ALA	ALA	ALA	GLY		ALA				ALA				
	75	ILE	ILE	ILE		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE				ILE				
	76		THR	SER		THR	THR	THR	SER	SER	SER	SER	SER	SER	THR		SER				SER				
	77	GLY	GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
	78	LEU	LEU	LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU				LEU				
	79		GLN	ARG		GLN	ARG	GLN	ARG	GLN	GLN	GLU	GLN	GLN	GLN		GLN				HIS				
	80		ALA	SER		THR	THR	THR	SER	SER	SER	SER	PRO	SER	THR		SER				SER				
	81		GLU	GLU		GLY	GLY	GLY	GLU	GLU	GLU	GLU	GLU	GLU	GLY		GLU				GLU				
	82		ASP	ASP		ASP	ASP	ASP	ASP	ASP	ASN	ASP	ASP	ASP	ASP		ASP				ASP				
	83	GLU	GLU	GLU		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU		GLU				GLU				
	84		ALA	ALA		ALA	ALA	ALA	ALA	THR	ALA	ALA	THR	ALA	ALA		SER				ALA				
	85		ASP	HIS		ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ILE		ASP				ASP				
	86	TYR	TYR	TYR		TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR		TYR				TYR				
	87		TYR	HIS		TYR	TYR	TYR	TYR	TYR	PHE	TYR	TYR	TYR	TYR		TYR				PHE				
	88	CYS	CYS	CYS		CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		CYS				CYS				
	89		GLN	ALA		GLY	ALA	GLY	ALA	ALA	ALA	ALA	ALA	ALA	GLY		ALA				ALA				
	90		SER	ALA		THR	THR	THR	ALA	THR	THR	ALA	ALA	ALA	THR		SER				THR				
	91		TYR	TRP		TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TYR		TRP				TRP				
	92		ASP	ASP		ASP	ASP	ASN	ASP	ASP	ASP	ASN	ASP	ASP	ASP		ASP				ASP				
	93		ARG	TYR		SER	SER	ASN	ASP	ASP	ASP	ASP	ASP	ASP	ASN		ASP				ASP				
	94		SER	ARG		SER	SER	SER	SER	SER	SER	SER	SER	SER	ARG		SER				SER				
CDR3	95		LEU	LEU		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	ARG		LEU				LEU				
	95A		---	SER		SER	ASN	SER	---	ASN	ASP	ASP	ASP	ASP	---		ASP				ASP				
	95B		---	ALA		VAL	ALA	GLY	---	GLY	GLY	GLU	VAL	GLY	---		GLY				GLY				
	95C		---	---		---	---	---	---	---	---	---	---	---	---		---				---				
	95D		---	---		---	---	---	---	---	---	---	---	---	---		---				---				
	95E		---	---		---	---	---	---	---	---	---	---	---	---		---				---				
	95F		---	---		---	---	---	---	---	---	---	---	---	---		---				---				
	96		ARG	VAL		GLY	VAL	TRP	TRP	PRO	PRO	PRO	ALA	PRO	SER		PRO				PRO				
	97		VAL	VAL		MET	VAL	VAL	VAL	VAL	VAL	GLY	VAL	VAL	VAL		VAL				VAL				
	98	PHE	PHE	PHE		PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE		PHE				PHE				
	99	GLY	GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
	100		GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	THR	GLY	GLY		GLY				GLY				
	101	GLY	GLY	GLY		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
FR4	102	THR	THR	THR		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR		THR				THR				
	103		LYS	GLN		ARG	LYS	LYS	THR	LYS	LYS	LYS	LYS	LYS	ASN		LYS				LYS				
	104		LEU	LEU		VAL	VAL	LEU	LEU	VAL	VAL	LEU	VAL	LEU	VAL		VAL				LEU				
	105	THR	THR	THR		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR		THR				THR				
	106	VAL	VAL	VAL		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		VAL				VAL				
	106A		LEU	LEU		LEU	LEU	LEU	LEU	GLN	LEU	LEU	LEU	LEU	VAL		LEU				LEU				
	107		ARG	ARG		GLY	GLY	GLY	SER	GLY	GLY	GLY	GLY	GLY	GLY		GLY				GLY				
	108	GLN	GLN	GLN			GLN		GLN	GLN	GLN	GLN	GLN	GLN	GLN		GLN				GLN				
	109	PRO	PRO	PRO			PRO		PRO	PRO	PRO	PRO	PRO	PRO	PRO		PRO				PRO				

HUMAN LAMBDA LIGHT CHAINS SUBGROUP I (cont'd)

		24 FUL #	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0		20	2	19(PCA)	2.1
	1		20	1	20(SER)	1.
	2		21	2	20(VAL)	2.1
	3		21	1	21(LEU)	1.
	4					
	5		22	1	22(THR)	1.
	6		21	1 : 2	21(GLN) : 20(GLN)	1. : 2.1
	7		21	1	21(PRO)	1.
	8		21	1	21(PRO)	1.
	9		21	1	21(SER)	1.
	10					
FR1	11		21	3	11(ALA)	5.7
	12		22	1	22(SER)	1.
	13		22	2	16(GLY)	2.8
	14		22	3	11(THR)	6.
	15		21	2	20(PRO)	2.1
	16		21	1	21(GLY)	1.
	17		21	2	20(GLN) : 19(GLN)	2.1 : 2.2
	18		21	6	14(ARG)	9.
	19		20	2	19(VAL)	2.1
	20		20	4	16(THR)	5.
	21		19	2	18(ILE)	2.1
	22		19	2	18(SER)	2.1
	23	CYS	19	1	19(CYS)	1.
	24	SER	18	3	15(SER)	3.8
	25	GLY	18	1	18(GLY)	1.
	26	ASN	17	3	13(SER)	3.9
	27	SER	16	5	12(SER)	6.7
	27A	---				
	27B	---				
	27C	---				
CDR1	27D	SER	15	3	12(SER)	
	27E		15	3	12(ASN)	
	27F		4	3	2(ILE)	
	28		15	5	10(ILE)	7.5
	29		14	3	12(GLY)	3.5
	30		14	7	4(SER)	25.
	31		14	4	11(ASN)	5.1
	32		14	6	5(TYR)	17.
	33		14	1	14(VAL)	1.
	34		14	7	4(+)	25.
	35		14	1	14(TRP)	1.
	36		14	2	13(TYR)	2.2
	37		14	3	12(GLN)	3.5
	38		14	3	9(GLN)	4.7
	39		14	4	9(LEU)	6.2
	40		14	1	14(PRO)	1.
FR2	41		14	1	14(GLY)	1.
	42		14	3	12(THR)	3.5
	43		14	2	13(ALA)	2.2
	44		14	1	14(PRO)	1.
	45		14	2	13(LYS)	2.2
	46		14	1	14(LEU)	1.
	47		14	2	13(LEU)	2.2
	48		14	2	13(ILE)	2.2
	49		14	2	12(TYR)	2.3
	50		14	6	4(SER)	28.
	51		14	3	8(ASN)	5.3
CDR2	52		14	3	8(ASN)	5.3
	53		14	5	6(GLN)	12.
	54		14	3	12(ARG)	3.5
	55		12	3	10(PRO)	3.6
	56		12	1	12(SER)	1.
	57		12	1	12(GLY)	1.
	58		12	2	9(VAL)	2.7
	59		12	2	10(PRO)	2.4
	60		12	2	11(ASP)	2.2
	61		13	1	13(ARG)	1.
	62		14	2	12(PHE)	2.3
	63		14	1	14(SER)	1.
	64		14	3	9(GLY)	4.7
	65		14	1	14(SER)	1.
	66		14	1	14(LYS)	1.
	67		14	1	14(SER)	1.
	68		14	1	14(GLY)	1.
	69		14	3	12(THR)	3.5
	70		14	1	14(SER)	1.
	71		14	1	14(ALA)	1.
FR3	72		14	2	9(SER)	3.1
	73		14	1	14(LEU)	1.
	74		14	2	11(ALA)	2.5
	75		14	1	14(ILE)	1.
	76		14	2	9(SER)	3.1
	77		14	1	14(GLY)	1.
	78		14	1	14(LEU)	1.
	79		14	4	9(GLN)	6.2
	80		14	4	8(SER)	7.
	81		14	2	10(GLU)	2.8
	82		14	2	13(ASP)	2.2
	83		14	1	14(GLU)	1.
	84		14	3	11(ALA)	3.8
	85		14	3	12(ASP)	3.5
	86		14	1	14(TYR)	1.
	87		14	3	11(TYR)	3.8
	88		14	1	14(CYS)	1.
	89		14	3	10(ALA)	4.2
	90		14	3	7(THR)	6.
	91		14	2	12(TRP)	2.3
	92		14	2	12(ASP)	2.3
	93		14	5	8(ASP)	8.8
	94		14	2	12(SER)	2.3
	95		14	2	13(LEU)	2.2
CDR3	95A		11	3	6(ASP)	
	95B		11	4	6(GLY)	
	95C					
	95D					
	95E					
	95F					
	96		14	7	6(PRO)	16.
	97		14	3	12(VAL)	3.5
	98		14	1	14(PHE)	1.
	99		14	1	14(GLY)	1.
	100		14	2	13(GLY)	2.2
	101		14	1	14(GLY)	1.
	102		14	1	14(THR)	1.
	103		14	5	10(LYS)	7.
FR4	104		14	2	7(+)	4.
	105		14	1	14(THR)	1.
	106		14	1	14(VAL)	1.
	106A		14	3	12(LEU)	
	107		14	3	11(GLY)	3.8
	108		12	1	12(GLN)	1.
	109		12	1	12(PRO)	1.

ANTIBODY SPECIFICITIES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP I

1) **NEWM:** ANTI-3-(3'-HYDROXY-3',7',11',15'-TETRAMETHYL HEXADECYL) 2-METHYL 1,4 NAPHTHOQUINONE(VIT.K1OH)
16) **KOH:** ANTI-HUMAN GAMMA G GLOBULIN

REFERENCE: HUMAN LAMBDA LIGHT CHAINS SUBGROUP I

1) **NEWM:** CHEN,B.L. & POLJAK,R.J. (1974) BIOCHEMISTRY,13,1295-1302. (CHECKED BY AUTHOR 01/24/78)
2) **HA:** SHINODA,T.,TITANI,K. & PUTNAM,F.W. (1970) J.BIOL.CHEM.,245,4475-4487. (CHECKED BY AUTHOR 06/15/83)
3) **LR:** CAULIN-GLASER,T.,PRELLI,F. & FRANKLIN,E.C. (1982) J.LAB.CLIN.MED.,99,845-851. (CHECKED BY AUTHOR 12/10/82)
4) **NIG-64:** TONOIKE,H.,KAMETANI,F.,HOSHI,A.,SHINODA,T. & ISOBE,T. (1985) BIOCHEM.BIOPHYS.RES.COMMUN.,126,1228-1234.
5) **NEW:** LANGER,B.,STEINMETZ-KAYNE,M. & HILSCHMANN,N. (1968) Z.PHYSIOL.CHEM.,349,945-951.
6) **BL2 'CL:** TSUJIMOTO,Y. & CROCE,C.M. (1984) NUC.ACIDS RES.,12,8407-8414.
7) **WAH:** TAKAHASHI,Y.,TAKAHASHI,N.,TETAERT,D. & PUTNAM,F.W. (1983) PROC.NAT.ACAD.SCI.USA,80,3686-3690. (CHECKED BY AUTHOR 06/15/83)
8) **NIG-77:** TONOIKE,H.,KAMETANI,F.,HOSHI,A.,SHINODA,T. & ISOBE,T. (1985) BIOCHEM.BIOPHYS.RES.COMMUN.,126,1228-1234.
9) **VOR:** ENGELHARD,M.,HESS,M. & HILSCHMANN,N. (1974) Z.PHYSIOL.CHEM.,355,85-88; ENGELHARD,M. & HILSCHMANN,N. (1975) Z.PHYSIOL.CHEM.,356, 1413-1444.
10) **RHE:** FUREY,W. JR.,WANG,B.C.,YOO,C.S. & SAX,M. (1983) J.MOL.BIOL.,167,661-692. (CHECKED BY AUTHOR 05/15/84)
11) **LOC:** ZHU,D.,KIM,H.S. & DEUTSCH,H.F. (1983) MOL.IMMUNOL.,20,1107-1116.
12) **OKA:** ZHU,D.,KIM,H.S. & DEUTSCH,H.F. (1983) MOL.IMMUNOL.,20,1107-1116.
13) **AMYLOID EPS:** TOFT,K.G.,SLETTEN,K. & HUSBY,G. (1985) BIOL.CHEM.HOPPE-SEYLER,366,617-625.
14) **HBJ7:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.
15) **COX:** ZHU,D.,KIM,H.S. & DEUTSCH,H.F. (1983) MOL.IMMUNOL.,20,1107-1116.
16) **KOH:** KAPLAN,A.P. & METZGER,H. (1969) BIOCHEMISTRY,8,3944-3951.
17) **HS92:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767; (1968) SCIENCE,1662,679-681.
18) **HS78:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767; (1968) SCIENCE,1662,679-681.
19) **NIG-51:** TAKAHASHI,N.,TAKAYASU,T.,SHINODA,T.,ITO,S.,OKUYAMA,T. & SHIMIZU,A. (1980) BIOMED.RES.,1,321-333. (CHECKED BY AUTHOR 01/28/81)
20) **HS94:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767; (1968) SCIENCE,1662,679-681.
21) **HBJ11:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.
22) **BJ98:** BAGLIONI,C. (1967) BIOCHEM.BIOPHYS.RES.COMMUN.,26,82-89.
23) **MZ:** MILSTEIN,C.,FRANGIONE,B. & PINK,J.R.L. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,31-36. (CHECKED BY AUTHOR 10/17/77)
24) **FUL:** SOX,H.C.,JR. & HOOD,L. (1970) PROC.NAT.ACAD.SCI.USA,66,975-982.

NOTES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP I

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: WAH[7],NIG-77[8],VOR[9],RHE[10],LOC[11],OKA[12]. (6 IDENTICAL)

FR2: SET 1: NEWM[1],AMYLOID EPS[13]. (2 IDENTICAL)
SET 2: HA[2],NIG-64[4]. (2 IDENTICAL)
SET 3: NIG-77[8],LOC[11]. (2 IDENTICAL)

FR3: SET 1: NIG-64[4],BL2 'CL[6]. (2 IDENTICAL)

FR4: SET 1: NEWM[1]. (IDENTICAL TO 1 HUMAN V-LAMBDA-II: WH[3]; AND 1 HUMAN V-LAMBDA-V: BO[1].)
SET 2: NEW[5],VOR[9],COX[15]. (3 IDENTICAL HUMAN V-LAMBDA-I; ALSO 1 HUMAN V-LAMBDA-VI: AMYLOID-AR[1]; AND 6 MOUSE V-LAMBDA: MOPC315[25],TEPC952[26],MA8-13[27],S-7[29],MOPC315-26'CL'[30],MOPC315-37'CL[32].)
SET 3: BL2 'CL[6],RHE[10],OKA[12],NIG-51[19]. (4 IDENTICAL HUMAN V-LAMBDA-I; ALSO 5 HUMAN V-LAMBDA-II: MES[2],ES492[8],TRO[14], VIL[17],WIN[21]; 4 HUMAN V-LAMBDA-III: HIL[1],CAP[4],BAU[12],DEL[14]; 1 HUMAN V-LAMBDA-IV: SH[1]; 3 HUMAN V-LAMBDA-VI: SUT[2],THO[4],LBV'CL[5]; AND 24 MOUSE V-LAMBDA: MOPC104E[1],J558[2],XS104[3],HOPC1[4],J698[5],H2061[6],W3159[7], Y5431[8],Y5485[9],Y5830[10],Y5669[11],MOPC511(L)[12],S178[13],Y5444[14],Y5606[15],S176[16],H2020[17],RPC20[18],IG 303LAMBDA'CL[19],S43'CL[21],S2H5'CL[38],S2E9'CL[39],S1F12'CL[40],IG 25LAMBDA'CL[41].)
SET 4: LOC[11]. (IDENTICAL TO 1 HUMAN V-LAMBDA-V: MCG[3].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1:

CDR2: SET 1: NIG-64[4],BL2 'CL[6]. (2 IDENTICAL)

CDR3: SET 1: VOR[9],NIG-51[19]. (2 IDENTICAL)

IDENTICAL SETS OF J-MINIGENES:

SET 1: NEW[5]. (IDENTICAL TO 1 HUMAN V-LAMBDA-VI: AMYLOID-AR[1].)
SET 2: BL2 'CL[6]. (IDENTICAL TO 2 HUMAN V-LAMBDA-VI: SUT[2],THO[4]; AND 24 MOUSE V-LAMBDA: MOPC104E[1],J558[2],XS104[3],HOPC1[4], J698[5],H2061[6],W3159[7],Y5431[8],Y5485[9],Y5830[10],Y5669[11],MOPC511(L)[12],S178[13],Y5444[14],Y5606[15],S176[16], H2020[17],RPC20[18],IG 303LAMBDA'CL[19],S43'CL[21],S2H5'CL[38],S2E9'CL[39],S1F12'CL[40],IG 25LAMBDA'CL[41].)
SET 3: VOR[9],COX[15]. (2 IDENTICAL)
SET 4: OKA[12],NIG-51[19]. (2 IDENTICAL)

SPECIFIC NOTES:

24) **FUL:** SOX AND HOOD HAVE REPORTED FOUR HUMAN V KAPPA AND ONE V LAMBDA CHAINS WITH ASN-SER/THR TO CONTAIN CARBOHYHDRATE.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
34	(SER,ASN)
104	(LEU,VAL)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP II

		INVARIANT RESIDUES	1 NIG -84	2 MES	3 WH /	4 NEI	5 KAR	6 RIM	7 SLA	8 ES492	9 WEIR	10 TOG	11 SM #	12 HS 68	13 HS 77	14 TRO	15 BOH	16 NIG -58	17 VIL	18 HBJ 15	19 HBJ 8	20 HS 70	21 WIN	22 BUR	23 PRE	24 HS 86
	0		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1		PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	his	PCA	PCA	PCA	PCA	PCA	PCA	PCA
	2	SER(.96)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	3		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	pro
	4	LEU(.96)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	5		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	ala	ser	THR	THR	THR	ala
	6	GLN(.96)	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN
	7		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	ser	PRO
	8		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	arg	arg	arg	ALA	ALA	ALA	ALA	pro	arg	pro	ALA
	9	SER(.96)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	arg	SER	SER	SER
FR1	10		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	11		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ala	VAL
	12	SER(.96)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	ala	glu	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	14	SER(.96)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	15	PRO(.96)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	leu	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	his	GLN	glu
	18		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	thr	SER	SER	SER	SER	SER	SER	SER
	19		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	val	leu	ILE	ILE	ILE	ILE	val	val	val	ILE
	20	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR
	21		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	val	ILE	ILE			ILE	ILE	ILE	ILE				ILE	ILE	ILE	
	22		SER	SER	SER	SER	SER	SER	SER		SER	SER	SER			SER	SER	SER	SER				SER	SER	SER	
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		CYS	CYS	CYS			CYS	CYS	CYS	CYS				CYS	CYS	CYS	
	24		THR	THR	THR	THR				ALA	ALA	THR	THR			THR	ALA	SER	THR				THR	ILE		
	25		GLY	GLY	GLY	GLY				GLY	GLY	GLY	GLY			GLY	GLY	GLY	GLY				GLY	GLY		
	26		THR	THR	THR	THR				THR	HIS	THR	ASX			THR	THR	ALA	THR				SER	THR		
	27		THR	SER	SER	THR				HIS	THR	THR	SER			SER	SER	PRO	SER				TYR	SER		
	27A		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	27B		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
CDR1	27C		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	27D		SER	SER	SER	SER				SER	SER	ASN	SER			SER	SER	CYS	SER				SER	SER		
	27E		ASP	ASP	ASP	ASP				ASP	ASP	ASP	VAL			ASP	ASP	ASP	ASP				ASN	ASN		
	27F		VAL	VAL	VAL	VAL				VAL	VAL	ILE	VAL			VAL	VAL	VAL	VAL				VAL	VAL		
	28		GLY	GLY	GLY	GLY				ASN	ALA	GLY	GLY			GLY	GLY	ASP	GLY				THR	GLY		
	29		GLY	GLY	SER	SER				PHE	ASP	SER	---			ALA	GLY	GLY	GLY				GLY	ASP		
	30		TYR	TYR	TYR	TYR				THR	SER	TYR	---			TYR	ASN	CYS	TYR				TYR	TYR		
	31		ASP	ASN	ASN	ASN				ASX	ASN	SER	---			ASN	HIS	GLU	ASN				ASN	LYS		
	32		PHE	TYR	PHE	PHE				ALA	SER	TYR	---			SER	PHE	SER	TYR				HIS	TYR		
	33		VAL	VAL	VAL	VAL					ILE	VAL	---			VAL	VAL	VAL	VAL				VAL	VAL		
	34		SER	SER	SER	SER					SER	SER	---			SER	SER	SER	SER				SER	SER		
	35	TRP	TRP	TRP	TRP	TRP				TRP	TRP	TRP	---			TRP	TRP	TRP	TRP				TRP	TRP		
	36		TYR	PHE	TYR	TYR				TYR	PHE	TYR	---			TYR	TYR	TYR	PHE				TYR	TYR		
	37		GLN	GLN	GLN	GLN				GLN	GLN	GLN	---			GLN	GLN	GLN	GLN				GLN	GLX		
	38		GLN	GLN	GLN	GLN				LEU	GLN	GLN	---			GLN	GLN	GLN	GLN				GLN	GLX		
	39		HIS	HIS	HIS	ASN				HIS	HIS	TYR	---			HIS	HIS	HIS	HIS				ASP	HIS		
	40	PRO	PRO	PRO	PRO	PRO				PRO	PRO	PRO	---			PRO	PRO	PRO	PRO				PRO	PRO		
	41		GLY	GLY	GLY	GLY				GLY	ASP	GLY	---			GLY	GLY	GLY	GLY				GLY	GLY		
FR2	42		LYS	LYS	LYS	LYS				ILE	LYS	LYS	---			LYS	LYS	LYS	THR				LYS	LYS		
	43		ALA	ALA	ALA	ALA				ALA	ALA	ALA	---			ALA	ALA	ALA	ALA				VAL	ALA		
	44	PRO	PRO	PRO	PRO	PRO				PRO	PRO	PRO	---			PRO	PRO	PRO	PRO				PRO	PRO		
	45		LYS	LYS	LYS	LYS				LYS	LYS	LYS	---			LYS	LYS	LYS	LYS				LYS	LYS		
	46		LEU	LEU	LEU	LEU				LEU	LEU	VAL	---			LEU	LEU	LEU	LEU				LEU	LEU		
	47		LEU	MET	ILE	MET				MET	LEU	LEU	---			MET	ILE	ILE	ILE				MET	ILE		
	48	ILE	ILE	ILE	ILE	ILE				ILE	ILE	ILE	---			ILE	ILE	ILE	ILE				ILE	ILE		
	49		TYR	PHE	TYR	TYR				PHE	TYR	PHE	---			PHE	TYR	TYR	SER				TYR	TYR		
	50		ASP	ASP	ASP	GLU				ASP	ALA	ASP	---			ASP	GLY	GLY	GLU				ASP	GLU		
	51		VAL	VAL	VAL	GLY				VAL	VAL	VAL	---			VAL	VAL	PHE	VAL				VAL	VAL		
	52		ASN	SER	THR	ASN				SER	THR	ASN	---			THR	ASN	SER	ARG				ASP	SER		
	53		SER	GLU	TYR	LYS				ASN	PHE	SER	---			LYS	LYS	ASN	ASN				LYS	SER		
CDR2	54		ARG	ARG	ARG	ARG				ARG	ARG	ARG	---			ARG	ARG	ARG	ARG				ARG	ARG		
	55		PRO	PRO	PRO	PRO				PRO	PRO	PRO	---			PRO	PRO	PRO	PRO				PRO	PRO		
	56	SER	SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER				SER	SER		
	57		GLY	GLY	GLY	GLY				GLY	GLY	GLY	---			GLY	GLY	GLY	GLY				GLY	GLY		
	58		ILE	VAL	ILE	VAL				VAL	ILE	VAL	---			VAL	VAL	VAL	VAL				VAL	VAL		
	59		SER	SER	SER	SER				SER	PRO	SER	---			PRO	PRO	PRO	SER				PRO	PRO		
	60		ASN	ASP	SER	ASN				ASN	LEU	HIS	---			ASP	TYR	LEU	ASP				ASP	ASP		
	61	ARG	ARG	ARG	ARG	ARG				ARG	ARG	ARG	---			ARG	ARG	ARG	ARG				ARG	ARG		
	62		PHE	PHE	PHE	PHE				PHE	PHE	PHE	---			LEU	PHE	PHE	PHE		PHE		PHE	PHE		
	63	SER	SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER		SER		SER	SER		
	64	GLY	GLY	GLY	GLY	GLY				GLY	GLY	GLY	---			GLY	GLY	GLY	GLY		GLY		GLY	GLY		
	65	SER	SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER		SER		SER	SER		
	66		LYS	LYS	ARG	LYS				LYS	LYS	LYS	---			LYS	LYS	LYS	LYS		LYS		LYS	LYS		
	67		SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER				SER	SER		
	68		GLY	GLY	GLY	GLY				GLY	GLY	GLY	---			GLY	GLY	GLY	ALA				ALA	GLY		
	69		ASN	ASN	ASN	LYS				ASN	ASN	ASN	---			ASP	ASN	ASP	ASN				ASN	ASX		
	70		THR	THR	THR	THR				THR	THR	THR	---			THR	THR	ALA	THR				THR	THR		
	71	ALA	ALA	ALA	ALA	ALA				ALA	ALA	ALA	---			ALA	ALA	ALA	ALA				ALA	ALA		
FR3	72		SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER				SER	SER		
	73	LEU	LEU	LEU	LEU	LEU				LEU	LEU	LEU	---			LEU	LEU	LEU	LEU				LEU	LEU		
	74	THR	THR	THR	THR	THR				THR	THR	THR	---			THR	THR	THR	THR				THR	THR		
	75		ILE	ILE	ILE	ILE				ILE	ILE	ILE	---			ILE	ILE	ILE	ILE				ILE	ILE		
	76	SER	SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER				SER	SER		
	77	GLY	GLY	GLY	GLY	GLY				GLY	GLY	GLY	---			GLY	GLY	GLY	GLY				GLY	GLY		
	78		LEU	LEU	LEU	LEU				LEU	LEU	LEU	---			LEU	LEU	LEU	LEU				LEU	LEU		
	79		GLN	GLN	GLN	GLN				GLN	LEU	GLN	---			ARG	GLN	GLN	GLN				GLN	GLN		
	80		ALA	ALA	ALA	VAL				ALA	PRO	ALA	---			ALA	ALA	VAL	ALA				ALA	ALA		
	81		GLU	GLU	GLU	GLU				GLU	ASP	GLU	---			ASP	GLU	GLU	GLU				ASN	GLU		
	82		ASP	ASP	ASP	ASP				ASP	ASP	ASP	---			ASP	ASP	ASP	ASP				ASN	ASP		
	83	GLU	GLU	GLU	GLU	GLU				GLU	GLU	GLU	---			GLU	GLU	GLU	GLU				GLU	GLU		
	84	ALA	ALA	ALA	ALA	ALA				ALA	ALA	ALA	---			ALA	ALA	ALA	ALA				ALA	ALA		
	85		ASP	ASP	ASP	ASP				ASP	ASP	HIS	---			ASP	HIS	ASP	ASP				ASP	ASX		
	86	TYR	TYR	TYR	TYR	TYR				TYR	TYR	TYR	---			TYR	TYR	TYR	TYR				TYR	TYR		
	87		TYR	TYR	TYR	TYR				TYR	PHE	PHE	---			TYR	TYR	TYR	TYR				TYR	TYR		
	88	CYS	CYS	CYS	CYS	CYS				CYS	CYS	CYS	---			CYS	CYS	CYS	CYS				CYS	CYS		
	89		SER	SER	SER	CYS				SER	MET	SER	---			CYS	CYS	SER	SER				SER	CYS		
	90		SER	SER	SER	SER				SER	SER	SER	---			SER	SER	SER	SER				SER	SER		
	91		PHE	TYR	TYR	TYR				PHE	TYR	TYR	---			TYR	TYR	TYR	TYR				TYR	TYR		
	92		THR	ALA	THR	ALA				THR	LEU	ARG	---			ALA	ALA	ALA	THR				GLY	ILE		
	93		THR	GLY	SER	GLY				ASP	SER	THR	---			GLY	GLY	ASP	SER				GLY	GLY		
	94		THR	SER	ASX	ASX				THR	ASP	SER	---			ARG	ARG	SER	SER				THR	SER		
	95		ASN	ASN	SER	SER				THR	ALA	GLY	---			TYR	PHE	SER	ASN				TYR	---		
	95A		SER	THR	THR	THR				GLN	SER	THR	---			SER	THR	---	SER				SER	---		
CDR3	95B		ARG	---	---	---				LEU	---	---	---			---	---	---	---				---	---		
	95C		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	95D		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	95E		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	95F		---	---	---	---				---	---	---	---			---	---	---	---				---	---		
	96		ALA	VAL	ARG	ARG				VAL	PHE	ILE	---			VAL	TRP	VAL	VAL				LEU	TYR		
	97		VAL	ILE	LEU	VAL	VAL	VAL		VAL	VAL	ILE	---			ILE	VAL	ILE	VAL				ILE	VAL		
	98	PHE	PHE	PHE	PHE	PHE	PHE	PHE		PHE	PHE	PHE	---			PHE	PHE	PHE	PHE				PHE	PHE		
	99	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	---			GLY	GLY	GLY	GLY				GLY	GLY	GLY	
	100		GLY	GLY	GLY	GLY	THR	THR	THR	GLY	SER	GLY	---			GLY	GLY	ALA	GLY				GLY	THR	THR	
	101	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	---			GLY	GLY	GLY	GLY				GLY	GLY	GLY	
FR4	102	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	---			THR	THR	THR	THR				THR	THR	THR	
	103		LYS	LYS	LYS	ARG	GLN	ARG	LYS	LYS	LYS	TYR	---			LYS	ASN	LYS	LYS				LYS	LYS	LYS	
	104		LEU	LEU	LEU	VAL	VAL			LEU	VAL	VAL	---			LEU	LEU	LEU	LEU				LEU	VAL		
	105		SER	THR	THR	THR	THR			THR	THR	THR	---			THR	THR	THR	THR				THR	ILE		
	106	VAL	VAL	VAL	VAL	VAL				VAL	VAL	VAL	---			VAL	VAL	VAL	VAL				VAL	VAL		
	106A	LEU	LEU	LEU	LEU	LEU				LEU	LEU	LEU	---			LEU	LEU	LEU	LEU				LEU	LEU		
	107		GLY	GLY	ARG	SER				GLY	ARG	ARG	---			GLY	GLY	ARG	GLY				GLY	GLY		
	108		GLN	GLN		GLN				GLN	GLN		GLN				GLN		GLN				GLN	GLX		
	109	PRO	PRO	PRO		PRO				PRO	PRO		PRO				PRO		PRO				PRO	PRO		

