

LABORATORY
NOTEBOOK



Ig LIGHT VAR

XIGE

GENENTECH, INC.

Celltrion v. Genentech
IPR2017-01374
Genentech Exhibit 2002

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NOTEBOOK NO. 10823
ISSUED TO LEONARD PRESTA
ON December 5 **19** 89
DEPARTMENT BIOMOL. CHEM
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STEVENSVILLE, MI 49127
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Genentech Laboratory Notebook Procedures

Important steps for maintenance of your notebooks:

- 1) Use dark permanent ink to record all of your work in your notebook on a daily basis. Sign and date each day's entries.
- 2) Permanently affix all attachments without covering any other entries. Please attach copies of any computer data entered into your computer files. These data are considered part of your experimental record.
- 3) Make any changes in data in dark permanent ink and, if appropriate, initial and date in the margin. Ensure that the original entry remains visible. Leave no open areas. When the book is completed line out any unused portion of a page at the end of each experiment.
- 4) Have a witness who understands and is aware of your work, but who is not directly involved in your project, sign and date your notebook entries (not later than one month after you do the work).
- 5) Don't hold back data for later entry and don't keep a "rough draft" notebook.
- 6) Report the quantitative or qualitative results only. Avoid over broad and potentially inflammatory comments like "failed experiment", "doesn't work", or "toxic compound."
- 7) The source and character of starting materials should be described. Preferably, refer to the notebook pages describing the starting material and its method of preparation.
- 8) Be sure your notebook record is understandable. Omit abbreviations or slang that would not be understood by others working in your field. It is helpful to introduce each experiment with a statement of purpose, and make liberal use of cross-references to related experiments. While sufficient detail should be included to enable reproduction of experiments, it is acceptable to refer to conventional or published procedures. However, record any changes you may make to such procedures.
- 9) Record your ideas too, not just experimental data. This is important to demonstrate when an invention or thought occurred to you, and is an important part of establishing priority in inventorship contests. Don't hesitate to broaden the scope of your ideas; there is no reason to limit them to specific experiments planned for the next few days, although you should include as much detail as possible. Your notebook will not be published and there is no penalty for guessing wrong on notebook *idea* entries, so don't hesitate to let your imagination run.
- 10) Try to keep a different notebook for each product and/or project. Please complete the table of contents indicating which product and/or project this work concerns.

Genentech's success, and with it your own prosperity and research support, depends upon the quality and timing of your work. This may require that we prove what you did and when you did it in the face of a contrary challenge. Such challenges have and will continue to arise in judicial proceedings, in patent validity or infringement or challenge, inventorship priority contests and product liability actions. The key to winning in such cases is the ability to supply appropriate evidence.

1. ...
 2-7 ...
 8-10 ...
 11-13 ...
 14 ...
 15 ...
 16-18 ...
 19-21 ...
 22-24 ...
 25-27 ...
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Using Biosym Insight program; all superimposed
 on IFB4 VL (output files = *.NEWROT)

IFB4	2RHE	2MCP	3FAB
V18-A24	V18-A24	V19-S25	V18-A24
V32-Q37	V34-Q39	L39-Q44	V32-Q37
R60-S66	R62-S68	R67- S73 S72	R53-S66
S69-I74	S71-I76	D76-I81	S69-I74
D84-A88	D86-A90	V91-Q95	D84-Q88
RMS NCαC	0.40	0.60	0.53

IFBJ	2HFL	IREI(molA)	(molB)
V19-A25	V19-A25	V19-A25	
L32-Q37	M32-Q37	L33-Q38	
R60- S65 S65	R60-S65	R61-S66	
S69-I74	S69-I74	D70-I75	
I84-Q88	E84-Q88	T85-Q89	
0.54	0.48	0.50	0.47

Superimposed on IFBJ (output files = *.ONFBJ)

	RMS NCαC
2MCP	0.470
2HFL	0.388
IREI(molA)	0.499
(molB)	0.444

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Recorded by _____

Leonard Presta

12-15-88

From Page No. _____

From PDB files: lfb4.test 2mcp.test
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 112 118