HUMAN LAMBDA LIGHT CHAINS SUBGROUP II (cont'd)

		25 WAL	26 4A CL	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0	---	---				
	1	PCA	gln	26	3	24(PCA)	3.3
	2	SER	thr	26	2	25(SER)	2.1
	3	val	val	26	3	23(ALA)	3.4
	4	LEU	val	26	2	25(LEU)	2.1
	5	THR	THR	26	3	23(THR)	3.4
	6	GLN	GLN	26	1 : 2	26(GLN) : 25(GLN)	1. : 2.1
	7	PRO	glu	26	3	24(PRO)	3.3
	8	pro	pro	26	3	18(ALA)	4.3
	9	SER	SER	26	2	25(SER)	2.1
	10	---	---				
FR1	11	ala	leu	26	3	23(VAL)	3.4
	12	SER	thr	26	2	25(SER)	2.1
	13	GLY	val	26	4	23(GLY)	4.5
	14	thr	SER	26	2	25(SER)	2.1
	15	PRO	PRO	26	2	25(PRO)	2.1
	16	GLY	GLY	26	1	26(GLY)	1.
	17	GLN	gly	26	4	23(GLN)	4.5
	18	arg	thr	26	3	23(SER)	3.4
	19		val	25	3	18(ILE)	4.2
	20		THR	25	1	25(THR)	1.
	21		leu	19	3	17(ILE)	3.4
	22		thr	18	2	17(SER)	2.1
	23		CYS	18	1	18(CYS)	1.
	24		ALA	15	4	9(THR)	6.7
	25		SER	15	2	14(GLY)	2.1
	26		SER	15	5	10(THR)	7.5
	27		THR	15	5	7(SER)	11.
	27A		---				
	27B		---				
	27C		---				
CDR1	27D		GLY	15	4	12(SER)	
	27E		ALA	15	4	11(ASP)	
	27F		VAL	15	2	14(VAL)	
	28		THR	15	5	10(GLY)	7.5
	29		SER	14	5	6(GLY)	12.
	30		GLY	14	6	9(TYR)	9.3
	31		TYR	14	7	8(ASN) : 7(ASN)	12. : 14.
	32		TYR	14	5	5(TYR)	14.
	33		PRO	13	3	11(VAL)	3.5
	34		ASN	13	2	12(SER)	2.2
	35		TRP	14	1	14(TRP)	1
	36		PHE	14	2	10(TYR)	2.8
	37		GLN	14	1 : 2	14(GLN) : 13(GLN)	1. : 2.2
	38		GLN	14	2 : 3	13(GLN) : 12(GLN)	2.2 : 3.5
	39		LYS	14	5	10(HIS)	7.
	40		PRO	14	1	14(PRO)	1.
FR2	41		GLY	14	2	13(GLY)	2.2
	42		GLN	14	4	11(LYS)	5.1
	43		ALA	14	2	13(ALA)	2.2
	44		PRO	14	1	14(PRO)	1.
	45		ARG	14	2	13(LYS)	2.2
	46		ALA	14	3	12(LEU)	3.5
	47		LEU	14	3	5(+)	8.4
	48		ILE	14	1	14(ILE)	1.
	49		TYR	14	3	9(TYR)	4.7
	50		SER	14	5	7(ASP)	10.
	51		THR	14	4	11(VAL)	5.1
CDR2	52		SER	14	5	5(SER)	14.
	53		ASN	14	6	4(+)	21.
	54		LYS	14	2	13(ARG)	2.2
	55		HIS	14	2	13(PRO)	2.2
	56		SER	14	1	14(SER)	1.
	57		TRP	14	2	13(GLY)	2.2
	58		THR	14	3	10(VAL)	4.2
	59		PRO	14	2	7(+)	4.
	60		ALA	14	7	5(ASP)	20.
	61		ARG	14	1	14(ARG)	1.
	62		PHE	15	2	14(PHE)	2.1
	63		SER	15	1	15(SER)	1.
	64		GLY	15	1	15(GLY)	1.
	65		SER	15	1	15(SER)	1.
	66		LEU	15	3	13(LYS)	3.5
	67		LEU	14	2	13(SER)	2.2
	68		GLY	14	2	12(GLY)	2.3
	69		GLY	14	4	10(ASN) : 9(ASN)	5.6 : 6.2
	70		LYS	14	3	12(THR)	3.5
FR3	71		ALA	14	1	14(ALA)	1.
	72		ALA	14	2	13(SER)	2.2
	73		LEU	14	1	14(LEU)	1.
	74		THR	14	1	14(THR)	1.
	75		LEU	14	2	13(ILE)	2.2
	76		SER	14	1	14(SER)	1.
	77		GLY	14	1	14(GLY)	1.
	78		VAL	14	2	13(LEU)	2.2
	79		GLN	14	3	12(GLN)	3.5
	80		PRO	14	3	10(ALA)	4.2
	81		GLU	14	3	11(GLU)	3.8
	82		ASP	14	2	13(ASP)	2.2
	83		GLU	14	1	14(GLU)	1.
	84		ALA	14	1	14(ALA)	1.
	85		GLU	14	3 : 4	11(ASP) : 10(ASP)	3.8 : 5.6
	86		TYR	14	1	14(TYR)	1.
	87		TYR	14	2	12(TYR)	2.3
	88		CYS	14	1	14(CYS)	1.
	89		LEU	14	4	8(SER)	7.
	90		LEU	14	2	13(SER)	2.2
	91		TYR	14	2	12(TYR)	2.3
	92		TYR	14	7	5(ALA)	20.
	93		GLY	14	4	7(GLY)	8.
	94		GLY	14	5 : 6	5(SER)	14. : 17.
	95		ALA	13	7	3(+)	30.
CDR3	95A		---	11	3	5(+)	
	95B		---	2	2	1(+)	
	95C		---				
	95D		---				
	95E		---				
	95F		---				
	96		---	13	8	5(VAL)	21.
	97	VAL	---	16	3	10(VAL)	4.8
	98	PHE	---	16	1	16(PHE)	1.
	99	GLY	---	18	1	18(GLY)	1.
	100	SER	---	18	4	10(GLY)	7.2
	101	GLY	---	18	1	18(GLY)	1.
	102	THR	---	18	1	18(THR)	1.
FR4	103	LYS	---	18	5	13(LYS)	6.9
	104	VAL	---	15	2	9(LEU)	3.3
	105	THR	---	15	3	13(THR)	3.5
	106		---	13	1	13(VAL)	1.
	106A		---	13	1	13(LEU)	
	107		---	13	3	8(GLY)	4.9
	108		---	10	1 : 2	10(GLN) : 9(GLN)	1. : 2.2
	109		---	10	1	10(PRO)	1.

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6) **RIM:** FETT,J.W. & DEUTSCH,H.F. (1976) IMMUNOCHEM.,13,149-155. (CHECKED BY AUTHOR)
7) **SLA:** FETT,J.W. & DEUTSCH,H.F. (1976) IMMUNOCHEM.,13,149-155. (CHECKED BY AUTHOR)
8) **ES492:** TVETERAAS,T.,SLETTEN,K. & WESTERMARK,P. (1985) BIOCHEM.J.,232,183-190.
9) **WEIR:** FETT,J.W. & DEUTSCH,H.F. (1976) IMMUNOCHEM.,13,149-155. (CHECKED BY AUTHOR); JABUSCH,J.R. & DEUTSCH,H.F. (1982) MOL.IMMUNOL., 19,901-906.
10) **TOG:** NABESHIMA,Y. & IKENAKA,T. (1979) MOL.IMMUNOL.,16,439-444. (CHECKED BY AUTHOR 10/10/79)
11) **SM:** GARVER,F.A.,CHANG,L.,MENDICINO,J.,ISOBE,T. & OSSERMAN,E.F. (1975) PROC.NAT.ACAD.SCI.USA,72,4559-4563. (CHECKED BY AUTHOR 05/31/83)
12) **HS68:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767.
13) **HS77:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767.
14) **TRO:** SCHOLZ,R. & HILSCHMANN,N. (1975) Z.PHYSIOL.CHEM.,356,1333-1335.
15) **BOH:** KOHLER,H.,RUDOFSKY,S. & KLUSKENS,L. (1975) J.IMMUNOLOGY,114,415-421. (CHECKED BY AUTHOR)
16) **NIG-58:** TAKAYASU,T.,TAKAHASHI,N.,SHINODA,T.,OKUYAMA,T. & TOMIOKA,H. (1980) J.BIOCHEM.,89,421-436. (CHECKED BY AUTHOR 05/24/84)
17) **VIL:** PONSTINGL,H. & HILSCHMANN,N. (1969) Z.PHYSIOL.CHEM.,350,1148-1152; (1971) Z.PHYSIOL.CHEM.,352,859-877. (CHECKED BY AUTHOR)
18) **HBJ15:** STANTON,T.,SLEDGE,C.,CAPRA,J.D.,WOODS,R.,CLEM,W. & HOOD,L. (1974) J.IMMUNOL.,112,633-640.
19) **HBJ8:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145; STANTON,T.,SLEDGE, C.,CAPRA,J.D.,WOODS,R.,CLEM,W. & HOOD,L. (1974) J.IMMUNOL.,112,633-640.
20) **HS70:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767.
21) **WIN:** CHEN,B.L.,CHIU,Y.Y.H.,HUMPHREY,R.L. & POLJAK,R.J. (1978) BIOCHIM.BIOPHYS.ACTA,537,9-21. (CHECKED BY AUTHOR 07/16/79)
22) **BUR:** LIU,V.Y.S.,LOW,T.L.K.,INFANTE,A. & PUTNAM,F.W. (1976) SCIENCE,193,1017-1020; INFANTE,A. & PUTNAM,F.W. (1979) J.BIOL.CHEM.,254,9006-9016. (CHECKED BY AUTHOR 07/28/79)
23) **PRE:** FETT,J.W. & DEUTSCH,H.F. (1976) IMMUNOCHEM.,13,149-155. (CHECKED BY AUTHOR)
24) **HS88:** HOOD,L. & EIN,D. (1968) NATURE,220,764-767.
25) **WAL:** FETT,J.W. & DEUTSCH,H.F. (1976) IMMUNOCHEM.,13,149-155. (CHECKED BY AUTHOR)
26) **4A'CL:** ANDERSON,M.L.M.,SZAJNERT,M.F.,KAPLAN,J.C.,MCCOLL,L. & YOUNG,B.D. (1984) NUC.ACIDS RES.,12,6647-6661. (CHECKED BY AUTHOR 05/16/85)

NOTES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP II

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: NIG-84[1],MES[2],WH[3],NEI[4],KAR[5],RIM[6],SLA[7]. (7 IDENTICAL)
SET 2: TRO[14],BOH[15]. (2 IDENTICAL)

FR2: SET 1: WH[3],BOH[15],NIG-58[16],BUR[22]. (4 IDENTICAL)

FR3:

FR4: SET 1: WH[3]. (IDENTICAL TO 1 HUMAN V-LAMBDA-I: NEWM[1]; AND 1 HUMAN V-LAMBDA-V: BO[1].)
SET 2: MES[2],ES492[8],TRO[14],VIL[17],WIN[21]. (5 IDENTICAL HUMAN V-LAMBDA-II; ALSO 4 HUMAN V-LAMBDA-I: BL2 'CL[6],RHE[10], OKA[12],NIG-51[19]; 4 HUMAN V-LAMBDA-III: HIL[1],CAP[4],BAU[12],DEL[14]; 1 HUMAN V-LAMBDA-IV: SH[1]; 3 HUMAN V-LAMBDA-VI: SUT[2],THO[4],LBV'CL[5]; AND 24 MOUSE V-LAMBDA: MOPC104E[1],J558[2],XS104[3],HOPC1[4],J606[5],H2061[6], W3159[7],Y5431[8],Y5485[9],Y5830[10],Y5669[11],MOPC511(L)[12],S178[13],Y5444[14],Y5606[15],S176[16],H2020[17], RPC20[18],IG 303LAMBDA'CL[19],S43'CL[21],S2H5'CL[38],S2E9'CL[39],S1F12'CL[40],IG 25LAMBDA'CL[41].)
SET 3: NIG-84[1]. (IDENTICAL TO 1 HUMAN V-LAMBDA-III: GAR[7].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1: SET 1: MES[2],VIL[17]. (2 IDENTICAL HUMAN V-LAMBDA-II; ALSO 1 HUMAN V-LAMBDA-V: MCG[3].)

CDR2: SET 1: NIG-84[1],TOG[10]. (2 IDENTICAL)

CDR3:

IDENTICAL SETS OF J-MINIGENES:

SET 1: MES[2],TRO[14]. (2 IDENTICAL HUMAN V-LAMBDA-II; ALSO 1 HUMAN V-LAMBDA-III: BAU[12].)
SET 2: ES492[8],VIL[17]. (2 IDENTICAL HUMAN V-LAMBDA-II; ALSO 1 HUMAN V-LAMBDA-III: DEL[14].)

SPECIFIC NOTES:

11) **SM:** IT HAS O-LINKED CARBOHYDRATE ATTACHED TO SER AT POSITION 22 AND N-LINKED CARBOHYDRATE ATTACHED TO ASX AT POSITION 25.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
47	(ILE,MET)
53	(LYS,ASN)
59	(PRO,SER)
95	(SER,ASN)
95A	(THR,SER)
95B	(LEU,ARG)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP III

		INVARIANT RESIDUES	1 HIL	2 YO	3 PS	4 CAP	5 LOY A	6 LOY G	7 GAR	8 CH	9 X (PET)	10 KERN	11 TA	12 BAU	13 AMYLOID 758	14 DEL	15 LYN	16 NIG -68	17 AMYLOID 808	18 MOT #	19 WIG	20 WHI	21 DU	22 LON
	0		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	#	---	---	---	---
	1		SER	SER	SER	SER	SER	SER	SER	SER	---	---	SER	---	---	---	---	---	---	phe	SER	---	---	---
	2	TYR(.96)	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	phe	TYR	TYR	TYR
	3		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp	ala	ala	gly	asp	val	GLU	asp	asp	GLU	gly	val	GLX	ser
	4	LEU(.96)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	val	LEU	LEU	LEU
	5		THR	THR	THR	THR	THR	THR	lys	THR	THR	THR	THR	THR	THR	ser	THR	THR	THR	THR	ser	THR	THR	THR
	6		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLX	GLN
	7		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	ala		PRO	PRO	ala	PRO	PRO
	8	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	9	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
FR1	10		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	11		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	leu	met	VAL	VAL	leu	VAL	VAL	VAL	leu	VAL	VAL
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	13	VAL(.96)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	leu	VAL	VAL	VAL	VAL
	14		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	ala	phe	SER	SER	ala	SER	ala	SER	SER
	15	PRO(.95)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	ala	PRO	PRO	PRO	PRO
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	
	17		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLX	GLN	GLN	GLN		GLN	GLN	GLX	GLX	
	18		THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	pro	THR	THR	THR	THR	THR		
	19	ALA(.95)	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	gly	ALA	ALA	ALA	ALA	ALA		
	20		ARG	ARG	ARG	ARG	ser	ser	ARG	ARG	ser	val		ser	ser	ARG	thr	tyr		met	ser	ARG		
	21	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		ILE	ILE		ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE		
	22	THR	THR	THR	THR	THR	THR	THR	THR		THR	THR		THR	THR	THR	THR	THR	THR	THR	THR	THR		
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		CYS	CYS		CYS		CYS	CYS	CYS		CYS	CYS	CYS		
	24		SER	SER	SER	SER	SER	SER	SER		SER	SER		SER	SER	GLY	SER	SER		GLU		GLX		
	25		ALA	GLY	GLY	GLY	GLY	GLY	GLY		GLY	GLY		GLY	GLY	GLY	GLY	GLY		GLY				
	26		ASN	ASP	ASP	ASP	ASP	ASX	ASP		ASP	ASP		ASP	GLX	ASP	ASP	ASP		ASN		ASX		
	27		ALA	ALA	ALA	ALA	---	---	VAL		LYS	ASN		LYS	ASX	GLY	ALA	ASN		ASP		ASX		
	27A		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
	27B		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
CDR1	27C		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
	27D		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
	27E		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
	27F		---	---	---	---	---	---	---		---	---		---	---	---	---	---		---		---		
	28		LEU	LEU	LEU	LEU	LEU	LEU	LEU		LEU	LEU		LEU	LEU	ILE	LEU	LEU		ILE		ILE		
	29		PRO	PRO	THR	PRO	---	---	PRO		GLY	GLU		GLY		GLY	SER	GLY		GLY		GLX		
	30		ASN	ASP	ASN	ALA	GLX	GLX	LYS		ASP	LYS		GLU		GLY	ASP	ASN		GLU		GLX		
	31		GLN	LEU	LYS	GLU	GLX	GLX	LYS		LYS	THR		GLN		LYS	LYS	GLU		ARG				
	32		TYR	TYR	TYR	TYR			TYR		ASP	PHE		TYR		SER	TYR	PHE		SER			TYR	
	33		ALA	VAL	ALA	ALA			ALA		VAL	VAL		VAL		VAL	VAL	VAL		VAL			VAL	
	34		TYR		TYR	TYR			TYR		CYS	SER		CYS		HIS		SER		HIS			CYS	
	35	TRP	TRP	TRP	TRP	TRP			TRP		TRP	TRP		TRP		TRP	TRP	TRP		TRP			TRP	
	36		TYR	TYR		TYR			TYR		TYR	PHE		TYR		TYR	TYR	TYR		TYR				
	37		GLN	GLN		GLN			GLN		GLN	GLN		GLN		GLN	GLX	GLN		GLN				
	38		GLN	GLN		GLN			GLU		GLN	GLN		GLN		GLN	HIS	GLN		GLN				
	39		LYS	LYS		LYS			ARG		ARG	ARG		LYS		LYS	LYS	ARG		LYS				
	40		PRO			PRO			SER		PRO	PRO		PRO		PRO	PRO	PRO		PRO				
FR2	41	GLY	GLY			GLY			GLY		GLY	GLY		GLY		GLY	GLY	GLY		GLY				
	42		ARG			GLN			GLN		GLN	GLN		GLN		GLN		GLX		GLN				
	43		ALA			ALA			ALA		SER	SER		SER		ALA		SER		ALA				
	44	PRO	PRO			PRO			PRO		PRO	PRO		PRO		PRO	PRO	PRO		PRO				
	45		VAL			VAL			VAL		VAL	LEU		VAL		VAL	LEU	ALA		VAL				
	46		MET			MET			LEU		LEU	LEU		LEU		LEU		LEU		PRO				
	47	VAL	VAL			VAL			VAL		VAL	VAL		VAL		VAL	VAL	VAL		VAL				
	48		ILE			ILE			VAL		ILE	ILE		ILE		VAL	ILE	ILE		ILE				
	49		TYR			TYR			TYR		TYR	TYR		TYR		HIS	TYR	TYR		TYR				
	50		LYS			GLU			GLU		GLN	HIS		HIS		GLU	GLX	ASX		ASP				
	51		ASP			THR			ASP	ASP	ASP	THR		ASP		ASP		THR		ASP				
CDR2	52		THR			ASN			SER	THR	ASN	SER		SER		ASN	THR	SER		ALA				
	53		GLN			LYS			GLY	GLY	GLN	GLU		LYS		ASP	LYS	LYS		ASP				
	54	ARG	ARG			ARG			ARG	ARG	ARG	ARG		ARG		ARG	ARG	ARG		ARG				
	55		PRO			PRO			PRO	PRO	SER	PRO		PRO		PRO	PRO	PRO		PRO				
	56		SER			SER			SER	SER	SER	SER		SER		ALA		SER		SER				
	57		GLY			GLY			GLU	THR	GLY	GLU		GLY		GLY	GLY	GLY		GLY				
	58		ILE			ILE			ILE	ILE	ILE	ILE		ILE		ILE		ILE		VAL				
	59	PRO	PRO			PRO			PRO	PRO	PRO	PRO		PRO		PRO		PRO		PRO				
	60		GLN			GLU			GLU	GLU	GLU	GLU		GLU		GLU	GLX	GLU		ALA				
	61	ARG	ARG			ARG			ARG	ARG	ARG	ARG		ARG		ARG	ARG	ARG		ARG				
	62	PHE	PHE			PHE			PHE	PHE	PHE	PHE		PHE		PHE	PHE	PHE		PHE				
	63	SER	SER			SER			SER	SER	SER	SER		SER		SER		SER		SER				
	64		SER			GLY			GLY	GLY	GLY	GLY		GLY		GLY		GLY		GLY				
	65		SER			SER			SER	SER	SER	SER		SER		SER		SER		TYR				
	66		THR			THR			SER	THR	ASN	SER		ASN		ASN		LYS		ASN				
	67	SER	SER			SER			SER	SER	SER	SER		SER		SER		SER		SER				
	68	GLY	GLY			GLY			GLY	GLY	GLY	GLY		GLY		GLY		GLY		GLY				
	69		THR			THR			THR	THR	ASN	ALA		THR		ASN		ASN		ASN				
	70		THR			THR			LYS	THR	THR	THR		THR		THR		THR		SER				
	71		VAL			VAL			ALA	ALA	ALA	ALA		ALA		ALA		ALA		ALA				
FR3	72		THR			THR			THR	THR	THR	THR		THR		ALA		THR		ILE				
	73	LEU	LEU			LEU			LEU	LEU	LEU	LEU		LEU		LEU		LEU		LEU				
	74	THR	THR			THR			THR	THR	THR	THR		THR		THR		THR		THR				
	75	ILE	ILE			ILE			ILE	ILE	ILE	ILE		ILE		ILE		ILE		ILE				
	76		SER			SER			SER	SER	SER	SER		SER		SER		SER		ASN				
	77		GLY			GLY			GLY	GLY	GLY	GLY		GLY		ARG		GLY		ARG				
	78		VAL			VAL			ALA	VAL	THR	ALA		THR		VAL		THR		VAL				
	79		GLN			GLN			GLN	GLN	GLN	GLN		GLN		GLU		GLU		GLU				
	80		ALA			ALA			VAL	ALA	ALA	SER		ALA		ALA		SER		ALA				
	81		GLU			GLU			GLU	ASN	MET	VAL		MET		GLY		MET		GLY				
	82		ASP			ASP			ASP	ASX	ASP	ASP		ASP		ASP		ASX		ASP				
	83		GLU			GLU			GLU	GLX	GLU	GLU		GLU		GLU		GLU		GLU				
	84	ALA	ALA			ALA			ALA	ALA	ALA	ALA		ALA		ALA		ALA		ALA				
	85		ASP			ASP			ASP	ASX	ASP	ASP		ASP		ASP		ASX		ASP				
	86	TYR	TYR			TYR			TYR	TYR	TYR	TYR		TYR		TYR		TYR		TYR				
	87		TYR			TYR			TYR	TYR	TYR	PHE		TYR		TYR		TYR		PHE				
	88	CYS	CYS			CYS			CYS	CYS	CYS	CYS		CYS		CYS		CYS		CYS				
	89		GLN			SER			SER	GLX	GLN	GLN		GLN		GLU		GLX		GLN				
	90		ALA			SER			THR	SER	ALA	THR		ALA		VAL		ALA		SER				
	91		TRP			ALA			ASP	ALA	TRP	TRP		TRP		TRP		TRP		TRP				
	92		ASP			ASP			ILE	ASN	ASP	ASP		ASP		ASP		ASX		ASP				
	93		ASN			SER			ASN	SER	SER	THR		SER		ASP		GLX		ASN				
	94		SER			SER			GLY	ARG	MET	ILE		TYR		ARG		ILE		GLY				
	95		ALA			GLN			TYR		SER	THR		THR		THR		ARG		SER				
CDR3	95A		---			GLY			---		---	---		---		ALA		ASP		TYR				
	95B		---			---			---		---	---		---		HIS		---		GLU				
	95C		---			---			---		---	---		---		---		---		---				
	95D		---			---			---		---	---		---		---		---		---				
	95E		---			---			---		---	---		---		---		---		---				
	95F		---			---			---		---	---		---		---		---		---				
	96		SER			MET			PRO		VAL	ALA		VAL		VAL		VAL		VAL				
	97		ILE			VAL			LEU		VAL	ILE		ILE		VAL		VAL		VAL	VAL			
	98	PHE	PHE			PHE			PHE		PHE	PHE		PHE		PHE		PHE		PHE	PHE			
	99	GLY	GLY			GLY			GLY	GLY	GLY	GLY		GLY		GLY		GLY		GLY	GLY			
	100		GLY			GLY			GLY	GLY	GLY	GLY		GLY		GLY		GLY		THR	ALA			
	101	GLY	GLY			GLY			GLY	GLY	GLY	GLY		GLY		GLY		GLY		GLY	GLY			
FR4	102	THR	THR			THR			THR	THR	THR	THR		THR		THR		THR		THR	THR			
	103		LYS			LYS			LYS	LYS	ARG	LYS		LYS		LYS		LYS		MET	THR			
	104		LEU			LEU			LEU	LEU	LEU	LEU		LEU		LEU		LEU		VAL				
	105		THR			THR			SER	THR	THR	THR		THR		THR		THR		THR				
	106	VAL	VAL			VAL			VAL	VAL	VAL	VAL		VAL		VAL		VAL		VAL				
	106A	LEU	LEU			LEU			LEU	LEU	LEU	LEU		LEU		LEU		LEU		LEU				
	107		GLY			GLY			GLY		SER	SER		GLY		GLY				GLY				
	108	GLN	GLN			GLN			GLN		GLN	GLN		GLN						GLN				
	109	PRO	PRO			PRO			PRO		PRO	PRO		PRO						PRO				

HUMAN LAMBDA LIGHT CHAINS SUBGROUP III (cont'd)

		23 SG	24 GIM	25 111	26 119	27 VIN	28 MIL	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0	---	---	---	---	---		12	3	10(SER)	3.6
	1	tyr	---	---	---	---		27	2	26(TYR)	2.1
	2	TYR	TYR	TYR	TYR	TYR		26	6 : 7	13(GLU) : 11(GLU)	12. : 17.
	3	val	val	GLU	GLX			26	2	25(LEU)	2.1
	4	LEU	LEU	LEU	LEU						
	5	THR	THR	THR	THR			26	3	23(THR)	3.4
	6	GLN	GLX	GLN	GLX			26	1 : 2	26(GLN) : 22(GLN)	1. : 2.4
	7	PRO	PRO	PRO	PRO			25	2	23(PRO)	2.2
	8	PRO	PRO	PRO	PRO			26	1	26(PRO)	1.
	9	SER	SER					24	1	24(SER)	1.
FR1	10	---	---								
	11	VAL	VAL					24	3	20(VAL)	3.6
	12	SER	SER					24	1	24(SER)	1.
	13	VAL	VAL					24	2	23(VAL)	2.1
	14							22	3	18(SER)	3.7
	15							22	2	21(PRO)	2.1
	16							21	1	21(GLY)	1.
	17							20	1 : 2	20(GLN) : 17(GLN)	1. : 2.4
	18					met		21	3	19(THR)	3.3
	19							20	2	19(ALA)	2.1
	20							18	6	8(ARG)	14.
	21						ILE	19	1	19(ILE)	1.
	22						THR	19	1	19(THR)	1.
	23						CYS	17	1	17(CYS)	1.
	24						GLY	17	3 : 4	13(SER)	3.9 : 5.2
	25						GLY	16	2	15(GLY)	2.1
	26						ASP	17	3	14(ASP) : 12(ASP)	3.6 : 4.3
	27						GLU	15	7	5(ALA)	21.
	27A										
	27B										
CDR1	27C										
	27D										
	27E										
	27F										
	28							16	2	13(LEU)	2.5
	29							13	5 : 6	5(GLY)	13. : 16.
	30							15	6 : 7	5(GLU) : 3(+)	18. : 35.
	31							14	6	5(LYS)	17.
	32							13	4	8(TYR)	6.5
	33							13	2	9(VAL)	2.9
	34							11	4	4(TYR)	11.
	35							13	1	13(TRP)	1.
	36							11	2	10(TYR)	2.2
	37							11	1 : 2	11(GLN) : 10(GLN)	1. : 2.2
	38							11	3	9(GLN)	3.7
	39							11	2	7(LYS)	3.1
	40							10	2	9(PRO)	2.2
	41							10	1	10(GLY)	1.
FR2	42							9	2 : 3	8(GLN) : 7(GLN)	2.3 : 3.9
	43							9	2	5(ALA)	3.6
	44							10	1	10(PRO)	1.
	45							10	3	7(VAL)	4.3
	46							9	3	6(LEU)	4.5
	47							10	1	10(VAL)	1.
	48							10	2	8(ILE)	2.5
	49							10	2	9(TYR)	2.2
	50							10	5 : 6	4(GLU) : 3(GLU)	13. : 20.
	51							10	2	7(ASP)	2.9
	52							11	4	4(SER)	11.
CDR2	53							11	5	4(LYS)	14.
	54							11	1	11(ARG)	1.
	55							11	2	10(PRO)	2.2
	56							10	2	9(SER)	2.2
	57							11	3	8(GLY)	4.1
	58							10	2	9(ILE)	2.2
	59							10	1	10(PRO)	1.
	60							11	3	9(GLU) : 8(GLU)	3.7 : 4.1
	61							11	1	11(ARG)	1.
	62							11	1	11(PHE)	1.
	63							10	1	10(SER)	1.
	64							10	2	9(GLY)	2.2
	65							10	2	9(SER)	2.2
	66							10	4	4(ASN)	10.
	67							10	1	10(SER)	1.
	68							10	1	10(GLY)	1.
	69							10	3	5(THR)	6.
	70							10	3	8(THR)	3.8
FR3	71							10	2	8(ALA)	2.5
	72							10	3	8(THR)	3.8
	73							10	1	10(LEU)	1.
	74							10	1	10(THR)	1.
	75							10	1	10(ILE)	1.
	76							10	2	9(SER)	2.2
	77							10	2	8(GLY)	2.5
	78							10	3	5(VAL)	6.
	79							10	2	7(GLN)	2.9
	80							10	3	7(ALA)	4.3
	81							10	5	3(+)	17.
	82							10	1 : 2	10(ASP) : 8(ASP)	1. : 2.5
	83							10	1 : 2	10(GLU) : 9(GLU)	1. : 2.2
	84							10	1	10(ALA)	1.
	85							10	1 : 2	10(ASP) : 8(ASP)	1. : 2.5
	86							10	1	10(TYR)	1.
	87							10	2	8(TYR)	2.5
	88							10	1	10(CYS)	1.
	89							10	3	7(GLN) : 5(GLN)	4.3 : 6.
	90							10	4	4(ALA)	10.
	91							10	3	7(TRP)	4.3
	92							10	3	8(ASP) : 7(ASP)	3.8 : 4.3
	93							10	5	4(SER)	13.
	94							10	6	2(+)	30.
	95							9	6	3(THR)	18.
	95A							4	4	1(+)	
CDR3	95B							2	2	1(+)	
	95C										
	95D										
	95E										
	95F										
	96							9	5	5(VAL)	9.
	97							10	3	6(VAL)	5.
	98							10	1	10(PHE)	1.
	99							11	1	11(GLY)	1.
	100							11	3	9(GLY)	3.7
	101							11	1	11(GLY)	1.
	102							11	1	11(THR)	1.
FR4	103							11	4	8(LYS)	5.5
	104							10	2	9(LEU)	2.2
	105							10	2	9(THR)	2.2
	106							10	1	10(VAL)	1.
	106A							10	1	10(LEU)	
	107							8	2	6(GLY)	2.7
	108							7	1	7(GLN)	1.
	109							7	1	7(PRO)	1.

ANTIBODY SPECIFICITIES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP III

7) **GAR:** ANTI-RIBOFLAVIN

REFERENCE: HUMAN LAMBDA LIGHT CHAINS SUBGROUP III

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5) **LOY A:** WOLFENSTEIN-TODEL,C.,FRANKLIN,E.C. & RUDDERS,R.A. (1974) J.IMMUNOL.,112,871-876. (CHECKED BY AUTHOR)
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10) **KERN:** PONSTINGL,H.,HESS,M. & HILSCHMANN,N. (1968) Z.PHYSIOL.CHEM.,349,867-871; (1971) Z.PHYSIOL.CHEM.,352,247-266. (CHECKED BY AUTHOR)
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NOTES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP III

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: HIL[1],YO[2],PS[3],CAP[4]. (4 IDENTICAL)
SET 2: LOY A[5],LOY G[6]. (2 IDENTICAL)

FR2:

FR3:

FR4: SET 1: HIL[1],CAP[4],BAU[12],DEL[14]. (4 IDENTICAL HUMAN V-LAMBDA-III; ALSO 4 HUMAN V-LAMBDA-I: BL2 'CL[6],RHE[10],OKA[12]. NIG-51[19]; 5 HUMAN V-LAMBDA-II: MES[2],ES492[8],TRO[14],VIL[17],WIN[21]; 1 HUMAN V-LAMBDA-IV: SH[1]; 3 HUMAN V-LAMBDA-VI: SUT[2],THO[4],LBV'CL[5]; AND 24 MOUSE V-LAMBDA: MOPC104E[1],J558[2],XS104[3],HOPC1[4],J698[5],H2061[6], W3159[7],Y5431[8],Y5485[9],Y5830[10],Y5669[11],MOPC511(L)[12],S178[13],Y5444[14],Y5606[15],S176[16],H2020[17], RPC20[18],IG 303LAMBDA'CL[19],S43'CL[21],S2H5'CL[38],S2E9'CL[39],S1F12'CL[40],IG 25LAMBDA'CL[41].)
SET 2: GAR[7]. (IDENTICAL TO 1 HUMAN V-LAMBDA-II: NIG-84[1].)
SET 3: KERN[10]. (IDENTICAL TO 1 HUMAN V-LAMBDA-VI: NIG-48[10].)

IDENTICAL SETS OF J-MINIGENES:

SET 1: BAU[12]. (IDENTICAL TO 2 HUMAN V-LAMBDA-II: MES[2],TRO[14].)
SET 2: DEL[14]. (IDENTICAL TO 2 HUMAN V-LAMBDA-II: ES492[8],VIL[17].)

SPECIFIC NOTES:

18) **MOT:** THERE ARE TWO RESIDUES IN FRONT OF POSITION 1; THEY ARE VAL AND THR.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
30	(ASP,ASN,GLN)
81	(MET,GLU)
94	(ILE,ARG,SER,GLY)
95A	(TYR,ALA,GLY,ASP)
95B	(HIS,GLU)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP IV

		INVARIANT RESIDUES	1 SH	2 NEV	3 USH	4 PFA	5 FRA	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0		---	---	---	---	---				
	1		---	---	---	---	---				
	2	SER	SER	SER	SER	SER	---	4	1	4(SER)	1.
	3		GLU	GLU	GLU	GLU	ala	5	2	4(GLU)	2.5
	4	LEU	LEU	LEU	LEU	LEU	LEU	5	1	5(LEU)	1.
	5		THR	THR	THR	THR	val	5	2	4(THR)	2.5
	6	GLN	GLN	GLN	GLN	GLN	GLN	5	1	5(GLN)	1.
	7		ASP	ASX	pro	pro	pro	5	2 : 3	3(PRO)	3.3 : 5.
	8		PRO	PRO	PRO	PRO	ala	5	2	4(PRO)	2.5
	9		ALA	ALA	ser	ser	ser	5	2	3(SER)	3.3
	10		---	---	---	---	---				
FR1	11	VAL	VAL	VAL	VAL	VAL	VAL	5	1	5(VAL)	1.
	12		SER	SER	SER	SER	glx	5	2	4(SER)	2.5
	13		VAL	VAL	VAL	VAL	gly	5	2	4(VAL)	2.5
	14		ALA	ALA	ser	ser	ALA	5	2	3(ALA)	3.3
	15		LEU	LEU	pro	pro	pro	5	2	3(PRO)	3.3
	16	GLY	GLY	GLY	GLY	GLY	GLY	5	1	5(GLY)	1.
	17		GLN	GLX	GLN	GLN	GLX	5	1 : 2	5(GLN) : 3(GLN)	1. : 3.3
	18		THR	THR	THR	THR	ser	5	2	4(THR)	2.5
	19		VAL	VAL	ala	ala	ile	5	3	2(+)	7.5
	20		ARG	ARG	ser	val	ala	5	4	2(ARG)	10.
	21	ILE	ILE	ILE	ILE	ILE	ILE	5	1	5(ILE)	1.
	22		THR	THR	THR	THR	gly	5	2	4(THR)	2.5
	23	CYS	CYS		CYS	CYS	CYS	4	1	4(CYS)	1.
	24		GLN		SER	SER	ILE	4	3	2(SER)	6.
	25	GLY	GLY		GLY	GLY	GLY	4	1	4(GLY)	1.
	26		ASP		ASP	ASP	ILE	4	2	3(ASP)	2.7
	27		SER		LYS	LYS	SER	4	2	2(+)	4.
	27A		---		---	---	---				
	27B		---		---	---	---				
CDR1	27C		---		---	---	---				
	27D		---		---	---	---				
	27E		---		---	---					
	27F		---		---	---	ASX	1	1	1(ASN) : 1(ASP)	
	28		LEU		LEU	LEU	ILE	4	2	3(LEU)	2.7
	29		ARG		GLY	GLY	GLY	4	2	3(GLY)	2.7
	30		GLY		ASP	GLN	ALA	4	4	1(+)	16.
	31		TYR		ASN	ALA	TYR	4	3	2(TYR)	6.
	32		ASP		TYR		ASX	3	2 : 3	2(ASP) : 1(+)	3. : 9.
	33		ALA		ALA		TYR	3	2	2(ALA)	3.
	34		ALA		SER		ILE	3	3	1(+)	9.
	35	TRP	TRP		TRP	TRP		3	1	3(TRP)	1.
	36	TYR	TYR		TYR	TYR		3	1	3(TYR)	1.
	37	GLN	GLN		GLN			2	1	2(GLN)	1.
	38	GLN	GLN		GLN			2	1	2(GLN)	1.
	39	LYS	LYS		LYS			2	1	2(LYS)	1.
	40		PRO					1	1	1(PRO)	
FR2	41		GLY					1	1	1(GLY)	
	42		GLN					1	1	1(GLN)	
	43		ALA					1	1	1(ALA)	
	44		PRO					1	1	1(PRO)	
	45		LEU					1	1	1(LEU)	
	46		LEU					1	1	1(LEU)	
	47		VAL					1	1	1(VAL)	
	48		ILE					1	1	1(ILE)	
	49		TYR					1	1	1(TYR)	
	50		GLY					1	1	1(GLY)	
	51		ARG					1	1	1(ARG)	
CDR2	52		ASN					1	1	1(ASN)	
	53		ASN					1	1	1(ASN)	
	54		ARG					1	1	1(ARG)	
	55		PRO					1	1	1(PRO)	
	56		SER					1	1	1(SER)	
	57		GLY					1	1	1(GLY)	
	58		ILE					1	1	1(ILE)	
	59		PRO					1	1	1(PRO)	
	60		ASP					1	1	1(ASP)	
	61		ARG					1	1	1(ARG)	
	62		PHE					1	1	1(PHE)	
	63		SER					1	1	1(SER)	
	64		GLY					1	1	1(GLY)	
	65		SER					1	1	1(SER)	
	66		SER					1	1	1(SER)	
	67		SER					1	1	1(SER)	
	68		GLY					1	1	1(GLY)	
	69		HIS					1	1	1(HIS)	
	70		THR					1	1	1(THR)	
FR3	71		ALA					1	1	1(ALA)	
	72		SER					1	1	1(SER)	
	73		LEU					1	1	1(LEU)	
	74		THR					1	1	1(THR)	
	75		ILE					1	1	1(ILE)	
	76		THR					1	1	1(THR)	
	77		GLY					1	1	1(GLY)	
	78		ALA					1	1	1(ALA)	
	79		GLN					1	1	1(GLN)	
	80		ALA					1	1	1(ALA)	
	81		GLU					1	1	1(GLU)	
	82		ASP					1	1	1(ASP)	
	83		GLU					1	1	1(GLU)	
	84		ALA					1	1	1(ALA)	
	85		ASP					1	1	1(ASP)	
	86		TYR					1	1	1(TYR)	
	87		TYR					1	1	1(TYR)	
	88		CYS					1	1	1(CYS)	
	89		ASN					1	1	1(ASN)	
	90		SER					1	1	1(SER)	
	91		ARG					1	1	1(ARG)	
	92		ASP					1	1	1(ASP)	
	93		SER					1	1	1(SER)	
	94		SER					1	1	1(SER)	
	95		GLY					1	1	1(GLY)	
CDR3	95A		LYS					1	1	1(LYS)	
	95B		HIS					1	1	1(HIS)	
	95C		---								
	95D		---								
	95E		---								
	95F		---								
	96		VAL					1	1	1(VAL)	
	97		LEU					1	1	1(LEU)	
	98		PHE					1	1	1(PHE)	
	99		GLY					1	1	1(GLY)	
	100		GLY					1	1	1(GLY)	
	101		GLY					1	1	1(GLY)	
FR4	102		THR					1	1	1(THR)	
	103		LYS					1	1	1(LYS)	
	104		LEU					1	1	1(LEU)	
	105		THR					1	1	1(THR)	
	106		VAL					1	1	1(VAL)	
	106A		LEU					1	1	1(LEU)	
	107		GLY					1	1	1(GLY)	
	108		GLN					1	1	1(GLN)	
	109		PRO					1	1	1(PRO)	

REFERENCE: HUMAN LAMBDA LIGHT CHAINS SUBGROUP IV

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NOTES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP IV

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: SH[1],NEV[2]. (2 IDENTICAL)

FR2:

FR3:

FR4: SET 1: SH[1]. (IDENTICAL TO 4 HUMAN V-LAMBDA-I: BL2 'CL[6],RHE[10],OKA[12],NIG-51[19]; 5 HUMAN V-LAMBDA-II: MES[2],ES492[8], TRO[14],VIL[17],WIN[21]; 4 HUMAN V-LAMBDA-III: HIL[1],CAP[4],BAU[12],DEL[14]; 3 HUMAN V-LAMBDA-VI: SUT[2],THO[4], LBV'CL[5]; AND 24 MOUSE V-LAMBDA: MOPC104E[1],J558[2],XS104[3],HOPC1[4],J698[5],H2061[6],W3159[7],Y5431[8],Y5485[9], Y5830[10],Y5669[11],MOPC511(L)[12],S178[13],Y5444[14],Y5606[15],S176[16],H2020[17],RPC20[18],IG 303LAMBDA'CL[19], S43'CL[21],S2H5'CL[38],S2E9'CL[39],S1F12'CL[40],IG 25LAMBDA'CL[41].)