lfb4 Res	2mcp Res	Dist
GLU 1	ASP 1	2.31
VAL 3	VAL 3	2.46
LEU 4	MET 4	0.30
THR 5	THR 5	0.62
GLN 6	GLN 6	0.74
PRO 7	SER 7	1.60
PRO 7	PRO 8	2.49
PRO 8	SER 9	0.93
SER 9	SER 10	1.08
ALA 10	LEU 11	1.91
SER 11	SER 12	2.48
GLY 12	VAL 13	1.83
THR 13	SER 14	1.68
PRO 14	ALA 15	1.05
GLY 15	GLY 16	1.06
GLN 16	GLU 17	1.12
ARG 17	ARG 18	0.91
VAL 18	VAL 19	0.40
THR 19	THR 20	0.47
ILE 20	MET 21	0.40
SER 21	SER 22	0.18
CYS 22	CYS 23	0.33
THR 23	LYS 24	1.21
GLY 24	SER 25	0.84
THR 25	SER 26	2.16
THR 25	GLN 27	2.49
GLY 28	SER 28	1.67
THR 31	ASN 37	2.18
THR 31	PHE 38	2.28
VAL 32	LEU 39	1.41
ASN 33	ALA 40	0.73
TRP 34	TRP 41	0.37
TYR 35	TYR 42	0.30
GLN 36	GLN 43	0.35
GLN 37	GLN 44	0.31
ALA 42	PRO 49	0.56
PRO 43	PRO 50	0.33
LYS 44	LYS 51	0.24
LEU 45	LEU 52	0.48
LEU 46	LEU 53	0.76
ILE 47	ILE 54	0.56
TYR 48	TYR 55	0.67
ARG 49	GLY 56	0.79
ASP 50	ALA 57	0.67
ALA 51	SER 58	0.57
MET 52	THR 59	0.59
ARG 53	ARG 60	1.25
PRO 54	GLU 61	1.43
SER 55	SER 62	1.37
GLY 56	GLY 63	1.01
VAL 57	VAL 64	0.25
PRO 58	PRO 65	0.19
THR 59	ASP 66	0.24
ARG 60	ARG 67	0.48
PHE 61	PHE 68	0.22
SER 62	THR 69	0.28
GLY 63	GLY 70	0.51
SER 64	SER 71	0.49
LYS 65	GLY 72	1.14
THR 68	THR 75	1.01
SER 69	ASP 76	0.65

ALA 70	PHE 77	0.35
SER 71	THR 78	0.55
LEU 72	LEU 79	0.44
ALA 73	THR 80	0.64
ILE 74	ILE 81	0.21
SER 75	SER 82	0.21
GLY 76	SER 83	0.72
LEU 77	VAL 84	0.73
LEU 78	GLN 85	0.74
ALA 79	ALA 86	0.88
GLU 80	GLU 87	0.80
ASP 81	ASP 88	0.85
GLU 82	LEU 89	1.15
SER 83	ALA 90	0.70
ASP 84	VAL 91	0.37
TYR 85	TYR 92	0.38
TYR 86	TYR 93	0.28
CYS 87	CYS 94	0.37
ALA 88	GLN 95	0.80
SER 89	ASN 96	1.48
TRP 90	HIS 98	1.73
SER 96	TYR 100	1.26
SER 96	PRO 101	2.29
TYR 97	LEU 102	1.35
VAL 98	THR 103	1.51
PHE 99	PHE 104	0.82
GLY 100	GLY 105	1.38
THR 101	GLY 105	2.48
THR 101	ALA 106	1.56
GLY 102	GLY 107	0.81
THR 103	THR 108	0.66
LYS 104	LYS 109	0.59
VAL 105	LEU 110	0.74
THR 106	GLU 111	0.92
VAL 107	ILE 112	1.26
LEU 108	LYS 113	1.82

From PDB files: lfb4.test lfbj.test
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 112 111

lfb4 Res	lfbj Res	Dist
GLU 1	GLU 1	1.53
LEU 4	LEU 4	1.23
THR 5	THR 5	0.93
GLN 6	GLN 6	0.57
PRO 7	SER 7	1.28
PRO 7	PRO 8	2.34
PRO 8	ALA 9	0.68
SER 9	ILE 10	1.37
ALA 10	THR 11	1.91
SER 11	ALA 12	1.43
GLY 12	ALA 13	0.88
THR 13	SER 14	0.44
PRO 14	LEU 15	0.62
GLY 15	GLY 16	0.17
GLN 16	GLN 17	0.30
ARG 17	LYS 18	0.25
VAL 18	VAL 19	0.68
THR 19	THR 20	0.85
ILE 20	ILE 21	0.12
SER 21	THR 22	0.46
CYS 22	CYS 23	0.28
THR 23	SER 24	0.99
GLY 24	ALA 25	0.37
THR 25	SER 26	1.95
THR 25	SER 27	2.33
SER 26	SER 27	1.77
SER 27	SER 28	2.44
ILE 30	SER 30	1.00
THR 31	SER 31	1.47
VAL 32	LEU 32	1.00
ASN 33	HIS 33	0.26
TRP 34	TRP 34	0.47
TYR 35	TYR 35	0.53
GLN 36	GLN 36	0.38
GLN 37	GLN 37	0.41
LEU 38	LYS 38	2.15
LEU 38	SER 39	2.13
MET 41	THR 41	2.21
ALA 42	SER 42	0.50
PRO 43	PRO 43	0.96
LYS 44	LYS 44	0.63
LEU 45	PRO 45	0.83
LEU 46	TRP 46	0.75
ILE 47	ILE 47	0.14
TYR 48	TYR 48	0.51
ARG 49	GLU 49	1.61
ASP 50	ILE 50	1.22
ALA 51	SER 51	0.40
MET 52	LYS 52	0.74
ARG 53	LEU 53	1.02
PRO 54	ALA 54	2.21
PRO 54	SER 55	2.33
SER 55	SER 55	2.19
GLY 56	GLY 56	1.26
VAL 57	VAL 57	1.16
PRO 58	PRO 58	0.92
THR 59	ALA 59	0.52
ARG 60	ARG 60	0.59
PHE 61	PHE 61	0.56
SER 62	SER 62	0.33
GLY 63	GLY 63	0.55