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
19	(VAL,ALA)
27	(LYS,SER)
30	(ALA,GLY,ASP,GLN)
32	(TYR,ASP,ASN)
34	(ILE,ALA,SER)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP V

	*	INVARIANT RESIDUES	1 BO	2 HBJ 2	3* MCG	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0		---	---	---				
	1	PCA	PCA	PCA	PCA	3	1	3(PCA)	1.
	2	SER	SER	SER	SER	3	1	3(SER)	1.
	3	ALA	ALA	ALA	ALA	3	1	3(ALA)	1.
	4	LEU	LEU	LEU	LEU	3	1	3(LEU)	1.
	5	THR	THR	THR	THR	3	1	3(THR)	1.
	6	GLN	GLN	GLN	GLN	3	1	3(GLN)	1.
	7	PRO	PRO	PRO	PRO	3	1	3(PRO)	1.
	6	PRO	PRO	PRO	PRO	3	1	3(PRO)	1.
	9	SER	SER	SER	SER	3	1	3(SER)	1.
	10		---	---	---				
FR1	11	ALA	ALA	ALA	ALA	3	1	3(ALA)	1.
	12	SER	SER	SER	SER	3	1	3(SER)	1.
	13	GLY	GLY	GLY	GLY	3	1	3(GLY)	1.
	14	SER	SER	SER	SER	3	1	3(SER)	1.
	15		PRO	PRO	leu	3	2	2(PRO)	3.
	16	GLY	GLY	GLY	GLY	3	1	3(GLY)	1.
	17	GLN	GLN	GLN	GLN	3	1	3(GLN)	1.
	18	SER	SER	SER	SER	3	1	3(SER)	1.
	19	VAL	VAL	VAL	VAL	3	1	3(VAL)	1.
	20	THR	THR	THR	THR	3	1	3(THR)	1.
	21	ILE	ILE	ILE	ILE	3	1	3(ILE)	1.
	22	SER	SER	SER	SER	3	1	3(SER)	1.
	23	CYS	CYS	CYS	CYS	3	1	3(CYS)	1.
	24	THR	THR	THR	THR	3	1	3(THR)	1.
	25	GLY	GLY	GLY	GLY	3	1	3(GLY)	1.
	26	THR	THR	THR	THR	3	1	3(THR)	1.
	27	SER	SER		SER	2	1	2(SER)	1.
	27A		---		---				
	27B		---		---				
	27C		---		---				
CDR1	27D	SER	SER		SER	2	1	2(SER)	
	27E	ASP	ASP		ASP	2	1	2(ASP)	
	27F	VAL	VAL		VAL	2	1	2(VAL)	
	26	GLY	GLY		GLY	2	1	2(GLY)	1.
	29		ASP		GLY	2	2	1(+)	4.
	30		ASN		TYR	2	2	1(+)	4.
	31		LYS		ASN	2	2	1(+)	4.
	32	TYR	TYR		TYR	2	1	2(TYR)	1.
	33	VAL	VAL		VAL	2	1	2(VAL)	1.
	34	SER	SER		SER	2	1	2(SER)	1.
	35	TRP	TRP		TRP	2	1	2(TRP)	1.
	36	TYR	TYR		TYR	2	1	2(TYR)	1.
	37	GLN	GLN		GLN	2	1	2(GLN)	1.
	38	GLN	GLN		GLN	2	1	2(GLN)	1.
	39	HIS	HIS		HIS	2	1	2(HIS)	1.
	40		PRO		ALA	2	2	1(+)	4.
FR2	41	GLY	GLY		GLY	2	1	2(GLY)	1.
	42		ARG		LYS	2	2	1(+)	4.
	43	ALA	ALA		ALA	2	1	2(ALA)	1.
	44	PRO	PRO		PRO	2	1	2(PRO)	1.
	45	LYS	LYS		LYS	2	1	2(LYS)	1.
	46		LEU		VAL	2	2	1(+)	4.
	47		VAL		ILE	2	2	1(+)	4.
	48	ILE	ILE		ILE	2	1	2(ILE)	1.
	49		PHE		TYR	2	2	1(+)	4.
	50	GLU	GLU		GLU	2	1	2(GLU)	1.
	51	VAL	VAL		VAL	2	1	2(VAL)	1.
CDR2	52		SER		ASN	2	2	1(+)	4.
	53		GLY		LYS	2	2	1(+)	4.
	54	ARG	ARG		ARG	2	1	2(ARG)	1.
	55	PRO	PRO		PRO	2	1	2(PRO)	1.
	56	SER	SER		SER	2	1	2(SER)	1.
	57	GLY	GLY		GLY	2	1	2(GLY)	1.
	58	VAL	VAL		VAL	2	1	2(VAL)	1.
	59	PRO	PRO		PRO	2	1	2(PRO)	1.
	60	ASP	ASP		ASP	2	1	2(ASP)	1.
	61	ARG	ARG		ARG	2	1	2(ARG)	1.
	62	PHE	PHE		PHE	2	1	2(PHE)	1.
	63	SER	SER		SER	2	1	2(SER)	1.
	64	GLY	GLY		GLY	2	1	2(GLY)	1.
	65	SER	SER		SER	2	1	2(SER)	1.
	66	LYS	LYS		LYS	2	1	2(LYS)	1.
	67	SER	SER		SER	2	1	2(SER)	1.
	68		ASP		GLY	2	2	1(+)	4.
	69	ASN	ASN		ASN	2	1	2(ASN)	1.
	70	THR	THR		THR	2	1	2(THR)	1.
	71	ALA	ALA		ALA	2	1	2(ALA)	1.
FR	72	SER	SER		SER	2	1	2(SER)	1.
3	73	LEU	LEU		LEU	2	1	2(LEU)	1.
	74	THR	THR		THR	2	1	2(THR)	1.
	75	VAL	VAL		VAL	2	1	2(VAL)	1.
	76	SER	SER		SER	2	1	2(SER)	1.
	77	GLY	GLY		GLY	2	1	2(GLY)	1.
	78	LEU	LEU		LEU	2	1	2(LEU)	1.
	79		ARG		GLN	2	2	1(+)	4.
	80	ALA	ALA		ALA	2	1	2(ALA)	1.
	81	GLU	GLU		GLU	2	1	2(GLU)	1.
	82	ASP	ASP		ASP	2	1	2(ASP)	1.
	83	GLU	GLU		GLU	2	1	2(GLU)	1.
	84	ALA	ALA		ALA	2	1	2(ALA)	1.
	85	ASP	ASP		ASP	2	1	2(ASP)	1.
	86	TYR	TYR		TYR	2	1	2(TYR)	1.
	87	TYR	TYR		TYR	2	1	2(TYR)	1.
	88	CYS	CYS		CYS	2	1	2(CYS)	1.
	89	SER	SER		SER	2	1	2(SER)	1.
	90	SER	SER		SER	2	1	2(SER)	1.
	91	TYR	TYR		TYR	2	1	2(TYR)	1.
	92		VAL		GLU	2	2	1(+)	4.
	93		ASP		GLY	2	2	1(+)	4.
	94		ASN		SER	2	2	1(+)	4.
	95		ASN		ASP	2	2	1(+)	4.
CDR	95A	ASN	ASN		ASN	2	1	2(ASN)	
3	95B		---		---				
	95C		---		---				
	95D		---		---				
	95E		---		---				
	95F		---		---				
	96	PHE	PHE		PHE	2	1	2(PHE)	1.
	97	VAL	VAL		VAL	2	1	2(VAL)	1.
	98	PHE	PHE		PHE	2	1	2(PHE)	1.
	99	GLY	GLY		GLY	2	1	2(GLY)	1.
	100		GLY		THR	2	2	1(+)	4.
	101	GLY	GLY		GLY	2	1	2(GLY)	1.
FR	102	THR	THR		THR	2	1	2(THR)	1.
4	103	LYS	LYS		LYS	2	1	2(LYS)	1.
	104		LEU		VAL	2	2	1(+)	4.
	105	THR	THR		THR	2	1	2(THR)	1.
	106	VAL	VAL		VAL	2	1	2(VAL)	1.
	106A	LEU	LEU		LEU	2	1	2(LEU)	
	107		ARG		GLY	2	2	1(+)	4.
	108	GLN	GLN		GLN	2	1	2(GLN)	1.
	109	PRO	PRO		PRO	2	1	2(PRO)	1.

ANTIBODY SPECIFICITIES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP V

3) **MCG:** ANTI-EPSILON-DNP-LYS, EPSILON-DNP-AMINOCAPROATE, DNP-LEU, TRIACETIN, SODIUM MERTHIOLATE, METHADONE, 1,10-PHENANTHROLINE, CAFFEINE, THEOPHYLLINE, DI-DNP-LYS, DNP-TRP, DNP-PHE, DI-DNP-TYR, COLCHICINE, P-NITROANILINE, P-NITROPHENYLPHOSPHORYL CHOLINE, 5-ACETYLURACIL, MENADIONE, MEPERIDINE, TRIBUTYRIN, OMEGA-BROMOHEPTANOATE, O-CHLOROMERCURIPHENOL, P-CHLOROMERCURIPHENOL, PHENYLMERCURIC COMPOUNDS, METHYL-MERCURIC CHLORIDE.

REFERENCE: HUMAN LAMBDA LIGHT CHAINS SUBGROUP V

1) **BO:** WIKLER,M. & PUTNAM,F.W. (1970) J.BIOL.CHEM.,245,4488-4507. (CHECKED BY AUTHOR 06/15/83)

2) **HBJ2:** HOOD,L.,GRAY,W.R.,SANDERS,B.G. & DREYER,W.J. (1967) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,32,133-145.

3) **MCG:** FETT,J.W. & DEUTSCH,H.F. (1974) BIOCHEMISTRY,13,4102-4114. (CHECKED BY AUTHOR)

NOTES: HUMAN LAMBDA LIGHT CHAINS SUBGROUP V

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: BO[1],HBJ2[2]. (2 IDENTICAL)

FR2:

FR3:

FR4: SET 1: BO[1]. (IDENTICAL TO 1 HUMAN V-LAMBDA-I: NEWM[1]; AND 1 HUMAN V-LAMBDA-II: WH[3].)
SET 2: MCG[3]. (IDENTICAL TO 1 HUMAN V-LAMBDA-I: LOC[11].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1: SET 1: MCG[3]. (IDENTICAL TO 2 HUMAN V-LAMBDA-II: MES[2],VIL[17].)

CDR2:

CDR3:

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
29	(GLY,ASP)
30	(TYR,ASN)
31	(LYS,ASN)
40	(PRO,ALA)
42	(LYS,ARG)
46	(LEU,VAL)
47	(ILE,VAL)
49	(TYR,PHE)
52	(SER,ASN)
53	(LYS,GLY)
68	(GLY,ASP)
79	(ARG,GLN)
92	(VAL,GLU)
93	(GLY,ASP)
94	(SER,ASN)
95	(ASP,ASN)
100	(THR,GLY)
104	(LEU,VAL)
107	(ARG,GLY)

HUMAN LAMBDA LIGHT CHAINS SUBGROUP VI

*		INVARIANT RESIDUES	1 AMYLOID -AR #	2 SUT #	3 AMYLOID -RS	4 THO #	5 LBV -CL #	6 GIO	7 YAM	8 WAN	9 WIN	10 NIG -48 #	11 JAM	12 MOR	13 KIN	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0		---	---	---	---	---	---	---	---	---	---	---	---	---				
	1		ASP	ASP	ASP	asn	asn	asn	ASP	asn	asn	asn	ASP	asn	asn	13	2	8(ASN)	3.3
	2		PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	leu	PHE	leu	PHE	13	2	11(PHE)	2.4
	3		MET	MET	MET	MET	MET	MET	MET	ile	MET	MET	MET	MET	MET	13	2	12(MET)	2.2
	4	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	13	1	13(LEU)	1.
	5		THR	THR	THR	THR	THR	THR	THR	THR	THR	ile	THR	THR	leu	13	3	11(THR)	3.5
	6		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	glu	GLN	GLN	13	2	12(GLN)	2.2
	7	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	13	1	13(PRO)	1.
	8		HIS	HIS	HIS	HIS	HIS	HIS	HIS			pro	HIS	HIS	HIS	11	2	10(HIS)	2.2
	9	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	13	1	13(SER)	1.
	10		---	---	---	---	---	---	---	---	---	---	---	---	---				
FR1	11		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	leu	VAL	13	2	12(VAL)	2.2
	12	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	13	1	13(SER)	1.
	13		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp		12	2	11(GLU)	2.2
	14	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER	SER		11	1	11(SER)	1.
	15	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		12	1	12(PRO)	1.
	16	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		12	1	12(GLY)	1.
	17		LYS	LYS	gln	LYS	LYS	LYS	gly	LYS	LYS	LYS	LYS	LYS		12	3	10(LYS)	3.6
	18		THR	THR	THR	THR	THR	THR	lys	THR	THR	THR		THR		11	2	10(THR)	2.2
	19		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		ile		11	2	10(VAL)	2.2
	20		THR	ile	THR	THR	THR	THR	ser	THR	THR	THR		ile		11	3	8(THR)	4.1
	21		PHE	ile	ile	ile	ile	ile	ile	ile		met		ile		10	3	8(ILE)	3.8
	22	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER		SER		10	1	10(SER)	1.
	23	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		CYS		CYS		10	1	10(CYS)	1.
	24		THR	THR	THR	THR	THR	THR	SER			THR		THR		9	2	8(THR)	2.3
	25		GLY	ARG	GLY	ARG	GLY					ARG		ALA		7	3	3(+)	7.
	26		SER	SER	SER	SER	ASN					THR		ASN		7	3	4(SER)	5.3
	27		GLY	ASP	GLY	SER	SER					SER		GLY		7	3	3(+)	7.
	27A		GLY	GLY	ASP	GLY	GLY		ALA			---		GLY		7	3	5(GLY)	
	27B		SER	THR	SER	SER	SER					---		ASN		6	3	4(SER)	
CDR1	27C		---	---	---	---	---					---		---					
	27D		---	---	---	---	---					---		---					
	27E		---	---	---	---	---					ASP		---		1	1	1(ASP)	
	27F		---	---	---	---	---					SER		---		1	1	1(SER)	
	28	ILE	ILE	ILE	ILE	ILE	ILE					ILE		ILE		7	1	7(ILE)	1.
	29		ALA	ALA	ALA	ALA	ALA					ALA		GLY		7	2	6(ALA)	2.3
	30		ASP	GLY		SER	SER					SER		SER		6	3	4(SER)	4.5
	31		SER	TYR	SER	TYR	ASN					ASN		HIS		7	4	2(+)	14.
	32		PHE	TYR	TYR	TYR	TYR					TYR		PRO		7	3	5(TYR)	4.2
	33	VAL	VAL	VAL	VAL	VAL	VAL					VAL		VAL		7	1	7(VAL)	1.
	34	GLN	GLN	GLN		GLN	GLN					GLN				5	1	5(GLN)	1.
	35	TRP	TRP	TRP		TRP	TRP					TRP		TRP		6	1	6(TRP)	1.
	36	TYR	TYR	TYR		TYR	TYR					TYR		TYR		6	1	6(TYR)	1.
	37		GLN	GLN		GLN	GLN					ARG		LYS		6	3	4(GLN)	4.5
	38		GLN	GLN		LEU	GLN					GLN				5	2	4(GLN)	2.5
	39	ARG	ARG	ARG		ARG	ARG					ARG				5	1	5(ARG)	1.
	40		PRO	PRO		PRO	ARG					PRO		PRO		6	2	5(PRO)	2.4
FR2	41		GLY	GLY		GLY	VAL					GLY		ASP		6	3	4(GLY)	4.5
	42		SER	ARG		SER	SER					GLY		SER		6	3	4(SER)	4.5
	43	ALA	ALA	ALA		ALA	ALA					ALA				5	1	5(ALA)	1.
	44	PRO	PRO	PRO		PRO	PRO					PRO				5	1	5(PRO)	1.
	45	THR	THR	THR		THR	THR					THR				5	1	5(THR)	1.
	46		THR	THR		THR	ILE					THR				5	2	4(THR)	2.5
	47		VAL	VAL		VAL	VAL					LEU				5	2	4(VAL)	2.5
	48	ILE	ILE	ILE		ILE	ILE					ILE				5	1	5(ILE)	1.
	49		TYR	PHE		TYR	TYR					TYR				5	2	4(TYR)	2.5
	50		ASP	GLU		GLU	GLU					ASP				5	2	3(GLU)	3.3
	51		ASP	ASP		ASP	ASP					THR				5	2	4(ASP)	2.5
CDR2	52		ASN	THR		ASN	ASN					ASN				5	2	4(ASN)	2.5
	53	GLN	GLN	GLN		GLN	GLN					GLN				5	1	5(GLN)	1.
	54	ARG	ARG	ARG		ARG	ARG					ARG				5	1	5(ARG)	1.
	55	PRO	PRO	PRO		PRO	PRO					PRO				5	1	5(PRO)	1.
	56		SER	SER		SER	LEU					TYR				5	3	3(SER)	5.
	57	GLY	GLY	GLY		GLY	GLY					GLY				5	1	5(GLY)	1.
	58	VAL	VAL	VAL		VAL	VAL					VAL				5	1	5(VAL)	1.
	59	PRO	PRO	PRO		PRO	PRO					PRO				5	1	5(PRO)	1.
	60		ASP	ASP		ASP	ASP					ASN				5	2	4(ASP)	2.5
	61	ARG	ARG	ARG		ARG	ARG					ARG				5	1	5(ARG)	1.
	62	PHE	PHE	PHE		PHE	PHE					PHE				5	1	5(PHE)	1.
	63	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	64	GLY	GLY	GLY		GLY	GLY					GLY				5	1	5(GLY)	1.
	65	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	66		#	#		#	#					#							
	67	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	68		ALA	SER		SER	SER					SER				5	2	4(SER)	2.5
	69	ASN	ASN	ASN		ASN	ASN					ASN				5	1	5(ASN)	1.
	70	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	71	ALA	ALA	ALA		ALA	ALA					ALA				5	1	5(ALA)	1.
FR3	72	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	73	LEU	LEU	LEU		LEU	LEU					LEU				5	1	5(LEU)	1.
	74	THR	THR	THR		THR	THR					THR				5	1	5(THR)	1.
	75		ILE	ILE		VAL	ILE					ILE				5	2	4(ILE)	2.5
	76	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	77		GLY	GLY		GLU	GLY					GLY				5	2	4(GLY)	2.5
	78	LEU	LEU	LEU		LEU	LEU					LEU				5	1	5(LEU)	1.
	79		LYS	GLN		LYS	LYS					THR				5	3	3(LYS)	5.
	80		THR	THR		THR	THR					ASN				5	2	4(THR)	2.5
	81		GLU	GLU		GLU	GLU					ASP				5	2	4(GLU)	2.5
	82	ASP	ASP	ASP		ASP	ASP					ASP				5	1	5(ASP)	1.
	83		GLU	GLU		GLU	GLU					THR				5	2	4(GLU)	2.5
	84	ALA	ALA	ALA		ALA	ALA					ALA				5	1	5(ALA)	1.
	85		ASP	ASP		ASP	ASP					MET				5	2	4(ASP)	2.5
	86	TYR	TYR	TYR		TYR	TYR					TYR				5	1	5(TYR)	1.
	87		TYR	TYR		TYR	TYR					PHE				5	2	4(TYR)	2.5
	88	CYS	CYS	CYS		CYS	CYS					CYS				5	1	5(CYS)	1.
	89	GLN	GLN	GLN		GLN	GLN					GLN				5	1	5(GLN)	1.
	90	SER	SER	SER		SER	SER					SER				5	1	5(SER)	1.
	91		TYR	TYR		TYR	PHE					TYR				5	2	4(TYR)	2.5
	92		ASN	ASP		ASP	ASP					ASP				5	2	4(ASP)	2.5
	93		SER	ARG		SER	ASN					SER				5	3	3(SER)	5.
	94		ASN	ASP		ASN	THR					SER				5	4	2(ASN)	10.
CDR3	95		HIS	HIS		ASN	ASN					ASN				5	2	3(ASN)	3.3
	95A		HIS	---		---	GLN					LEU				3	3	1(+)	
	95B		---	---		---	---					---							
	95C		---	---		---	---					---							
	95D		---	---		---	---					---							
	95E		---	---		---	---					---							
	95F		---	---		---	---					---							
	96		VAL	TRP		TRP	GLY					TRP				5	3	3(TRP)	5.
	97	VAL	VAL	VAL		VAL	VAL					VAL				5	1	5(VAL)	1.
	98	PHE	PHE	PHE		PHE	PHE					PHE				5	1	5(PHE)	1.
	99	GLY	GLY	GLY		GLY	GLY					GLY				5	1	5(GLY)	1.
	100	GLY	GLY	GLY		GLY	GLY					GLY				5	1	5(GLY)	1.
	101	GLY	GLY	GLY		GLY	GLY					GLY				5	1	5(GLY)	1.
FR4	102	THR	THR	THR		THR	THR					THR				5	1	5(THR)	1.
	103	LYS	LYS	LYS		LYS	LYS					LYS				5	1	5(LYS)	1.
	104		VAL	LEU		LEU	LEU					LEU		LEU		6	2	5(LEU)	2.4
	105	THR	THR	THR		THR	THR					THR		THR		6	1	6(THR)	1.
	106	VAL	VAL	VAL		VAL	VAL					VAL		VAL		6	1	6(VAL)	1.
	106A	LEU	LEU	LEU		LEU	LEU					LEU		LEU		6	1	6(LEU)	
	107		GLY	GLY		GLY	GLY					SER		SER		6	2	4(GLY)	3.
	108	GLN	GLN	GLN		GLN	GLN					GLN		GLN		6	1	6(GLN)	1.
	109	PRO	PRO	PRO		PRO	PRO					PRO		PRO		6	1	6(PRO)	1.

HUMAN HEAVY CHAINS SUBGROUP I

		INVARIANT RESIDUES	1 EU	2* SIE	3 HG3 CL #	4* WOL	5 CA	6 ND CL #	7 MOT #	8 BRO IGG	9 THO	10* STE	11 BEN (I)	12 ZUC #	13 DI	14 BOT #	15 OMM CL #	16* MAR	17 FI	18 VU	19 WAR	20 VIL	21 DUN	22 ADA	23 NOR	24 SAW
	0		---	---	#	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1		PCA	PCA	gln	PCA	PCA	gln	PCA	glu	glu	PCA	glu	PCA	PCA	asp	gln	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA	PCA
	2		VAL	VAL	VAL	VAL	VAL	thr	VAL	VAL	VAL	VAL	leu	VAL	VAL	ser	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	3		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	his	GLN	GLN	GLN	pro	his	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	glu
	4	LEU(.96)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	val	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU			LEU
	5		VAL	VAL	VAL	met	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		glu	gln									
	6		GLN	GLN	GLN	GLN	glu	GLN	GLN	GLN	GLN	glu	GLN	glu		GLN	glu									
	7	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		SER	SER									
	8		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	ser	GLY	GLY	GLY	GLY	GLY									
	9		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	gly	his	pro									
	10		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp		GLU	gly									
	11		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	leu		VAL	leu									
	12		LYS	LYS	LYS	LYS	arg	arg	LYS	LYS	LYS	LYS	ser	val	LYS	gly	gly									
	13		LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS		LYS	LYS	ile	LYS									
	14		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO		leu	PRO									
FR1	15		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		lys	pro									
	16		SER	SER	ala	SER	ala	ala	SER	glu	glu	ala		gly		glu	---									
	17		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER		---		thr	---									
	18		VAL	VAL	VAL	VAL	VAL	VAL	ala	leu	leu	met		---		glu	---									
	19		LYS	arg	LYS	arg	LYS	arg	arg	LYS	arg	LYS		---	LYS	ala	---									
	20		VAL	VAL	VAL	VAL	ile	VAL	leu	ile	ile	VAL		---		glu	---									
	21		SER	thr	SER	SER	SER	SER	SER	SER	SER	SER		---		asp	---									
	22		CYS	CYS	CYS	CYS	CYS	CYS	CYS			CYS		---		arg	---									
	23		LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	arg		---		ile	---									
	24		ALA	thr	ALA	thr	thr	ALA	val	gly	gly	ALA		---		ile	---									
	25		SER	SER	SER	SER	SER	SER	SER	SER	phe			---		lys	---									
	26		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY			---		glu	---									
	27		GLY	GLY	tyr	GLY	tyr	tyr	asp	tyr	tyr			---		glu	---									
	28		THR	THR	THR	THR	THR	THR	asp					---		glu	---									
	29		PHE	PHE	PHE	PHE	PHE	PHE	PHE					---		ala	---									
	30		SER	SER	asn	val	SER	ile	asn					---		arg	---									
CDR1	31		ARG	GLY	SER	ASP	HIS	ASP	THR					---		LEU	---									
	32		SER	TYR	TYR	TYR	TYR	SER	TYR					---		SER	---									
	33		ALA	THR	TYR	LYS	ALA	TYR	ASP					---		GLY	---									
	34		ILE	ILE	MET	GLY	MET	ILE	ILE					---		ARG	---									
	35		ILE	SER	HIS	LEU		HIS	HIS					---	SER	ASP	---									
	35A		---	---	---	---		---	---					---	---	---	---									
	35B		---	---	---	---		---	---					---	---	---	---									
	36		TRP	TRP	TRP	TRP		TRP	TRP					---	TRP	MET	---									
	37		VAL	VAL	VAL	VAL		ILE	VAL					---	ILE	GLN	---									
	38		ARG	ARG	ARG	ARG		ARG	ARG					---	ARG	VAL	---									
	39		GLN	GLN	GLN	GLN		GLN	GLN					---	GLN	THR	---									
	40		ALA	ALA	ALA	ALA		ALA	ALA					---	PRO	SER	---									
	41		PRO	PRO	PRO	PRO		PRO	PRO					---	PRO	GLN	---									
FR2	42		GLY	GLY	GLY	GLY		GLY	GLY					---	GLY	PRO	---									
	43		GLN	ARG	GLN	LYS		HIS	ARG					---	LYS	---	---									
	44	GLY	GLY	GLY	GLY	GLY		GLY	GLY					---	GLY	---	---									
	45	LEU	LEU	LEU	LEU	LEU		LEU	LEU					---	LEU	---	---									
	48	GLU	GLU	GLU	GLU	GLU		GLU	GLU					---	GLU	---	---									
	47	TRP	TRP	TRP	TRP	TRP		TRP	TRP					---	TRP	---	---									
	48		MET	VAL	MET	VAL		VAL	MET					---	VAL	---	---									
	49		GLY	GLY	GLY	GLY		GLY	ALA					---	GLY	---	---									
	50		GLY	SER	ILE	GLN		TRP	VAL					---	GLU	---	---									
	51		ILE	PRO	ILE	ILE		ILE	VAL					---	ILE	---	---									
	52		VAL	ALA	ASN	PRO		ASN	HIS					---	ASP	---	---									
	52A		PRO	LYS	PRO	LEU		PRO	PRO					---	---	---	---									
	52B		---	---	---	---		---	---					---	---	---	---									
	52C		---	---	---	---		---	---					---	---	---	---									
	53		MET	TRP	SER	ARG		ASN	SER					---	TYR	---	---									
	54		PHE	THR	GLY	PHE		SER	ASP					---	SER	---	---									
CDR2	55		GLY	ASP	GLY	ASN		GLY	ASP					---	GLY	---	---									
	56		PRO	PRO	SER	GLY		GLY	ARG					---	THR	---	---									
	57		PRO	PHE	THR	GLU		THR	THR					---	THR	---	---									
	58		ASN	GLN	SER	VAL		ASP	THR					---	ASP	---	---									
	59		TYR	GLY	TYR	LYS		TYR	TYR					---	TYR	---	---									
	60		ALA	VAL	ALA	ASN		ALA	GLY					---		---	---									
	61		GLN	TYR	GLN	PRO		PRO	PRO					---		---	---									
	62		LYS	ILE	LYS	GLY		ARG	ARG					---		---	---									
	63		PHE	LYS	PHE	SER		PHE	SER					---		---	---									
	64		GLN	TRP	GLN	VAL		GLN	GLN					---	LYS	---	---									
	65		GLY	GLU	GLY	VAL		GLY	ALA					---	SER	---	---									
	66	ARG	ARG	ARG	ARG	ARG		ARG	ARG					---	ARG	---	---									
	67		VAL	VAL	VAL	VAL		VAL	PHE					---		---	---									
	68		THR	THR	THR	SER		THR	THR					---		---	---									
	69		ILE	VAL	MET	VAL		MET	VAL					---	MET	---	---									
	70		THR	SER	THR	SER		THR	THR					---	SER	---	---									
	71		ALA	LEU	ARG	LEU		ARG	ARG					---	LEU	---	---									
	72		ASP	LYS	ASP	LYS		ASP	ASP					---	ASP	---	---									
	73		GLU	PRO	THR	PRO		ALA	SER					---	THR	---	---									
	74	SER	SER	SER	SER	SER		SER	SER					---	SER	---	---									
	75		THR	PHE	THR	PHE		PHE	THR					---	VAL	---	---									
	76		ASN	ASN	SER	ASN		SER	THR					---	ASN	---	---									
	77		THR	GLN	THR	GLN		THR	THR					---	LEU	---	---									
	78		ALA	ALA	VAL	ALA		ALA	VAL					---	PHE	---	---									
	79		TYR	TYR	TYR	HIS		TYR	TYR					---	SER	---	---									
FR3	80		MET	MET	MET	MET		MET	MET					---	LEU	---	---									
	81		GLU	GLU	GLU	GLU		ASP	GLU					---	SER	---	---									
	82		LEU	LEU	LEU	LEU		LEU	LEU					---	LEU	---	---									
	82A		SER	VAL	SER	SER		ARG	THR					---	THR	---	---									
	82B		SER	ASN	SER	SER		SER	ALA					---	SER	---	---									
	82C		LEU	LEU	LEU	LEU		LEU	LEU					---	VAL	---	---									
	83		ARG	PHE	ARG	PHE		ARG	ILE					---	THR	---	---									
	84		SER	ASN	SER	SER		SER	SER					---	ALA	---	---									
	85		GLU	GLU	GLU	GLU		ASP	ALA					---	ALA	---	---									
	86		ASP	ASP	ASP	ASP		ASP	ASP					---	ASP	---	---									
	87		THR	GLY	THR	THR		SER	THR					---	THR	---	---									
	88	ALA	ALA	ALA	ALA	ALA		ALA	ALA					---	ALA	---	---									
	89		PHE	VAL	VAL	VAL		VAL	ILE					---	VAL	---	---									
	90		TYR	TYR	TYR	TYR		PHE	TYR					---	TYR	---	---									
	91		PHE	TYR	TYR	TYR		TYR	TYR					---	TYR	---	---									
	92	CYS	CYS	CYS	CYS	CYS		CYS	CYS					---	CYS	---	---									
	93		ALA	ALA	ALA	ALA		ALA	ALA					---	ALA	---	---									
	94		GLY	ARG	ARG	ARG		LYS	ARG					---	ARG	---	---									
	95		GLY	GLU	#	GLU		SER	GLY					---		---	---									
	96		TYR	TRP	---	TYR		ASP	ALA					---		---	---									
	97		GLY	LYS	---	GLY		PRO	HIS					---		---	---									
	98		ILE	GLY	---	PHE		PHE	TYR					---		---	---									
	99		TYR	GLN	---	ASP		TRP	SER					---		---	---									
	100		SER	VAL	---	THR		SER	ASP					---		---	---									
	100A		---	ASN	---	SER		ASP	THR					---		---	---									
CDR3	100B		---	VAL	---	ASP		TYR	ASP					---		---	---									
	100C		---	ASN	---	TYR		TYR	ASP					---		---	---									
	100D		---	PRO	---	TYR		ASN	SER					---		---	---									
	100E		---	---	---	---		PHE	GLY					---		---	---									
	100F		---	---	---	---		ASP	THR					---		---	---									
	100G		---	---	---	---		TYR	SER					---		---	---									
	100H		---	---	---	---		SER	LEU					---		---	---									
	100I		---	---	---	---		TYR	---					---		---	---									
	100J		---	---	---	---		THR	---					---		---	---									
	100K		---	PHE	---	TYR		LEU	---					---		---	---									
	101		PRO	ASP	---	TYR		ASP	GLY					---		---	---									
	102		GLU	TYR	---	TYR		VAL	PRO					---	ARG	---	---									
	103		GLU	TRP	---	TRP		TRP	TRP					---	TRP	---	---									
	104		TYR	GLY	---	GLY		GLY	GLY					---	GLY	---	---									
	105		ASN	GLN	---	GLN		GLN	GLN					---	SER	---	---									
	106	GLY	GLY	GLY	---	GLY		GLY	GLY					---	GLY	---	---									
	107		GLY	VAL	---	THR		THR	THR					---	GLY	---	---									
FR4	108		LEU	LEU	---	LEU		THR	LEU					---	LEU	---	---									
	109		VAL	VAL	---	VAL		VAL	LEU					---	VAL	---	---									
	110		THR	THR	---	THR		---	ILE					---	THR	---	---									
	111	VAL	VAL	VAL	---	VAL		VAL	VAL					---	VAL	---	---									
	112		SER	SER	---	SER		SER	SER					SER	SER	---	---									
	113	SER	SER	SER	---	SER		SER	SER					SER	SER	---	---									

HUMAN HEAVY CHAINS SUBGROUP I (cont'd)

		25* KOH	26 RIC	27 WIS #	28 VAU #	29 LEB #	30 SAC #	31 DEE	32 LEA	33 HAR	34 HUS	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY
	0	---	---	---	---	---	---		---	---					
	1	gln	PCA	PCA	PCA	PCA	gly		---	---		30	5	21(PCA)	7.1
	2	VAL	VAL	met	VAL	VAL	ala		---	---		30	6	25(VAL)	7.2
	3	GLN	leu	GLN	---	---	---		pca	pca		29	6	22(GLN)	7.9
	4	LEU		---	---	---	---		LEU	LEU		25	2	24(LEU)	2.1
	5			---	---	---	---					14	4	11(VAL)	5.1
	6			---	---	---	---					14	2	10(GLN)	2.8
	7			---	---	---	---					14	1	14(SER)	1.
	8			---	---	---	---					15	2	14(GLY)	2.1
	9			---	---	---	---					15	4	12(ALA)	5.
	10			---	---	---	---					14	3	12(GLU)	3.5
	11			---	---	---	---					14	2	12(VAL)	2.3
	12			---	---	---	---					15	5	9(LYS)	8.3
	13			---	---	---	---					14	2	13(LYS)	2.2
	14			---	---	---	---					14	2	13(PRO)	2.2
FR1	15			---	---	---	---					14	3	12(GLY)	3.5
	16			---	---	---	---					12	4	4(+)	12.
	17			---	---	---	---					11	2	10(SER)	2.2
	18			---	---	---	---	VAL				12	5	7(VAL)	8.6
	19			---	---	---	---	arg				13	3	6(+)	6.5
	20			---	---	---	---	ile				12	4	6(VAL)	8.
	21			---	---	---	---					11	3	9(SER)	3.7
	22			---	---	---	---					9	2	8(CYS)	2.3
	23			---	---	---	---					11	3	9(LYS)	3.7
	24			---	---	---	---					11	5	4(ALA)	14.
	25			---	---	---	---					10	3	8(SER)	3.8
	26			---	---	---	---					10	2	9(GLY)	2.2
	27			---	---	---	---					10	4	5(TYR)	8.
	28			---	---	---	---					8	3	6(THR)	4.
	29			---	---	---	---					8	2	7(PHE)	2.3
	30			---	---	---	---					8	5	3(SER)	13.
CDR1	31			---	---	---	---					8	7	2(ASP)	28.
	32			---	---	---	---					8	2	5(TYR)	3.2
	33			---	---	---	---					8	6	2(+)	24.
	34			---	---	---	---					8	4	4(ILE)	8.
	35			---	---	---	---					8	5	3(HIS)	13.
	35A			---	---	---	---								
	35B			---	---	---	---								
	36			---	---	---	---					8	2	7(TRP)	2.3
	37			---	---	---	---					8	3	5(VAL)	4.8
	38			---	---	---	---					8	2	7(ARG)	2.3
	39			---	---	---	---					8	2	7(GLN)	2.3
	40			---	---	---	---					8	3	6(ALA)	4.
	41			---	---	---	---					8	2	7(PRO)	2.3
FR2	42			---	---	---	---					8	2	7(GLY)	2.3
	43			---	---	---	---					7	4	2(+)	14.
	44			---	---	---	---					7	1	7(GLY)	1.
	45			---	---	---	---					7	1	7(LEU)	1.
	46			---	---	---	---					7	1	7(GLU)	1.
	47			---	---	---	---					7	1	7(TRP)	1.
	48			---	---	---	---					7	2	4(VAL)	3.5
	49			---	---	---	---					7	2	6(GLY)	2.3
	50			---	---	---	---					7	7	1(+)	49.
	51			---	---	---	---					7	3	5(ILE)	4.2
	52			---	---	---	---					7	6	2(ASN)	21.
	52A			---	---	---	---					6	3	4(PRO)	
	52B			---	---	---	---								
	52C			---	---	---	---								
	53			---	---	---	---					7	6	2(SER)	21.
	54			---	---	---	---					7	5	2(+)	18.
CDR2	55			---	---	---	---					7	3	4(GLY)	5.3
	56			---	---	---	---					7	5	2(+)	18.
	57			---	---	---	---					7	4	4(THR)	7.
	58			---	---	---	---					7	6	2(ASN)	21.
	59			---	---	---	---					7	3	5(TYR)	4.2
	60			---	---	---	---					6	4	3(ALA)	8.
	61			---	---	---	---					6	3	3(PRO)	6.
	62			---	---	---	---					6	4	2(+)	12.
	63			---	---	---	---					6	3	3(PHE)	6.
	64			---	---	---	---					7	4	4(GLN)	7.
	65			---	---	---	---					7	5	3(GLY)	12.
	66			---	---	---	---					7	1	7(ARG)	1.
	67			---	---	---	---					6	2	5(VAL)	2.4
	68			---	---	---	---					6	2	5(THR)	2.4
	69			---	---	---	---					7	3	3(+)	7.
	70			---	---	---	---					7	2	4(THR)	3.5
	71			---	---	---	---					7	3	3(+)	7.
	72			---	---	---	---					7	2	5(ASP)	2.8
	73			---	---	---	---					7	5	2(+)	18.
	74			---	---	---	---					7	1	7(SER)	1.
	75			---	---	---	---					7	3	3(+)	7.
	76			---	---	---	---					7	3	4(ASN)	5.3
	77			---	---	---	---					7	3	4(THR)	5.3
	78			---	---	---	---					7	3	4(ALA)	5.3
	79			---	---	---	---					7	3	5(TYR)	4.2
	80			---	---	---	---					7	2	6(MET)	2.3
FR3	81			---	---	---	---					7	3	5(GLU)	4.2
	82			---	---	---	---				MET	8	2	7(LEU)	2.3
	82A			---	---	---	---				ASN	8	5	3(SER)	
	82B			---	---	---	---				SER	8	3	6(SER)	
	82C			---	---	---	---				LEU	8	2	7(LEU)	
	83			---	---	---	---				ARG	8	4	4(ARG)	8.
	84			---	---	---	---				VAL	8	4	5(SER)	6.4
	85			---	---	---	---				GLX	8	3 : 4	5(GLU) : 4(GLU)	4.8 : 8.
	86			---	---	---	---				ASX	8	1 : 2	8(ASP) : 7(ASP)	1. : 2.3
	87			---	---	---	---				THR	8	3	6(THR)	4.
	88			---	---	---	---				ALA	8	1	8(ALA)	1.
	89			---	---	---	---				VAL	8	3	6(VAL)	4.
	90			---	---	---	---	TYR			TYR	9	2	8(TYR)	2.3
	91			---	---	---	---	TYR			TYR	9	2	8(TYR)	2.3
	92			---	---	---	---	CYS			CYS	9	1	9(CYS)	1.
	93			---	---	---	---	THR			ALA	9	2	8(ALA)	2.3
	94			---	---	---	---	GLY			ARG	9	3	6(ARG)	4.5
	95			---	---	---	---	ARG			ASX	7	5	2(+)	18.
	96			---	---	---	---	GLY			ARG	7	6	2(TYR)	21.
	97			---	---	---	---	MET			ASX	7	6	2(GLY)	21.
	98			---	---	---	---				ASX	6	5	2(PHE)	15.
	99			---	---	---	---				TYR	6	5	2(TYR)	15.
	100			---	---	---	---				GLY	6	5	2(SER)	15.
	100A			---	---	---	---				ASX	5	4	2(ASN) : 2(ASP)	
	100B			---	---	---	---				PHE	5	4	2(ASP)	
CDR3	100C			---	---	---	---				---	4	3	2(TYR)	
	100D			---	---	---	---				---	4	4	1(+)	
	100E			---	---	---	---				---	2	2	1(+)	
	100F			---	---	---	---				---	2	2	1(+)	
	100G			---	---	---	---				---	2	2	1(+)	
	100H			---	---	---	---				---	2	2	1(+)	
	100I			---	---	---	---				---	1	1	1(TYR)	
	100J			---	---	---	---				---	1	1	1(THR)	
	100K			---	---	---	---				---	3	3	1(+)	
	101			---	---	---	PRO				ASX	7	4 : 5	3(ASP) : 2(+)	9.3 : 18.
	102			---	---	---	GLX				TYR	8	5 : 6	3(TYR)	13. : 16.
	103			---	---	---	GLX				TRP	8	2 : 3	6(TRP)	2.7 : 4.
	104			---	---	---	THR				GLY	8	3	6(GLY)	4.
	105			---	---	---	ASX				GLX	8	3 : 5	5(GLN) : 4(GLN)	4.8 : 10.
	106		GLY	---	---	---	---				GLY	8	1	8(GLY)	1.
FR4	107		VAL	---	---	---	LEU				THR	9	4	4(THR)	9.
	108		#	---	---	---	VAL				LEU	8	3	6(LEU)	4.
	109		#	---	---	---	ILE				VAL	8	3	6(VAL)	4.
	110		THR	---	---	---	THR				THR	9	2	8(THR)	2.3
	111		VAL	---	---	---	VAL				VAL	9	1	9(VAL)	1.
	112		SER	---	---	---	SER				THR	10	2	9(SER)	2.2
	113		SER	---	---	---	SER				SER	10	1	10(SER)	1.

ANTIBODY SPECIFICITIES: HUMAN HEAVY CHAINS SUBGROUP I

2) **SIE:** ANTI-HUMAN GAMMA G GLOBULIN; WA IDIOTYPE
4) **WOL:** ANTI-HUMAN GAMMA G GLOBULIN; WA IDIOTYPE
10) **STE:** COLD AGGLUTININ WITH ANTI-BLOOD GROUP I ACTIVITY
16) **MAR:** ANTI-LIPOPROTEIN LIPASE
25) **KOH:** ANTI-HUMAN GAMMA G GLOBULIN

CLASS: HUMAN HEAVY CHAINS SUBGROUP I

1) **EU:** IGG1-KAPPA
2) **SIE:** IGM-KAPPA
4) **WOL:** IGM-KAPPA
5) **CA:** IGG1-
6) **ND'CL:** IGE-
7) **MOT:** IGG-
8) **BRO'IGG:** IGG-KAPPA
10) **STE:** IGG1-
11) **BEN(I):** IGG3-
12) **ZUC:** IGG3-
13) **DI:** IGM-
14) **BOT:** IGM-
15) **OMM'CL:** IGG3-
16) **MAR:** IGM-
19) **WAR:** IGG1-
20) **VIL:** IGG3-LAMBDA
21) **DUN:** IGG4-
22) **ADA:** IGA-
23) **NOR:** IGA-
24) **SAW:** IGG2-
25) **KOH:** IGM-LAMBDA
26) **RIC:** IGG3-
27) **WIS:** IGG3-
28) **VAU:** IGG1-
29) **LEB:** IGG1-
30) **SAC:** IGG1-KAPPA
34) **HUS:** IGG3-

REFERENCE: HUMAN HEAVY CHAINS SUBGROUP I

1) **EU:** CUNNINGHAM,B.A.,RUTISHAUSER,U.,GALL,W.E.,GOTTLIEB,P.D.,WAXDAL,M.J. & EDELMAN,G.M. (1970) BIOCHEMISTRY,9,3161-3170. (CHECKED BY AUTHOR)
2) **SIE:** ANDREWS,D.W. & CAPRA,J.D. (1981) PROC.NAT.ACAD.SCI.USA,78,3799-3803; ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5816-5822. (CHECKED BY AUTHOR 11/15/82); ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5822-5830.
3) **HG3'CL:** RECHAVI,G.,RAM,.D.,GLAZER,L.,ZAKUT,R. & GIVOL,D. (1983) PROC.NAT.ACAD.SCI.USA,80,855-859. (CHECKED BY AUTHOR 01/04/83)
4) **WOL:** ANDREWS,D.W. & CAPRA,J.D. (1981) PROC.NAT.ACAD.SCI.USA,78,3799-3803; ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5816-5822. (CHECKED BY AUTHOR 11/15/82); ANDREWS,D.W. & CAPRA,J.D. (1981) BIOCHEMISTRY,20,5822-5830.
5) **CA:** PITCHER,S.E. & KONIGSBERG,W. (1970) J.BIOL.CHEM.,245,1267-1274. (CHECKED BY AUTHOR)
6) **ND'CL:** BENNICH,H. & VON BAHR-LINDSTROM,H. (1974) PROGRESS IN IMMUNOLOGY,1,49-58; BENNICH,H.H.,JOHANSSON,S.G.O. & VON BAHR-LINDSTROM,H. (1978) IN IMMEDIATE HYPERSENSITIVITY: MODERN CONCEPTS AND DEVELOPMENTS, BACH,M.K., ED.,PP.1-36, MARCEL DEKKER,NEW YORK; KENTEN,J.H.,MOLGAARD,H.V.,HOUGHTON,M.,DERBYSHIRE,R.B.,VINEY,J.,BELL,L.O. & GOULD,H.J. (1982) PROC.NAT.ACAD.SCI.USA,79,6661-6665.
7) **MOT:** KOJIMA,M.,ODANI,S. & ONO,T. (1982) MOL.IMMUNOL.,19,1095-1103; KOJIMA,M.,KOIDE,T.,ODANI,S. & ONO,T. (1986) MOL.IMMUNOL.,23,169-174 (CHECKED BY AUTHOR 08/08/86)
8) **BRO'IGG:** HOPPER,J.E.,NOYES,C.,HEINRIKSON,R. & KESSEL,J.W. (1976) J.IMMUNOL.,116,743-746; HOPPER,J.E. & BRAHN,E. (1977) J.IMMUNOL.,119, 847-849. (CHECKED BY AUTHOR 08/25/78 WHO POINTED OUT THAT BRO' IS SAME AS BRIGG AND SUGGESTED THAT IT SHOULD BE RENAMED AS BRO(GG)
9) **THO:** HOPPER,J.E. & BRAHN,E. (1977) J.IMMUNOL.,119,847-849. (CHECKED BY AUTHOR 08/25/78)
10) **STE:** FISHER,C.E.,PALM,W.H. & PRESS,E.M. (1969) FEBS LETTERS,5,20-22. (CHECKED BY AUTHOR)
11) **BEN(I):** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
12) **ZUC:** FRANGIONE,B. & MILSTEIN,C. (1969) NATURE,224,597-599. (CHECKED BY AUTHOR)
13) **DI:** KOHLER,H.,SHIMIZU,A.,PAUL,C.,MOORE,V. & PUTNAM,F.W. (1970) NATURE,227,1318-1320; FLORENT,G.,LEHMAN,D. & PUTNAM,F.W. (1974) BIOCHEMISTRY,13,2482-2498. (CHECKED BY AUTHOR 06/15/83)
14) **BOT:** BARNIKOL-WATANABE,S.,MIHAESCO,E.,MIHAESCO,C.,BARNIKOL,H.U. & HILSCHMANN,N. (1984) Z.PHYSIOL.CHEM.,365,105-118.
15) **OMM'CL:** ALEXANDER,A.,STEINMETZ,M.,BARRITAULT,D.,FRANGIONE,B.,FRANKLIN,E.C.,HOOD,L. & BUXBAUM,J.N. (1982) PROC.NAT.ACAD.SCI.USA,79, 3260-3264. (CHECKED BY AUTHOR 06/17/83)
16) **MAR:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
17) **FI:** MONTGOMERY,P.C.,BELLO,A.C. & ROCKEY,J.H. (1970) BIOCHIM.BIOPHYS.ACTA,200,258-268. (CHECKED BY AUTHOR)
18) **VU:** MONTGOMERY,P.C.,BELLO,A.C. & ROCKEY,J.H. (1970) BIOCHIM.BIOPHYS.ACTA,200,258-266. (CHECKED BY AUTHOR)
19) **WAR:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
20) **VIL:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
21) **DUN:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
22) **ADA:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
23) **NOR:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
24) **SAW:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
25) **KOH:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
26) **RIC:** KAPLAN,A.P.,HOOD,L.,TERRY,W.D. & METZGER,H. (1971) IMMUNOCHEMISTRY,8,801-811. (CHECKED BY AUTHOR)
27) **WIS:** FRANKLIN,E.C.,PRELLI,F. & FRANGIONE,B. (1979) PROC.NAT.ACAD.SCI.USA,76,452-456. (CHECKED BY AUTHOR 07/18/79)
28) **VAU:** FRANKLIN,E.C.,KYLE,R.,SELIGMANN,M. & FRANGIONE,B. (1979) MOL.IMMUNOL.,16,919-921. (CHECKED BY AUTHOR 12/10/82)
29) **LEB:** FRANKLIN,E.C.,KYLE,R.,SELIGMANN,M. & FRANGIONE,B. (1979) MOL.IMMUNOL.,16,919-921. (CHECKED BY AUTHOR 12/10/82)
30) **SAC:** PARR,D.M. (1981) MOL.IMMUNOL.,18,257-259. (CHECKED BY AUTHOR 03/02/82)
31) **DEE:** FRANGIONE,B. & MILSTEIN,C. (1967) NATURE,216,939-941. (CHECKED BY AUTHOR)
32) **LEA:** FRANGIONE,B. & FRANKLIN,E.C. (1977) PROG.IMMUNOL.,3,278-288. (CHECKED BY AUTHOR 07/18/79)
33) **HAR:** FRANGIONE,B. & FRANKLIN,E.C. (1977) PROG.IMMUNOL.,3,278-288. (CHECKED BY AUTHOR 07/18/79)
34) **HUS:** WANG,A.C. & FUDENBERG,H.H. (1975) ARCH.BIOCHEM.BIOPHYS.,168,657-664. (CHECKED BY AUTHOR 09/23/77)

NOTES: HUMAN HEAVY CHAINS SUBGROUP I

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1: SET 1: VAU[28],LEB[29]. (2 IDENTICAL)

FR2: SET 1: EU[1],HG3'CL[3]. (2 IDENTICAL)
SET 2: WOL[4]. (IDENTICAL TO 2 HUMAN V-H-III: TIL[4],TEI[10].)

FR3: SET 1: ND'CL[6]. (IDENTICAL TO 1 HUMAN V-H-III: U266'CL[106].)

FR4: SET 1: WOL[4]. (IDENTICAL TO 2 HUMAN V-H-II: MCE'[4],NZU[15]; 4 HUMAN V-H-III: TIL[4],DOB[31],WEA[33],NIE[34]; AND 1 MOUSE V-H-IIIA: MOPC47A[48].)
SET 2: ND'CL[6]. (IDENTICAL TO 1 HUMAN V-H-II: HIG1'CL[10]; 1 HUMAN V-H-III: U266'CL[106]; AND 1 MOUSE V-H-IIA: HDEX12[15].)

IDENTICAL SETS OF COMPLEMENTARITY DETERMINING REGIONS:

CDR1:

CDR2:

CDR3: SET 1: HG3'CL[3]. (IDENTICAL TO 1 HUMAN V-H-III: LAMBDA-VH26'CL[2]; 1 MOUSE V-H-IB: PJ14'CL[22]; AND 5 MOUSE V-H-IIB: 186-2'CL[3], 186-1'CL[5],102'CL[15],23'CL[18],3'CL[26].)
SET 2: ND'CL[6]. (IDENTICAL TO 1 HUMAN V-H-III: U266'CL[106].)

IDENTICAL SETS OF J-MINIGENES:

SET 1: ND'CL[6]. (IDENTICAL TO 1 HUMAN V-H-II: HIG1'CL[10]; AND 1 HUMAN V-H-III: U266'CL[106].)

NOTES: HUMAN HEAVY CHAINS SUBGROUP I (cont'd)

SPECIFIC NOTES:

3) **HG3'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN FETAL LIVER GENOMIC DNA.

6) **ND'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF MOUSE CDNA. IT CORRESPONDS TO THE AMINO ACID SEQUENCE DETERMINED EARLIER EXCEPT THAT THE AMINO ACID SEQUENCE DETERMINATION GAVE PCA AT POSITION 1, VAL AT 2, VAL AT 34, GLY AT 35, ILE AT 48 AND HIS AT 49.

7) **MOT:** PAPAIN CLEAVES BETWEEN ARG 56 AND THR 57, AND BETWEEN ARG 62 AND SER 63

12) **ZUC:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.

14) **BOT:** IT WAS FROM A CASE OF IGM HEAVY CHAIN DISEASE.

15) **OMM'CL:** THE AMINO ACID SEQUENCE IS OBTAINED BY TRANSLATING THE NUCLEOTIDE SEQUENCE OF A CLONE OF HUMAN CELL LINE CDNA. IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.

27) **WIS:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE. ITS RESIDUES AT POSITIONS 108 AND 109 ARE ASN AND CYS RESPECTIVELY, WHICH DO NOT CORRESPOND TO THE USUAL RESIDUES FOUND AT THESE POSITIONS IN HUMAN HEAVY CHAIN SUBGROUP I

28) **VAU:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.

29) **LEB:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.

30) **SAC:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
16	(ALA,SER)
19	(LYS,ARG)
33	(TYR,ALA)
43	(LYS,ARG,GLN)
50	(TRP,ILE,VAL,SER,GLY,GLU,GLN)
54	(PHE,SER)
56	(PRO,GLY)
62	(LYS,ARG)
69	(VAL,MET)
71	(LEU,ARG)
73	(PRO,THR)
75	(PHE,THR)
95	(GLY,GLU)
100D	(TYR,PRO,SER,ASN)
100E	(PHE,GLY)
100F	(THR,ASP)
100G	(TYR,SER)
100H	(LEU,SER)
100K	(TYR,PHE,LEU)
101	(PRO,ASP)

HUMAN HEAVY CHAINS SUBGROUP II

		INVARIANT RESIDUES	1 COR	2 DAW	3 OU	4 MCE #	5 CE-1 CL #	6 HE	7 SUP-T1 VH-JA CL #	8* NEWM	9 WAH	10 HIG1 CL	11 CAR	12 SA	13 IO	14 SPA #	15 NZU #	16 ERI	# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID
	0		---	---	---	---	---	---	---	---	---	---			---	---					
	1		PCA	PCA	PCA	PCA	gln	PCA	gln	PCA	arg	gln			PCA	PCA			12	3	8(PCA)
	2		VAL	VAL	VAL	ile	VAL	VAL	VAL	VAL	leu	VAL			VAL	glu			12	4	9(VAL)
	3		THR	THR	THR	THR	asn	THR	gln	gln	gln	gln			THR	glu			12	4	6(THR)
	4		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU			LEU	val			12	2	11(LEU)
	5		ARG	ARG	thr	lys	ARG	lys	gln	glx	gln	gln				ARG			11	4 : 5	4(+) : 4(ARG)
	6		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLX	GLU	gln				GLU			11	2	10(GLU) : 9(GLU)
	7		SER	SER	SER	SER	SER	SER	SER	SER	SER	trp				SER			11	3	9(SER)
	8	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY				---			10	1	10(GLY)
	9		PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	ala				---			10	2	9(PRO)
	10		ALA	ALA	ALA	thr	ALA	thr	gly	gly	gly	gly				---			10	3	4(+)
	11	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU				---			10	1	10(LEU)
	12	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL				---			10	1	10(VAL)
	13		LYS	arg	LYS	LYS	LYS	LYS	LYS	LYS	arg	LYS				---			10	2	8(LYS)
FR1	14		PRO	PRO	PRO	PRO	ala	PRO	PRO	PRO	PRO	PRO				---			10	2	9(PRO)
	15		THR	THR	lys	THR	THR	THR	ser	ser	ser	ser				---			10	3	5(THR)
	16		GLN	GLN	GLN	glu	his	glu	glu	GLN	glu	glu				---			10	3	5(GLU)
	17		THR	THR	pro	THR	THR	THR	THR	THR	THR	THR				---			10	2	9(THR)
	18	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU				---			10	1	10(LEU)
	19		THR	THR	THR	THR	THR	THR	ser	ser	ser	ser				---			10	2	6(THR)
	20	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU			---			11	1	11(LEU)
	21	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR		---			12	1	12(THR)
	22	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS		---			12	1	12(CYS)
	23		THR	THR	THR	THR	THR	THR	THR	THR	ile	ala	THR	THR		---			12	3	10(THR)
	24		PHE	PHE	PHE	PHE	PHE	leu	val	val	val	val	val	val		---			12	3	6(VAL)
	25		SER	SER	SER	SER	SER	SER	SER	SER	SER	phe	SER	SER		---			12	2	11(SER)
	26	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY		---			12	1	12(GLY)
	27		PHE	PHE	PHE	PHE	leu	leu	tyr	ser	gly	gly		gly		---			11	5	4(PHE)
	28		SER	SER	SER	SER	SER	SER	SER	thr	pro	SER		SER		---			11	3	9(SER)
	29		LEU	LEU	LEU	LEU	val	LEU	ile	phe	ile	phe				---			10	4	5(LEU)
	30		SER	SER	SER	SER	asn	thr	SER	SER	arg	SER				---			10	4	7(SER)
	31		SER	GLY	THR	THR	THR	THR	SER	ASN	ARG	GLY				---			10	5	4(THR)
	32		THR	GLU	SER	SER	ARG	ASP	GLY	ASP	THR	TYR				---			10	7	2(+)
	33		GLY	THR	ARG	GLY	GLY	GLY	TYR	TYR	GLY	TYR				---			10	4	5(GLY)
CDR1	34		MET	MET	MET	VAL	MET	VAL	TYR	TYR	TYR	TRP				---			10	4	4(MET)
	35		CYS	CYS	ARG	GLY	SER	ALA	TRP	THR	TYR	SER				---			10	8	2(+)
	35A		VAL	VAL	VAL	VAL	VAL	VAL	GLY	---	TRP	---				---			8	3	6(VAL)
	35B		GLY	ALA	SER	GLY	SER	GLY	---	---	GLY	---				---			7	3	4(GLY)
	36	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP				---			10	1	10(TRP)
	37		ILE	ILE	ILE	ILE	ILE	ILE	ILE	VAL	ILE	ILE				---			10	2	9(ILE)
	38	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG				---			10	1	10(ARG)
	39		GLN	GLN	ARG	GLN	GLN	GLN	GLN	GLN	GLN	GLN				---			10	2	9(GLN)
	40		PRO	PRO	PRO	ARG	PRO	GLY	PRO	PRO	PRO	PRO				---			10	3	8(PRO)
	41	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO				---			10	1	10(PRO)
FR2	42	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY				---			10	1	10(GLY)
	43		LYS	GLU	LYS	LYS	LYS	ARG	LYS	ARG	LYS	ARG				---			10	3	6(LYS)
	44		GLY	ALA	ALA	ALA	ALA	ALA	GLY	GLY	GLY	GLY				---			10	2	5(+)
	45	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU				---			10	1	10(LEU)
	46	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU				---			10	1	10(GLU)
	47	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP				---			10	1	10(TRP)
	48		LEU	LEU	LEU	LEU	LEU	LEU	ILE	ILE	ILE	ILE				---			10	2	6(LEU)
	49		ALA	ALA	ALA	ALA	ALA	ALA	GLY	GLY	GLY	GLY				---			10	2	6(ALA)
	50		ARG	TRP	ARG	PHE	ARG	TRP	SER	TYR	GLY	GLU				---			10	7	3(ARG)
	51		ILE	ASP	ILE	ILE	ILE	LEU	ILE	VAL	VAL	ILE				---			10	4	6(ILE)
	52		ASP	ILE	ASX	ASN	ASP	LEU	TYR	PHE	TYR	ASN				---			10	6	3(ASN) : 3(ASP)
	52A		---	---	---	---	---	TYR	HIS	---	---	---				---			2	2	1(+)
	52B		---	---	---	---	---	---	---	---	---	---				---					
	52C		---	---	---	---	---	---	---	---	---	---				---					
	53		TRP	LEU	ASX	TRP	TRP	TRP	---	TYR	TYR	HIS				---			9	5	4(TRP)
	54		ASP	ASN	ASX	ASP	ASP	ASP	SER	HIS	THR	SER				---			10	5	5(ASP) : 4(ASP)
	55		ASP	ASP	ASP	ASP	ASP	ASP	GLY	GLY	GLY	GLY				---			10	2	6(ASP)
	56		ASP	ASP	LYS	ASP	ASP	ASP	SER	THR	SER	SER				---			10	4	5(ASP)
	57		LYS	LYS	PHE	ASN	LYS	LYS	THR	SER	ILE	THR				---			10	6	4(LYS)
	58		TYR	TYR	TYR	ARG	TYR	ARG	TYR	ASP	TYR	ASN				---			10	4	6(TYR)
CDR2	59		TYR	TYR	TRP	TYR	TYR	PHE	TYR	ASP	TYR	TYR				---			10	4	7(TYR)
	60		ASX	GLY	SER	SER	GLY	SER	ASN	THR	ASN	LYS				---			10	5 : 6	3(+) : 3(SER)
	61		THR	ALA	THR	PRO	THR	PRO	PRO	THR	PRO	THR				---			10	3	5(THR)
	62		SER	SER	SER	SER	SER	SER	SER	PRO	SER	SER				---			10	2	9(SER)
	63	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU				---			10	1	10(LEU)
	64		GLU	GLU	ARG	ARG	GLU	LYS	LYS	ARG	ARG	LYS				---			10	3	4(ARG)
	65		THR	THR	THR	SER	THR	SER	SER	SER	GLY	SER				---			10	3	5(SER)
	66	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG				---			10	1	10(ARG)
	67		LEU	LEU	LEU	LEU	LEU	LEU	VAL	VAL	VAL	VAL				---			10	2	6(LEU)
	68		THR	ALA	SER	THR	THR	THR	THR	THR	THR	THR				---			10	3	8(THR)
	69		ILE	VAL	ILE	GLY	ILE	VAL	ILE	MET	ILE	ILE				---			10	4	6(ILE)
	70		SER	SER	SER	THR	SER	THR	SER	LEU	SER	SER				---			10	3	7(SER)
	71		LYS	LYS	LYS	LYS	LYS	ARG	VAL	VAL	VAL	LEU				---			10	4	5(LYS)
	72		ASP	ASP	ASN	ASP	ASP	ASP	ASP	ASP	ASP	ASP				---			10	2	9(ASP)
	73		THR	THR	ASP	THR	THR	THR	THR	THR	THR	THR				---			10	2	9(THR)
	74	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER				---			10	1	10(SER)
	75		ARG	LYS	LYS	ARG	LYS	LYS	LYS	LYS	ARG	LYS				---			10	2	7(LYS)
	76	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN				---			10	1	10(ASN)
	77		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	LEU				---			10	2	9(GLN)
	78		VAL	VAL	VAL	VAL	VAL	VAL	PHE	PHE	PHE	PHE				---			10	2	6(VAL)
	79		VAL	VAL	VAL	VAL	VAL	VAL	SER	SER	SER	SER				---			10	2	6(VAL)
	80	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU				---			10	1	10(LEU)
	81		THR	SER	ILE	THR	LYS	THR	LYS	ARG	ASN	LYS				---			10	6	3(+)
	82		MET	MET	MET	ILE	VAL	MET	LEU	LEU	LEU	LEU				---			10	4	4(+)
FR3	82A		---	ASN	ILE	THR	THR	THR	SER	SER	ARG	SER				---			9	5	3(+)
	82B		---	THR	ASN	ASN	ASN	ASN	SER	SER	SER	SER				---			9	3	4(+)
	82C		---	VAL	VAL	MET	MET	MET	VAL	VAL	MET	VAL				---	MET		10	2	5(+)
	83		ASP	GLY	ASN	ASP	ASP	ASP	THR	THR	SER	THR				---	ASP		11	5	5(ASP)
	84		PRO	PRO	PRO	PRO	PRO	PRO	ALA	ALA	ALA	ALA				---	PRO		11	2	7(PRO)
	85		VAL	GLY	VAL	VAL	ALA	VAL	ALA	ALA	ALA	ALA				---	VAL		11	3	5(+)
	86	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP				---	ASP		11	1	11(ASP)
	87		THR	THR	THR	SER	THR	THR	THR	THR	THR	THR				---	SER		11	2	9(THR)
	88		ALA	ALA	ALA	GLY	ALA	ALA	ALA	ALA	ALA	ALA				---	GLY		11	2	9(ALA)
	89		THR	THR	THR	THR	THR	THR	VAL	VAL	MET	VAL				---	THR		11	3	7(THR)
	90	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR	TYR				---	TYR		11	1	11(TYR)
	91		TYR	TYR	TYR	PHE	TYR	TYR	TYR	TYR	TYR	TYR				---	PHE		11	2	9(TYR)
	92	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS				---	CYS		11	1	11(CYS)
	93		ALA	ALA	ALA	ALA	ALA	VAL	ALA	ALA	ALA	ALA				---	ALA		11	2	10(ALA)
	94		ARG	ARG	ARG	HIS	ARG	HIS	ARG	ARG	ARG	ARG				---	HIS		11	2	8(ARG)
	95		ILE	SER	VAL	ARG	MET	ARG	VAL	ASN	GLY	GLY				---	ARG		11	7	3(ARG)
	96		THR	CYS	VAL	PRO	GLN	HIS	ARG	LEU	ASN	LEU				---	PRO		11	9	2(-)
	97		VAL	GLY	ASN	PRO	VAL	PRO	ARG	ILE	PRO	LEU				---	PRO		11	7	4(PRO)
	98		ILE	SER	SER	TRP	THR	ARG	ARG	ALA	PRO	ARG				---	TRP		11	7	3(ARG)
	99		PRO	GLN	VAL	ARG	MET	THR	---	GLY	PRO	GLY				---	ARG		10	7	2(+)
	100		ALA	TYR	MET	PHE	VAL	LEU	---	CYS	TYR	GLY				---	PHE		10	8	2(+)
	100A		PRO	PHE	ALA	THR	ARG	ALA	---	ILE	TYR	TRP				---	THR		10	8	2(+)
	100B		ALA	---	GLY	GLY	GLU	---	---	---	ASP	ASN				---	SER		7	6	2(GLY)
	100C		GLY	---	TYR	ASN	VAL	---	---	---	ILE	ASP				---	ASP		7	6	2(ASP)
	100D		TYR	---	TYR	LEU	MET	---	---	---	GLY	VAL				---	LEU		7	5	2(+)
CDR3	100E		---	---	TYR	GLY	ILE	---	---	---	THR	ASP				---	GLY		6	5	2(GLY)
	100F		---	---	TYR	GLY	THR	---	---	---	GLY	TYR				---	SER		6	4	2(+)
	100G		---	---	TYR	---	SER	---	TYR	---	SER	TYR				---	---		5	2	3(TYR)
	100H		---	---	---	---	ASN	---	SER	---	ASP	TYR				---	---		4	4	1(+)
	100I		---	---	---	---	---	---	SER	---	ASP	GLY				---	---		3	3	1(+)
	100J		---	---	---	---	ALA	---	ALA	---	GLY	MET				---	---		4	3	2(ALA)
	100K		MET	---	MET	PHE	PHE	PHE	SER	---	ILE	---				---	PHE		8	4	4(PHE)
	101		ASP	ASP	ASP	ASP	ASP	ASP	LYS	ASP	ASP	ASP				---	SER	ASP	12	3	10(ASP)
	102		VAL	TYR	VAL		ILE	VAL	ILE	VAL	VAL	VAL				---	PRO	VAL	11	4	7(VAL)
	103		TRP	TRP	TRP	TRP	TRP	TRP	ILE	TRP	TRP	TRP				---	TRP	TRP	12	2	11(TRP)
	104		GLY	GLY	GLY	GLY	GLY	GLY	PHE	GLY	GLY	GLY				---	GLY	GLY	12	2	11(GLY)
	105		ARG	GLN	LYS	GLN	GLN	GLN	GLY	GLN	GLN	GLN				---	GLN	ARG	12	4	8(GLN)
	106		GLY	GLY	GLY	GLY	GLY	GLY	SER	GLY	GLY	GLY				---	GLY	GLY	12	2	11(GLY)
FR4	107		THR	ILE	THR	THR	THR	THR	GLY	SER	THR	THR				---	THR	THR	12	4	9(THR)
	108		PRO	LEU	THR	LEU	MET	LYS	THR	LEU	THR	THR				---	LEU	THR	12	5	5(THR)
	109		VAL	VAL	VAL	VAL	VAL	VAL	ARG	VAL	VAL	VAL				---	VAL	VAL	12	2	11(VAL)
	110		THR	THR	THR	THR	THR	ALA	LEU	THR	HIS	THR				---	THR	THR	12	4	9(THR)
	111		VAL	VAL	VAL	VAL	VAL	VAL	SER	VAL	VAL	VAL				---	VAL	VAL	12	2	11(VAL)
	112		SER	SER	SER	SER	SER	SER	ILE	SER	SER	SER				---	SER	SER	12	2	11(SER)
	113					SER	SER		ARG	SER	SER	SER				---	SER	ALA	8	3	6(SER)

HUMAN HEAVY CHAINS SUBGROUP II (cont'd)

VARIABILITY

	0	
	1	4.5
	2	5.3
	3	8.
	4	2.2
	5	11. : 14.
	6	2.2 : 2.4
	7	3.7
	8	1.
	9	2.2
	10	7.5
	11	1.
	12	1.
	13	2.5
	14	2.2
FR1	15	6.
	16	6.
	17	2.2
	18	1.
	19	3.3
	20	1.
	21	1.
	22	1.
	23	3.6
	24	6.
	25	2.2
	26	1.
	27	14.
	28	3.7
	29	8.
	30	5.7
	31	13.
	32	35.
CDR1	33	8.
	34	10.
	35	40.
	35A	
	35B	
	36	1.
	37	2.2
	38	1.
	39	2.2
	40	3.8
	41	1.
FR2	42	1.
	43	5.
	44	4.
	45	1.
	46	1.
	47	1.
	48	3.3
	49	3.3
	50	23.
	51	6.7
	52	20.
	52A	
	52B	
	52C	
	53	11.
	54	10. : 13.
	55	3.3
	56	8.
CDR2	57	15.
	58	6.7
	59	5.7
	60	17. : 20.
	61	6.
	62	2.2
	63	1.
	64	7.5
	65	6.
	66	1.
	67	3.3
	68	3.8
	69	6.7
	70	4.3
	71	8.
	72	2.2
	73	2.2
	74	1.
	75	2.9
	76	1.
	77	2.2
	78	3.3
	79	3.3
	80	1.
FR3	81	20.
	82	10.
	82A	
	82B	
	82C	
	83	11.
	84	3.1
	85	6.6
	86	1.
	87	2.4
	88	2.4
	89	4.7
	90	1.
	91	2.4
	92	1.
	93	2.2
	94	2.8
	95	26.
	96	50.
	97	19.
	98	26.
	99	35.
	100	40.
	100A	
	100B	
	100C	
CDR3	100D	
	100E	
	100F	
	100G	
	100H	
	100I	
	100J	
	100K	
	101	3.6
	102	6.3
	103	2.2
	104	2.2
	105	6.
	106	2.2
	107	5.3
FR4	108	12.
	109	2.2
	110	5.3
	111	2.2
	112	2.2
	113	4.

ANTIBODY SPECIFICITIES: HUMAN HEAVY CHA[redacted]UBGROUP II

8) **NEWM:** ANTI-3-(3'-HYDROXY-3',7',11',15',TETRAMETHYL HEXADECYL) 2-METHYL 1,4 NAPHTHOQUINONE(VIT.K1OH)

CLASS: HUMAN HEAVY CHAINS SUBGROUP II

1) **COR:** IGG1-
2) **DAW:** IGG1-LAMBDA
3) **OU:** IGM-KAPPA
4) **MCE':** IGM-KAPPA
6) **HE:** IGG1-
8) **NEWM:** IGG1-LAMBDA
9) **WAH:** IGD-LAMBDA
12) **SA:** IGG2-LAMBDA
15) **NZU:** IGM-
16) **ERI:** IGD-

REFERENCE: HUMAN HEAVY CHAINS SUBGROUP II

1) **COR:** PRESS,E.M. & HOGG,N.M. (1970) BIOCHEM.J.,117,641-660. (CHECKED BY AUTHOR)
2) **DAW:** PRESS,E.M. & HOGG,N.M. (1970) BIOCHEM.J.,117,641-660. (CHECKED BY AUTHOR)
3) **OU:** PUTNAM,F.W.,SHIMIZU,A.,PAUL,,C.,SHINODA,T. & KOHLER,H. (1971) ANN.N.Y.ACAD.SCI.,190,83-103. (CHECKED BY AUTHOR 06/15/83)
4) **MCE':** GERBER-JENSON,B.,KAZIN,A.,KEHOE,J.M.,SCHEFFEL,C.,ERICKSON,B.W. & LITMAN,G.W. (1981) J.IMMUNOL.,126,1212-1216. (CHECKED BY AUTHOR 12/15/80)
5) **CE-1 'CL:** TAKAHASHI,N.,NOMA,T. & HONJO,T. (1984) PROC.NAT.ACAD.SCI.USA,81,5194-5198.
6) **HE:** CUNNINGHAM,B.A.,GOTTLIEB,P.D.,PFLUMM,M.N. & EDELMAN,G.M. (1971) PROGRESS IN IMMUNOLOGY (B.AMOS,ED.),ACADEMIC PRESS,N.Y.,PP.3-24. (CHECKED BY AUTHOR)
7) **SUP-T1 VH-JA'CL:** DENNY,C.T.,YOSHIKAI,Y.,MAK,T.W.,SMITH,S.D.,HOLLIS,G.F. & KIRSCH,I.R. (1986) NATURE,320,549-551.
8) **NEWM:** POLJAK,R.J.,AMZEL,L.M.,CHEN,B.L.,PHIZACKERLEY, R.P. & SAUL,F. (1974) PROC.NAT.ACAD.SCI.USA,71,3440-3444. (CHECKED BY AUTHOR WHO CORRECTED RESIDUES 6,9,15,16,24,26,27,29 THROUGH 35B,59,60 AS GIVEN IN TABLE OF THE FIRST EDITION OF THIS BOOK, AND HAS MORE RECENTLY REVISED RESIDUES 5,24,28,29,30,31,33,34,35,35A,35B,59,60 AND 101); POLJAK,R.J.,AMZEL,L.M.,CHEN,B.L.,CHIU,Y.Y., PHIZACKERLEY,R.P.,SAUL,F. & YSERN,X. (1976) COLD SPRING HARBOR SYMP. QUANTITATIVE BIOL.,41,639-645; POLJAK,R.J.,NAKASHIMA,Y.,CHEN, B.L. & KONIGSBERG,W. (1977) BIOCHEMISTRY,16,3412-3420. THE SEQUENCE LISTED IN THE LAST REFERENCE IS GIVEN IN THE TABLE. (CHECKED BY AUTHOR, W.K., 09/30/78)
9) **WAH:** PUTNAM,F.W.,TAKAHASHI,N.,TETAERT,D.,DEBUIRE,B. & LIN,L.C. (1981) PROC.NAT.ACAD.SCI.USA,78,6168-6172. (CHECKED BY AUTHOR 11/30/81); TAKAHASHI,N.,TETAERT,D.,DEBUIRE,B.,LIN,L. & PUTNAM,F.W. (1982) PROC.NAT.ACAD.SCI.USA,79,2850-2854.
10) **HIG1'CL:** KUDO,A.,ISHIHARA,T.,NISHIMURA,Y. & WATANABE,T. (1985) GENE,33,181-189. (CHECKED BY AUTHOR 10/01/85)
11) **CAR:** FRANGIONE,B. (1968) PH.D. THESIS, UNIVERSITY OF CAMBRIDGE. (CHECKED BY AUTHOR)
12) **SA:** MILSTEIN,C. & FRANGIONE,B. (1971) BIOCHEM.J.,121,217-225. (CHECKED BY AUTHOR)
13) **IO:** MONTGOMERY,P.C.,BELLO,A.C. & ROCKEY,J.H. (1970) BIOCHIM.BIOPHYS.ACTA,200,258-266. (CHECKED BY AUTHOR)
14) **SPA:** FRANGIONE,B. & FRANKLIN,E.C. (1979) J.IMMUNOL.,122,1177-1179. (CHECKED BY AUTHOR 07/18/79)
15) **NZU:** ERICKSON,B.W.,GERBER-JENSON,B.,WANG,A.C. & LITMAN,G.W. (1981) MOL.IMMUNOL.,19,357-365. (CHECKED BY AUTHOR 11/30/81)
16) **ERI:** MILSTEIN,C.P. & DEVERSON,E.V. (1980) IMMUNOLOGY,40,657-664. (CHECKED BY AUTHOR 11/30/82)

NOTES: HUMAN HEAVY CHAINS SUBGROUP II

IDENTICAL SETS OF FRAMEWORK SEGMENTS:

FR1:
FR2: SET 1: SUP-T1 VH-JA'CL[7],WAH[9]. (2 IDENTICAL)
FR3:
FR4: SET 1: MCE'[4],NZU[15]. (2 IDENTICAL HUMAN V-H-II: ALSO 1 HUMAN V-H-I: WOL[4]; 4 HUMAN V-H-III: TIL[4],DOB[31],WEA[33],NIE[34]; AND 1 MOUSE V-H-IIIA: MOPC47A[48].)
SET 2: HIG1'CL[10]. (IDENTICAL TO 1 HUMAN V-H-I: ND'CL[6]; 1 HUMAN V-H-III: U266'CL[106]; AND 1 MOUSE V-H-IIA: HDEX12[15].)

IDENTICAL SETS OF J-MINIGENES:

SET 1: HIG1'CL[10]. (IDENTICAL TO 1 HUMAN V-H-I: ND'CL[6]; AND 1 HUMAN V-H-III: U266'CL[106].)

SPECIFIC NOTES:

4) **MCE':** IT IS A CRYOIMMUNOGLOBULIN AND IS DESIGNATED BY THE AUTHORS AS MCE. IN ORDER TO DIFFERENTIATE IT FROM ANOTHER MCE SEQUENCED BY CAPRA ET AL., IT IS DENOTED AS MCE'.
5) **CE-1 'CL:** CELL LINE CESS
7) **SUP-T1 VH-JA'CL:** IT IS FROM A PATIENT SUFFERING FROM CHILDHOOD T-CELL LYMPHOMA WITH inv(14)(q11.2;q32.2). THE INVERSION ON CHROMOSOME 14 BRINGS THE VH GENE AND JA MINIGENE TOGETHER, GIVING RISE TO A HYBRID MOLECULE CONTAINING PART OF THE IMMUNOGLOBULIN GENE AND PART OF THE T-LYMPHOCYTE RECEPTOR FOR ANTIGEN GENE.
14) **SPA:** IT WAS FROM A CASE OF HEAVY CHAIN DISEASE.
15) **NZU:** IT IS A CRYOIMMUNOGLOBULIN.

+ THE FOLLOWING WERE EQUALLY AND MOST FREQUENTLY OCCURRING:

AT POSITION	RESIDUES
5	(ARG,GLN)
10	(ALA,GLY)
32	(THR,SER,ASP)
35	(CYS,SER)
44	(ALA,GLY)
52A	(TYR,HIS)
60	(SER,ASN)
81	(LYS,THR)
82	(LEU,MET)
82A	(THR,SER)
82B	(SER,ASN)
82C	(VAL,MET)
85	(VAL,ALA)
96	(PRO,LEU)
99	(PRO,ARG,GLY)
100	(TYR,PHE)
100A	(ALA,THR)
100D	(TYR,LEU)
100F	(TYR,GLY)
100H	(TYR,SER,ASP,ASN)
100I	(SER,GLY,ASP)

HUMAN HEAVY CHAINS SUBGROUP III

		INVARIANT RESIDUES	1* TUR	2 LAMBDA -VH26 -CL #	3* POM	4 TIL	5 WAS	6 HF2-1/13B	7 HF2-1/17	8 HF2-18/2	9 H11 'CL	10 TEI	11 BRO 'IGM	12 GR'	13 WAT	14* LAY	15 GRA' #	16* FR #	17 MU	18 VIN	19 HF3-16/6	20 BEN (III)	21 ZAP	22 JON	23 KEA
	0		---	#	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	1		GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	ala	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp	GLU
	2		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL
	3		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN
	4	LEU(.97)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	5		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	val	val	val	val	val	LEU	val	val	val	val	LEU	val	val	val	val
	6		GLU	GLU	GLU	GLU	GLU	GLU	GLU	gln	GLU	GLU	GLU	GLU	GLU	GLU	GLU	asp	GLU	GLU	gln	GLU	GLU	GLU	GLX
	7	SER(.97)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	8	GLY(.99)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	9	GLY(.98)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	10		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	ala	GLY	GLY
	11		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	12		VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	ile	VAL	ala	VAL	VAL	VAL
	13		GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	lys	GLN	GLN	GLN	GLN	lys	lys
FR 1	14	PRO(.95)	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO
	15	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	16		GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	17	SER(.97)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	18	LEU(.97)	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	gly	LEU	LEU
	19		ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG
	20		LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU
	21		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	gln	ala	SER	SER	SER
	22	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS
	23		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	24		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA
	25	SER(.98)	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER
	26	GLY(.97)	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY
	27	PHE(.98)	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE
	28		THR	THR	THR	THR	ser	lys	lys	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	ser	THR	THR	THR	ile
	29		PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	ile	PHE	PHE	val	PHE	PHE	PHE	PHE	PHE
	30		SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	asx	SER	SER	SER	thr	SER	SER	SER	SER	SER	pro
	31		ARG	SER	SER	THR	THR	SER	SER	SER	SER	THR	TYR	ALA	THR	ALA	LYS	ASX	ARG	THR	PRO	THR	THR	THR	
	32		VAL	TYR	SER	TYR	ASP	TYR	TYR	TYR	TYR	SER	TYR	ASX	TYR	SER	THR	PHE	GLY	ASN	SER	THR	THR	ALA	TYR
CDR 1	33		LEU	ALA	ALA	VAL	ALA	ALA	ALA	ALA	TRP	ALA	ASN	TYR	THR	ALA	VAL	TYR	GLY	TYR	ALA	PHE	SER	TRP	
	34		SER	MET	MET	MET	MET	MET	MET	MET	MET	VAL	MET	MET	MET	MET	TYR	MET	LEU	MET	MET	MET	ARG	MET	
	35		SER	SER	SER	SER	TYR	SER	SER	SER	HIS	TYR	ASN		VAL	SER	GLU	ASP	GLU		SER	ARG	PHE	LYS	
	35A		---	---	---	---	---	---	---	---	---	---	---	---		---	---	---			---	---	---	---	
	35B		---	---	---	---	---	---	---	---	---	---	---	---		---	---	---			---	---	---	---	
	36	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP		TRP	TRP	TRP	TRP		TRP	TRP	TRP	TRP	
	37	VAL(.95)	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL		VAL	VAL	VAL	VAL		VAL	VAL	VAL	VAL	
	38	ARG(.97)	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	PRO		ARG	ARG	ARG	ARG		ARG	ARG	ARG	ARG	
	39	GLN(.97)	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLY		GLN	GLN	GLN	GLN		GLN		GLN	GLN	
	40		ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	VAL	ALA		ALA	ALA	ALA	ALA		ALA		ALA	ALA	
	41		PRO	PRO	PRO	PRO	PRO				PRO	PRO	THR	PRO		PRO	PRO	PRO	PRO				PRO	PRO	
FR 2	42	GLY	GLY	GLY	GLY	GLY	GLY				GLY	GLY	GLY	GLY		GLY	GLY	GLY	GLY				GLY	GLY	
	43	LYS(.97)	LYS	LYS	LYS	LYS	LYS				LYS	LYS	LYS	ARG		LYS	LYS	LYS	LYS				LYS	LYS	
	44		GLY	GLY	GLY	GLY	GLY				GLY	GLY	GLY	GLY		GLY	GLY	GLY	ALA				GLY	GLY	
	45	LEU(.97)	LEU	LEU	LEU	LEU	LEU				LEU	LEU	LEU	LEU		LEU	LEU	LEU	LEU				LEU	LEU	
	46		GLU	GLU	GLU	GLX	GLU				GLU	GLU	GLU			GLU	GLU	GLU	GLX				GLU	GLU	
	47	TRP	TRP	TRP	TRP	TRP	TRP				TRP	TRP	TRP			TRP	TRP	TRP	TRP				TRP	TRP	
	48		VAL	VAL	VAL	VAL	VAL				VAL	VAL	VAL			VAL	VAL	VAL	VAL				VAL	VAL	
	49		SER	SER	ALA	GLY	ALA				SER	GLY	SER			ALA	THR	ALA	LEU				GLU	VAL	
	50		GLY	ALA	TRP	ALA	TRP				ARG	TRP	ALA			TRP	TYR	ALA	VAL				PHE	TRP	
	51		ARG	ILE	LYS	ILE	LYS				ILE	ARG	ILE			LYS	VAL	ARG	PHE				ARG	ARG	
	52		LEU	SER	TYR	GLX	TYR				ASN	TYR	GLY			TYR	GLY		SER				VAL	VAL	
	52A		ASN	GLY	GLU	GLY	GLN				SER	GLU	---			GLU	GLN		VAL				GLN	GLU	
	52B	LYS	---	---	---	---	---				---	---	---			---	---		---				---	---	
	52C		---	---	---	---	---				---	---	---			---	---		---				---	---	
	53		ALA	SER	ASN	LEU	GLU				ASP	GLY	THR			ASN	VAL		THR				GLY	GLN	
	54		SER	GLY	GLY	SER	ALA				GLY	SER	ALA			GLY	SER						SER	VAL	
CDR 2	55		SER	GLY	ASN	VAL	SER				SER	SER	GLY			ASN	LYS						ALA	VAL	
	56		ASN	SER	ASP	SER	ASN				SER	LEU	ASP			ASP	PHE						ILE	GLU	
	57		LEU	THR	LYS	GLX	SER				THR	THR	GLN			LYS	SER		LYS				SER	LYS	
	58		HIS	TYR	HIS	SER	HIS				THR	HIS	TYR			HIS			PHE				HIS	ALA	
	59		PHE	TYR	TYR	TYR	PHE				TYR	TYR	TYR			TYR	TYR		TYR				TYR	PHE	
	60		ALA	GLY	ALA	ALA	ALA				ALA	ALA	ALA			ALA	ALA		THR				ALA	ALA	
	61		VAL	ASP	ASP	ASX	ASP				ASP	VAL	ASP			ASP	VAL		GLU				ASP	ASN	
	62		SER	SER	SER	SER	THR				SER	SER	SER			SER	SER		SER				SER	SER	
	63		ALA	VAL	VAL	VAL	VAL				VAL	VAL	VAL			VAL	VAL		LEU				VAL	VAL	
	64		GLN	LYS	ASN	LYS	ASN				LYS	GLN	LYS			ASN	GLN		ASN				GLN	ASN	
	65	GLY(.97)	GLY	GLY	GLY	GLY	GLY				GLY	GLY	GLY			GLY	GLY						ALA	GLY	
	66	ARG	ARG	ARG	ARG	ARG	ARG				ARG	ARG	ARG			ARG	ARG						ARG	ARG	
	67	PHE(.97)	PHE	PHE	PHE	PHE	PHE				PHE	PHE	PHE			PHE	PHE						PHE	PHE	
	68		THR	THR	THR	THR	THR				THR	THR	THR			THR	THR						THR	THR	
	69	ILE(.97)	ILE	ILE	ILE	ILE	ILE				ILE	ILE	ILE			ILE	ILE						ILE	ILE	
	70	SER(.97)	SER	SER	SER	SER	SER				SER	SER	SER			SER	SER						SER	SER	
	71	ARG	ARG	ARG	ARG	ARG	ARG				ARG	ARG	ARG			ARG	ARG						ARG	ARG	
	72		ASN	ASP	ASN	ASP	ASN				ASP	ASN	ASN			ASN	ASN						ASN	ASN	
	73		ASP	ASN	ASP	ASP	ASP				ASN	ASP	ASP			ASP	ASP						ASP	ASP	
	74		SER	SER	SER	SER	SER				ALA	SER	SER			SER	SER						SER	SER	
	75		LYS	LYS	LYS	LYS	LYS				LYS	LYS	LYS			LYS	LYS						LYS	LYS	
	76		ASN	ASN	ASN	ASN	ASN				ASN	ASN	ASN			ASN	ASN						ASN	ASN	
	77		THR	THR	THR	THR	THR				THR	THR	THR			THR	THR						THR	THR	
	78		LEU	LEU	LEU	---	LEU				LEU	LEU	LEU			LEU	LEU						LEU	LEU	
	79		TYR	TYR	TYR	---	TYR				TYR	TYR	TYR			TYR	TYR						TYR	TYR	
	80		LEU	LEU	LEU	---	LEU				LEU	LEU	LEU			LEU	LEU						LEU	LEU	
FR 3	81		GLN	GLN	LEU	---	GLN				GLN	GLN	ASN			GLN	GLU						GLN	GLN	
	82	MET(.95)	MET	MET	MET	MET	MET				MET	MET	MET			MET	MET	MET					MET	MET	MET
	82A		LEU	ASN	ASN	ASN	ASN				ASN	LEU	ASN			ASN	LYS	ASN					ASN	ILE	ASN
	82B		SER	SER	SER	SER	ARG				SER	SER	SER			GLY	THR	SER					THR	SER	ASN
	82C		LEU	LEU	LEU	LEU	LEU				LEU	LEU	LEU			LEU	GLY	LEU					GLY	VAL	LEU
	83		GLN	ARG	GLN	ARG	GLU				ARG	GLU	ARG			GLN	GLU	ARG					GLU	THR	ARG
	84		ALA	ALA	ALA	ALA	ALA				ALA	PRO	ALA			ALA	PRO	ALA		ALA			ALA	PRO	VAL
	85		GLU	GLU	GLU	GLU	GLU				GLU	GLU	GLU			GLU	GLU	GLX		GLU			GLU	GLU	GLX
	86		ASP	ASP	ASP	ASP	ASP				ASP	ASP	ASP			VAL	ASP	ASX		ASP			ASP	ASP	ASX
	87		THR	THR	THR	THR	THR				THR	THR	THR			SER	THR	THR		THR			THR	THR	THR
	88		ALA	ALA	ALA	ALA	ALA				ALA	ALA	ALA			ALA	ALA	ALA		ALA			ALA	ALA	ALA
	89		LEU	VAL	LEU	VAL	VAL				VAL	VAL	VAL			ILE	VAL	VAL		VAL			VAL	VAL	VAL
	90	TYR(.98)	TYR	TYR	TYR	TYR	TYR				TYR	TYR	TYR			TYR	TYR	TYR		TYR			TYR	TYR	TYR
	91	TYR(.95)	TYR	TYR	TYR	TYR	TYR				TYR	TYR	TYR			TYR	TYR	TYR		TYR			TYR	TYR	TYR
	92	CYS	CYS	CYS	CYS	CYS	CYS				CYS	CYS	CYS			CYS	CYS	CYS		CYS			CYS	CYS	CYS
	93		ALA	ALA	ALA	ALA	ALA				ALA	ALA	ALA			ALA	ALA	ALA		ALA			ALA	ALA	ALA
	94		ARG	LYS	ARG	LYS	ARG				ARG	ARG	ARG			ARG	ARG	ARG		ARG			ARG	ARG	ARG
	95		LEU	#	ASP	GLY	PHE				---	VAL	SER			ASP	HIS						THR	VAL	ASX
	96		SER	---	ALA	LYS	ARG				---	THR	PRO			ALA	ILE						ARG	VAL	ARG
	97		VAL	---	GLY	VAL	GLN				---	PRO	VAL			GLY	TYR						PRO	VAL	LEU
	98		THR	---	PRO	SER	PRO				---	ALA	SER			PRO	VAL						GLY	SER	GLY
	99		ALA	---	TYR	ALA	PHE				---	ALA	LEU			TYR	THR						GLY	THR	PRO
	100		VAL	---	VAL	TYR	VAL				---	ALA	VAL			VAL	LEU						TYR	SER	THR
	100A		ALA	---	SER	TYR	GLN				---	SER	ASP			SER	TYR						PHE	---	ALA
	100B		PHE	---	PRO	PHE	---				---	LEU	GLY			PRO	TYR						SER	---	CYS
	100C		---	---	THR	---	---				---	THR	TRP			THR	TYR						---	---	SER
	100D		---	---	PHE	---	---				---	---	LEU			PHE	---						---	---	VAL
	100E		---	---	---	---	---				---	---	TYR			---	---						---	---	
CDR 3	100F		---	---	---	---	---				---	---	TYR			---	---						---	---	
	100G		---	---	---	---	---				---	---	TYR			---	---						---	---	
	100H		---	---	---	---	---				---	---	TYR			---	---						---	---	
	100I		---	---	---	---	---				---	---	GLY			---	---						---	---	
	100J		---	---	---	---	PHE				---	PHE	---			---	PHE						---	MET	
	100K		---	---	PHE	---	PHE				---	SER	---			PHE	MET						---		
	101		ASP	---	ALA	ASX	ASP				---	ALA	SER			ALA	ALA						ASP	ASP	
	102		VAL	---	HIS	TYR	VAL				---	VAL				HIS	VAL						VAL	VAL	
	103		TRP	---	TYR	TRP	PHE				---	TRP	TRP			TRP	TRP						TRP	TRP	
	104	GLY(.97)	GLY	---	GLY	GLY	GLY				---	GLY	GLY			GLY	GLY						GLY	GLY	
	105		GLN	---	GLN	GLX	GLN				---	GLN	GLN			GLN	GLN						GLN	GLN	
	106	GLY(.97)	GLY	---	GLY	GLY	GLY				---	GLY	GLY			GLY	GLY						GLY	GLY	
FR 4	107		THR	---	THR	THR	THR				---	THR	THR			THR	THR						THR	THR	
	108		LYS	---	LEU	LEU	LEU				---	LEU	LEU			LEU	LEU						LEU	PRO	
	109	VAL(.97)	VAL	---	VAL	VAL	VAL				---	VAL				VAL							VAL	VAL	
	110		SER	---	THR	THR	THR				---	THR				THR							SER	THR	
	111			---		VAL					---														
	112	SER		---		SER					---														
	113			---		SER					---														

GP1806

PATENT DOCKET NO. 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#23 Appeal 9-13-93

In re Application of

Paul J. Carter et al.

Serial No. 07/715,272

Filed: 14 June 1991

For: Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. Feisee

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-1896

NOTICE OF APPEAL

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Applicant hereby appeals to the Board of Appeals and Interferences from the decision dated May 19, 1993, of the Primary Examiner finally rejecting claims 1-11 and 17-21.

The Commissioner is hereby authorized to charge Deposit Account No. 07-0630 in the amount of $270 to cover the fees for this appeal and to charge the deposit account for any further fees in regard to this patent application. A duplicate copy of this Notice is enclosed for this purpose.

Respectfully submitted,

GENENTECH, INC.

Janet E. Hasak

Janet E. Hasak
Reg. No. 28,616

Dated: October 15, 1993

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh
Louise Strasbaugh

Date: October 15, 1993

RP14167 11/04/93 07715272 07-0630 140 119 270.00CH
w020.u

GP1806

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

18D1/10/25/93

In re Application of

Paul J. Carter et al.

Serial No. 07/715,272

Filed: 14 June 1991

For: Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. Feisee

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-1896

PETITION AND FEE FOR EXTENSION OF TIME (37 CFR 1.136(a))

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Applicant petitions the Commissioner of Patents and Trademarks to extend the time for response to the Office action dated May 19, 1993 for an additional month, from September 19, 1993 to October 19, 1993. The extended time for response does not exceed the statutory period.

Please charge Deposit Account Number 07-0630 in the amount of $250 to cover the cost of the second month extension fee less the first month extension fee paid in relation to the request for a one month extension of time filed on September 20, 1993. Any deficiency or overpayment should be charged or credited to this deposit account. A duplicate of this sheet is enclosed.

Respectfully submitted,

GENENTECH, INC.

Janet E. Hasak

Janet E. Hasak
Reg. No. 28,616

Date: October 15, 1993

RP14166 11/04/93 07715272 07-0630 140 116 250.00CH

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Louise Strasbaugh

Louise Strasbaugh

Date: October 15, 1993

w021.u

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/715,272	06/14/91	CARTER	[illegible] 209

18M2/1021

GENENTECH, INC.
ATTN: CAROLYN R. ADLER
460 POINT SAN BRUNO BLVD.
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
[illegible]	
ART UNIT	PAPER NUMBER
1806	21

DATE MAILED: 10/21/93

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

[X] THE PERIOD FOR RESPONSE:

a) [X] is extended to run 4 months or continues to run ______ from the date of the final rejection

b) [ ] expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

[ ] Appellant's Brief is due in accordance with 37 CFR 1.192(a).

[X] Applicant's response to the final rejection, filed 9/23/93 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. [X] The proposed amendments to the claim and/or specification will not be entered and the final rejection stands because:

a. [ ] There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

b. [X] They raise new issues that would require further consideration and/or search. (See Note).

c. [X] They raise the issue of new matter. (See Note).

d. [X] They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

e. [ ] They present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: The language "of a human immunoglobulin subgroup" has not been defined with respect to the variable domain of a consensus antibody.

2. [ ] Newly proposed or amended claims ______ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. [X] Upon the filing an appeal, the proposed amendment [ ] will be entered [X] will not be entered and the status of the claims will be as follows:

Claims allowed: ~~None~~ 12 and 13
Claims objected to: None
Claims rejected: 1-11, 17-21

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
10/19/93

However;

[X] Applicant's response has overcome the following rejection(s): The rejection under 35 USC 112 first paragraph regarding "at least a portion" and "reasonably".

4. [X] The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because the introduction of the language "human subgroup" is defined in [illegible] but not in the application. Also, it is not clear

5. [ ] The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

[ ] The proposed drawing correction [ ] has [ ] has not been approved by the examiner.

[ ] Other

that the "consensus antibody" of the application would be identical to the antibody of Queen et al. The [illegible] [illegible] not add [illegible] different than that [illegible]

PATENT DOCKET 709

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Paul J. Carter et al.

Serial No. 07/715272

Filed: June 14, 1991

For: Immunoglobulin Variants

Group Art Unit: 1806

Examiner: L. FEISEE

1807

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 225-1896

AMENDMENT PURSUANT TO 37 CFR § 1.116(a)

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Pursuant to 37 CFR § 1.116(a), please cancel claims 1-11, 17, and 19-21 of the above application. Claim 18 was canceled in the Amendment filed September 20, 1993. Applicants trust that the above-mentioned application with allowed claims 12 and 13 will be in condition for allowance following the entry of this amendment and look forward to receiving the Notice to this effect.

Respectfully submitted,
GENENTECH, INC.

Janet E. Hasak

Dated: December 13, 1993

Janet E. Hasak
Reg. No. 28,616

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service in first class envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on the date shown below.

Dated: 13 DEC 1993

Louise Strasbaugh
Louise Strasbaugh

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	25

DATE MAILED:

EXAMINER INTERVIEW SUMMARY RECORD

All participants (applicant, applicant's representative, PTO personnel):

(1) Wendy Lee (3) _____

(2) Nils Eisen (4) _____

Date of interview 1/11/94

Type: ☒ Telephonic ☐ Personal (copy is given to ☐ applicant ☐ applicant's representative).

Exhibit shown or demonstration conducted: ☐ Yes ☐ No. If yes, brief description: _____

Agreement ☐ was reached with respect to some or all of the claims in question. ☐ was not reached.

Claims discussed: _____

Identification of prior art discussed: _____

Description of the general nature of what was agreed to if an agreement was reached, or any other comments: Finality would be withdrawn. Action forth coming.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

Unless the paragraphs below have been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW (e.g., items 1–7 on the reverse side of this form). If a response to the last Office action has already been filed, then applicant is given one month from this interview date to provide a statement of the substance of the interview.

☐ It is not necessary for applicant to provide a separate record of the substance of the interview.

☐ Since the examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action.

Examiner's Signature

PTOL-413 (REV. 1-84)

ORIGINAL FOR INSERTION IN RIGHT HAND FLAP OF FILE WRAPPER

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/715,272	06/14/91	CARTER	P 709

EXAMINER	
FEISEE, L.	
ART UNIT	PAPER NUMBER
1806	26

18M2/0203

GENENTECH, INC.
ATTN: CAROLYN R. ADLER
460 POINT SAN BRUNO BLVD.
SOUTH SAN FRANCISCO, CA 94080

DATE MAILED: 02/03/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/17/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 12 and 13 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-11, 14-21 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 12 and 13 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The finality of the previous Office action is withdrawn in view of the following new grounds of rejection.

Claims 12 and 13 are pending in this application, and these claims are humanized light and heavy chain variable regions of a previously referenced antibody 4D5.

Claims 12 and 13 are rejected under 35 U.S.C. § 103 as being unpatentable over Hudziak et. al. or Fendly et. al. in view of Queen et. al.

Hudziak et. al. and Fendly et. al. both teach the production and characterization of the 4D5 antibody (see Hudziak et. al. 1166-1167 and Fendly et. al. pages 1553-1554). Hudziak et. al. suggests the possible therapeutic role of the 4D5 antibody in human neoplasias which overexpress p185-HER2 (pages 1171, last paragraph) while Fendly et. al. disclose the possible use of anti-p185 HER2 antibodies for in vivo radioimaging for detection of relevant primary tumors. They do not describe the production of these antibodies in the humanized form.

Queen et. al. teach the production of antibodies against IL-2 receptor in the humanized form, using computer modeling in order to determine the modification of certain framework regions in conjunction with CDR grafting. The antibodies produced are than to be used for in vivo administration to human patients, either for diagnosis or therapy. It is known in the art that murine and even chimeric antibodies have characteristics which may severely limit their use in human therapy. As foreign proteins, murine and chimeric antibodies may elicit immune reactions that reduce or destroy their therapeutic efficacy and/or evoke allergic or hypersensitivity reactions in patients. The probable need for readministration of such therapeutic modalities in neoplastic

disorders increases these risks. The result would be tissue injury by virtue of antigen-antibody deposition.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make humanized antibodies having the sequences of the 4D5 antibody. The methods of Queen et. al. were clear and self explanatory, and resulted in a high affinity antibody. One of ordinary skill in the art would have been motivated to humanize the 4D5 antibody in light of its potential therapeutic and diagnostic applicability.

Although the claims are drawn to specific amino acid sequences, it is maintained that the differences in amino acid sequence which would have been obtained using the method of Queen et. al. would not have been patentably distinct from the claimed amino acid sequences. Absent sufficient factual evidence to the contrary the claims are obvious over the cited prior art.

35 U.S.C. § 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.**

Claims 12 and 13 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility. These claims are drawn to a light chain variable region polypeptide and a heavy chain variable region polypeptide which in and of themselves have no patentable utility. The specification does not disclose any

practical utility for the individual polypeptides and does not present evidence that these polypeptides are capable of binding in any particular manner when not in association with each other.

Claims 12 and 13 are directed to an invention not patentably distinct from claims 1, 3-9, and 40 of commonly assigned 07/977,453.

Specifically, the claims of the instant invention are drawn to the humanized version of the 4D5 antibody which is disclosed in copending application.

Commonly assigned 07/977,453, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. 1.78(c) and 35 U.S.C. § 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

Claims 12 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,3-9, and 40 of copending application Serial No. 07/977,453 in view of Queen et. al.. The instant claims are drawn to the heavy chain and light chain variable regions of the 4D5 antibody. Copending application 07/977,453 claims an antibody with the same characteristics as 4D5, and also states within the claims that 4D5 antibody was useful for diagnosis and therapy of tumors expressing the p185 HER2 antigen on their surface. The induction of HAMA responses upon repeated administration of rodent antibodies has led to the desirability of producing antibodies which are even more "near human" than chimeric antibodies. Queen et. al. describes the production of antibodies which contain essentially the CDR of rodents and are grafted into human framework regions. These antibodies are also mutated in certain framework residues in order to produce functional and high affinity molecules. The procedure in Queen et. al. clearly teaches the particular framework residues that need to be changed in order to yield high affinity antibodies, and they teach how to determine the appropriate residues using computer modeling programs. This protocol is adaptable to any number of antibodies. Therefore, not only was the production of non-immunogenic 4D5 antibodies desirable, but the procedure for producing the antibodies was also well known and practiced. It would have been <u>prima facie</u> obvious

to one of ordinary skill in the art at the time the invention was made to use the claims of the copending application in combination with the reference of Queen et. al. in order to obtain high affinity functional humanized antibodies.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 U.S.P.Q. 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.78(d).

Claims 12 and 13 are provisionally rejected under 35 U.S.C. § 103 as being obvious over copending application Serial No. 07/977,453 in view of Queen et. al.

The instant claims are drawn to the heavy chain and light chain variable regions of the 4D5 antibody. Copending application 07/977,453 discloses an antibody with the same characteristics as 4D5, and also discloses that 4D5 antibody is useful for diagnosis and therapy of tumors expressing the p185 HER2 antigen on their surface. The induction of HAMA responses upon repeated administration of rodent antibodies has led to the desirability of

producing antibodies which are even more "near human" than chimeric antibodies. Queen et. al. describes the production of antibodies which contain essentially the CDR of rodents and are grafted into human framework regions. These antibodies are also mutated in certain framework residues in order to produce functional and high affinity molecules. The procedure in Queen et. al. clearly teaches the particular framework residues that need to be changed in order to yield high affinity antibodies, and they teach how to determine the appropriate residues using computer modeling programs. This protocol is adaptable to any number of antibodies. Therefore, not only was the production of non-immunogenic 4D5 antibodies desirable, but the procedure for producing the antibodies was also well known and practiced. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the claims of the copending application in combination with the reference of Queen et. al. in order to obtain high affinity functional humanized antibodies.

Copending application Serial No. 07/977,453 has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. § 102(e) if patented. This provisional rejection under 35 U.S.C. § 103 is based upon a presumption of future patenting of the conflicting application.

Serial No. 715272

Art Unit 1806

This provisional rejection might be overcome either by a showing under 37 C.F.R. 1.132 that any unclaimed invention disclosed in the copending application was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention prior to the effective U.S. filing date of the copending application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lila Feisee whose telephone number is (703) 308-2731.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Feisee/lf
January 11, 1994

PAULA K. HUTZELL
PRIMARY EXAMINER
GROUP 1800

TO SEPARATE, [illegible] TOP AND BOTTOM EDGES, SNAP-APART AN[illegible] DISCARD CARBON

FORM PTO-892 (REV. 2-92) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
NOTICE OF REFERENCES CITED	07/715,272	1806	26
	APPLICANT(S) Carter et al.		

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A						
	B						
	C						
	D						
	E						
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R	Queen et al. PNAS 86: 10029-10033 (1989)
S	Fendly et al. Cancer Research 5: 1350-1358 (1
T	Hudziak et al. Molecular and Cellular Biology 1989 p. 1165-1172
U	

EXAMINER [signature] DATE 1/11/94

[illegible] with this office action. [illegible] on 707.05 (a).)

* A copy of this reference [illegible]

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/715,272	06/14/91	CARTER	709

EXAMINER: FEISEE, L

ART UNIT	PAPER NUMBER
1806	27

GENENTECH, INC.
ATTN: CAROLYN R. ADLER
460 POINT SAN BRUNO BLVD.
SOUTH SAN FRANCISCO, CA 94080

DATE MAILED: 09/06/94

NOTIFICATION OF DEFECTIVE NOTICE OF APPEAL OR DEFECTIVE BRIEF

1. ☐ The Notice of Appeal filed _____ is:

   A. ☐ Not acceptable for reason(s) that:

      (1) ☐ The Appeal fee required by 35 U.S.C. 41 (a)(6) and 37 CFR 1.17(e) was not submitted with the Notice of Appeal.

      (2) ☐ The submitted fee of $ _____ is insufficient. The appeal fee required by 37 CFR 1.17(e) is $ _____.

      (3) ☐ The Notice of Appeal was not timely filed.

      (4) ☐ The Appeal fee received on _____ was not timely filed.

      (5) ☐ The Appeal is not in compliance with 37 CFR 1.191 in that the claims have not been finally or twice rejected.

      (6) ☐ A Notice of Allowability was mailed by the Office on _____.

   B. ☐ Defective and should be corrected as indicated. Applicant is given a TIME LIMIT of ONE MONTH from the date of this letter OR the TIME REMAINING IN THE RESPONSE PERIOD OF THE LAST OFFICE ACTION, whichever is longer, to complete the appeal. NO EXTENSION OF THIS ONE MONTH PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a) or (b) BUT THE PERIOD FOR RESPONSE SET IN THE LAST ACTION MAY POSSIBLY BE EXTENDED. If the appeal is not timely completed, the application will be abandoned.

      (1) ☐ The Notice of Appeal is not signed.

      (2) ☐ Identification of the appealed claim or claims is required under 37 CFR 1.191 (b).

2. ☐ The Brief filed _____ is NOT acceptable for the reason(s) indicated below.

   The Appeal in this application will be dismissed unless the applicant makes the Brief acceptable. Extensions of time may be obtained under 37 CFR 1.136(a).

   A. ☐ The Brief and/or Brief fee is untimely. See 37 CFR 1.192.

   B. ☐ The requisite fee which must accompany the Brief has been omitted. See 37 CFR 1.17(f).

   C. ☐ The submitted Brief fee of _____ is not the proper amount. The Brief fee required by 37 CFR 1.17(f) is _____.

3. ☒ The Appeal in this application is DISMISSED because

   A. ☐ The fee for filing the Brief as required under 37 CFR 1.17(f) was not submitted or timely submitted and the period for obtaining an extension of time to file the brief under 37 CFR 1.136 has expired.

   B. ☒ The Brief was not filed, or was not timely filed and the period for obtaining an extension of time to file the brief under 37 CFR 1.136 has expired.

4. ☒ As the result of the dismissal in "3" above, this application:

   A. ☒ is abandoned since there are no allowed claims.

   B. ☐ is being returned to the examiner for disposition since it contains allowed claims. Prosecution on the merits is CLOSED.

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
9/1/94

(PTOL-461, Rev. 4/89)

REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

In re Application of		
Application Number		Filed
07/715,272		6-14-91
Group Art Unit	Examiner	

Paper No. #28

Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

___ (A) referred to in United States Patent Number 5821337, column 1

___ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____ filed _____, on page _____ of paper number _____.

___ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____, or

___ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

2001 Jefferson Davis Hwy Arl. Va. 22202
Suite # 806

Brian Willingham
Signature

10/18/99
Date

Brian Willingham
Typed or printed name

FOR PTO USE ONLY

Approved by: _____ (Initials)

Unit: _____

In re Application of	
Application Number: 07/715272	Filed: 6-14-91
Group Art Unit:	Examiner:

RECEIVED
NOV 3 0 1999
File Information Unit

Paper No. #29

Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

✓ (A) referred to in United States Patent Number 5821337, column _____

___ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____, on page _____ of paper number _____

___ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____, or

___ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

_____

_____

_____

Signature

11-30-99
Date

_____
Typed or printed name

FOR PTO USE ONLY

Approved by: DW (Initials)

Unit: 1751

PTO/SB/68 (11-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

In re Application of	
Application Number: 07/715272	Filed: 6/14/91
Group Art Unit:	Examiner:

Paper No. 30

Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE):

✓ (A) referred to in United States Patent Number 6054297, column _____.

___ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____, on page _____ of paper number _____.

___ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____ or

___ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

_____

_____

_____

Wayne Croteau
Signature

9-10-01
Date

WAYNE CROTEAU
Typed or printed name

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SEP 12 AM 11:15
TECH CENTER 1600/2900

FOR PTO USE ONLY

Approved by: _____ (initials)

Unit: _____

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PTO/SB/68 (11-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

In re Application of	
Application Number: 07/715272	Filed: 6-14-91
Group Art Unit:	Examiner:

Paper No. #31

Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

✓ (A) referred to in United States Patent Number 6054297 column _____.

___ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____, on page _____ of paper number _____.

___ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____ filed _____ or

___ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

_____

_____

_____

_____ 9-28-01
Signature Date

_____
Typed or printed name

FOR PTO USE ONLY
Approved by: _____ (Initials)
Unit: _____

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PTO/SB/68 (04-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)

In re Application of	
Carter	
Application Number 07/715,272	Filed 6/14/91
Art Unit	Examiner

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MAR 1 1 2002
File Information Unit

Paper No. #32

Assistant Commissioner for Patents
Washington, DC 20231

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REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)

In re Application of

Application Number	Filed
07/715,272	Jun. 14, 1991
Art Unit	Examiner

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Paper No. #33

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Chris Ruby
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REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)

In re Application of	
Application Number: 07/715,272	Filed: 6-14-91
Art Unit	Examiner

Paper No. #34

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REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)

In re Application of	
Application Number: 07/715,272	Filed: 6.14.91
Art Unit: 184	Examiner: Keisee

Paper No. 35

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Application Number 07/715,272	Filed 6-14-91
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Application Number	Filed
07-715272	06-14-91
Art Unit	Examiner

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US006407213B1

(12) **United States Patent**
Carter et al.

(10) **Patent No.: US 6,407,213 B1**
(45) **Date of Patent: Jun. 18, 2002**

(54) **METHOD FOR MAKING HUMANIZED ANTIBODIES**

(75) Inventors: **Paul J. Carter**; **Leonard G. Presta**, both of San Francisco, CA (US)

(73) Assignee: **Genentech, Inc.**, South San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/146,206**

(22) PCT Filed: **Jun. 15, 1992**

(86) PCT No.: **PCT/US92/05126**

§ 371 (c)(1),
(2), (4) Date: **Nov. 17, 1993**

Related U.S. Application Data

(63) Continuation-in-part of application No. 07/715,272, filed on Jun. 14, 1991, now abandoned.

(51) **Int. Cl.**[7] **C07K 16/00**

(52) **U.S. Cl.** **530/387.3**; 435/69.6; 435/69.7; 435/70.21; 435/91; 536/23.53; 424/133.1

(58) **Field of Search** 435/69.6, 69.7, 435/70.21, 91, 172.2, 240.1, 240.27, 252.3, 320.1, 328; 536/23.53; 424/133.1; 530/387.3

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(List continued on next page.)

Primary Examiner—Anthony C. Caputa
Assistant Examiner—Minh-Tam Davis
(74) *Attorney, Agent, or Firm*—Wendy M. Lee

(57) **ABSTRACT**

Variant immunoglobulins, particularly humanized antibody polypeptides are provided, along with methods for their preparation and use. Consensus immunoglobulin sequences and structural models are also provided.

82 Claims, 9 Drawing Sheets

PTO/SB/68 (04-01)
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REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)

In re Application of Carter	
Application Number 07/715,272	Filed June 14, 91
Art Unit	Examiner

Paper No. 38

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07/715272	6-14-91

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In re Application of: Crater

Application Number	Filed
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Ursula Boudreaux
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Application Number	Filed
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Application Number	Filed
07/715,272	6/14/91

Paper No. 142

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number 6,054,297, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

Direct access to pending applications is not available to the public but copies may be available and may be purchased from the Office of Public Records upon payment of the appropriate fee (37 CFR 1.19(b)), as follows:

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the pending application as originally filed.

Gary Wasserman
Signature

3/9/04
Date

GARY WASSERMAN
Typed or printed name

Registration Number, if applicable

(703) 931-4540
Telephone Number

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Unit: FIU

REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

In re Application of
Carter et al

Application Number: 07/715,272 | Filed: 6/14/91

Paper No. #43

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United States Patent Application Publication No. _____, page _____, line _____

United States Patent Number 6639055, column _____, line _____, or

WIPO Pub. No. _____, page _____, line _____

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Signature

4/2/04
Date

Rick Jensen
Typed or printed name

Registration Number, if applicable

703-418-2848
Telephone Number

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Initials

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REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

In re Application of
CARTER

Application Number: 07/715,272

Filed: 6/14/91

Paper No. #44

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United States Patent Application Publication No. _____, page _____ line _____

United States Patent Number 6407213, column _____, line _____ or

WIPO Pub. No. _____, page _____, line _____

Related Information about Access to Pending Applications (37 CFR 1.14):

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Signature

5/4/04
Date

Rick Jernigan
Typed or printed name

Registration Number, if applicable

703-418-2848
Telephone Number

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Unit: File Information Unit

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In re Application of: Carter

Application Number	Filed
07/715272	6/14/91

Paper No. 45

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number 6407213, column _____, line, _____ or

WIPO Pub. No. _____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

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Anita Myles
Signature

6/7/04
Date

Anita Myles
Typed or printed name

Registration Number, if applicable

(703) 415-4630
Telephone Number

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REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

In re Application of

Application Number	Filed
07/715,272	06-14-91

Paper No. #46

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United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number US 6,407,213 B1, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

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For unpublished applications that are still pending:

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(2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:
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Rachel Hale
Signature

06-09-04
Date

Rachel Hale
Typed or printed name

Registration Number, if applicable

703-486-1150
Telephone Number

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REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

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Telephone: (703) 308-2733

In re Application of: Carter

Application Number	Filed
07/715222	6/14/91

Paper No. #17

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____.

United States Patent Number 6407283, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

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(2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:
   - the pending application as originally filed.

Deborah Saunders
Signature

8/16/04
Date

Deborah Saunders
Typed or printed name

Registration Number, if applicable

414 486-1150
Telephone Number

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In re Application of

Application Number	Filed
07715272	Jun. 18th 91

Paper No. 48

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United States Patent Application Publication No. 6800730, page, _____ line _____,

United States Patent Number _____, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

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Kelvin Rodriguez
Signature

11-1-04
Date

Kelvin Rodriguez
Typed or printed name

Registration Number, if applicable

(703)418-2772
Telephone Number

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REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

In re Application of Carter

Application Number 07/715272 | Filed 7/14/91

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Paper No. #49

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. ________, page, ______ line ______,

United States Patent Number 6407213, column ______, line ______ or

WIPO Pub. No.________, page ______, line ______.

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[signature]
Signature

11/29/04
Date

Violetta Carter
Typed or printed name

Registration Number, if applicable

7486 1150
Telephone Number

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NOV 29 2004
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REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

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In re Application of

Application Number	Filed
07/713272	June 14, 1991

Paper No. 450

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is not within the file jacket of a pending Continued Prosecution Application (CPA) (37 CFR 1.53(d)) and which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number 6054297, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information About Access to Applications Maintained in the Image File Wrapper System (IFW) and Access to Pending Applications in General

A member of the public, acting without a power to inspect, cannot order applications maintained in the IFW system through the FIU. If the member of the public is entitled to a copy of the application file, then the file is made available through the Public Patent Application Information Retrieval system (Public PAIR) on the USPTO internet web site (www.uspto.gov). Terminals that allow access to Public PAIR are available in the Public Search Room. The member of the public may also be entitled to obtain a copy of all or part of the application file upon payment of the appropriate fee. Such copies must be purchased through the **Office of Public Records** upon payment of the appropriate fee (37 CFR 1.19(b)).

For **published** applications that are still pending, a member of the public may obtain **a copy** of: the file contents; the pending application as originally filed; or any document in the file of the pending application.

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Darlene Jones
Signature

Jan. 18, 05
Date

Darlene Jones
Typed or printed name

Registration Number, if applicable

713-418-0330
Telephone Number

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File Information Unit
Unit: _____

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In re Application of
Carter et al

Application Number	Filed
07/715,272	6/14/91

Paper No. #51

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number 6,800,738, column 1, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

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(2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a **copy** of:
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Rayline K. Petitt
Signature

Jan. 31, 2005
Date

Rayline K. Petitt
Typed or printed name

n/a
Registration Number, if applicable

703-415-3060
Telephone Number

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Unit: _____

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In re Application of

Application Number	Filed
07/715,272	6-14-91

Paper No. #52

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United States Patent Application Publication No. _____, page, _____ line _____.

United States Patent Number 5891337, column _____, line, _____ or

WIPO Pub. No._____, page _____, line _____.

Related Information about Access to Pending Applications (37 CFR 1.14):

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In re Application of

Application Number	Filed
07/715272	6/4/91

Paper No. 53

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Application Number 09/715272 Filed 11/15/00

Paper No. 459

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Application Number	Filed
07/715272	Jun 14, 1991

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07/715272	6-14-91

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US006407213B1

(12) **United States Patent**
Carter et al.

(10) **Patent No.: US 6,407,213 B1**
(45) **Date of Patent: Jun. 18, 2002**

(54) **METHOD FOR MAKING HUMANIZED ANTIBODIES**

(75) Inventors: **Paul J. Carter**; **Leonard G. Presta**, both of San Francisco, CA (US)

(73) Assignee: **Genentech, Inc.**, South San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/146,206**

(22) PCT Filed: **Jun. 15, 1992**

(86) PCT No.: **PCT/US92/05126**

§ 371 (c)(1),
(2), (4) Date: **Nov. 17, 1993**

Related U.S. Application Data

(63) Continuation-in-part of application No. 07/715,272, filed on Jun. 14, 1991, now abandoned.

(51) **Int. Cl.**[7] **C07K 16/00**

(52) **U.S. Cl.** **530/387.3**; 435/69.6; 435/69.7; 435/70.21; 435/91; 536/23.53; 424/133.1

(58) **Field of Search** 435/69.6, 69.7, 435/70.21, 91, 172.2, 240.1, 240.27, 252.3, 320.1, 328; 536/23.53; 424/133.1; 530/387.3

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(List continued on next page.)

Primary Examiner—Anthony C. Caputa
Assistant Examiner—Minh-Tam Davis
(74) *Attorney, Agent, or Firm*—Wendy M. Lee

(57) **ABSTRACT**

Variant immunoglobulins, particularly humanized antibody polypeptides are provided, along with methods for their preparation and use. Consensus immunoglobulin sequences and structural models are also provided.

82 Claims, 9 Drawing Sheets