SER 64	SER 64	0.33
LYS 65	GLY 65	0.90
SER 66	SER 66	2.13
THR 68	THR 68	0.85
SER 69	SER 69	0.96
ALA 70	TYR 70	0.31
SER 71	SER 71	0.45
LEU 72	LEU 72	0.25
ALA 73	THR 73	0.45
ILE 74	ILE 74	0.78
SER 75	ASN 75	1.03
GLY 76	THR 76	0.52
LEU 77	MET 77	0.69
GLU 78	GLU 78	0.75
ALA 79	ALA 79	0.95
GLU 80	GLU 80	0.61
ASP 81	ASP 81	1.24
GLU 82	ALA 82	1.40
SER 83	ALA 83	0.35
ASP 84	ILE 84	0.16
TYR 85	TYR 85	0.23
TYR 86	TYR 86	0.54
CYS 87	CYS 87	0.56
ALA 88	GLN 88	0.48
SER 89	GLN 89	0.53
TRP 90	TRP 90	1.58
ASN 95	PRO 93	2.10
SER 96	LEU 94	1.57
TYR 97	ILE 95	0.62
VAL 98	THR 96	0.70
PHE 99	PHE 97	0.64
GLY 100	GLY 98	0.77
THR 101	ALA 99	1.18
GLY 102	GLY 100	0.67
THR 103	THR 101	0.23
LYS 104	LYS 102	0.36
VAL 105	LEU 103	0.67
THR 106	GLU 104	1.08
VAL 107	LEU 105	0.65
LEU 108	LYS 106	0.65
GLY 109	ARG 107	2.30

Using MATCH program

Witnessed & Understood by me,

Date

Invented by

Date

Recorded by

TITLE _____

From Page No. 2

From PDB files: 1FB4.TEST IREI MOLECULE A
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 112 107

From PDB files: 1FB4.TEST IREI MOLECULE B
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 112 107

1FB4 Res	1REI Res	Dist
GLU 1	ASP 1	2.48
LEU 4	MET 4	0.65
THR 5	THR 5	0.57
GLN 6	GLN 6	0.56
PRO 7	SER 7	1.73
PRO 7	PRO 8	2.24
PRO 8	SER 9	0.70
SER 9	SER 10	1.42
ALA 10	LEU 11	2.40
SER 11	SER 12	2.38
GLY 12	ALA 13	1.67
THR 13	SER 14	2.18
PRO 14	VAL 15	1.41
GLY 15	GLY 16	0.43
GLN 16	ASP 17	1.03
ARG 17	ARG 18	0.62
VAL 18	VAL 19	0.45
THR 19	THR 20	0.68
ILE 20	ILE 21	0.48
SER 21	THR 22	0.36
CYS 22	CYS 23	0.34
THR 23	GLN 24	0.75
GLY 24	ALA 25	0.69
THR 25	SER 26	2.29
THR 25	GLN 27	2.19
SER 26	GLN 27	2.34
SER 26	ASP 28	2.04
GLY 28	ASP 28	2.09
THR 31	TYR 32	1.26
VAL 32	LEU 33	0.89
ASN 33	ASN 34	0.68
TRP 34	TRP 35	0.22
TYR 35	TYR 36	0.25
GLN 36	GLN 37	0.34
GLN 37	GLN 38	0.55
LEU 38	THR 39	2.29
ALA 42	ALA 43	0.78
PRO 43	PRO 44	0.39
LYS 44	LYS 45	0.35
LEU 45	LEU 46	0.40
LEU 46	LEU 47	0.61
ILE 47	ILE 48	0.43
TYR 48	TYR 49	0.44
ARG 49	GLU 50	1.04
ASP 50	ALA 51	0.78
ALA 51	SER 52	0.60
MET 52	ASN 53	0.53
ARG 53	LEU 54	0.58
PRO 54	GLN 55	1.13
SER 55	ALA 56	1.64
GLY 56	GLY 57	0.85
VAL 57	VAL 58	0.37
PRO 58	PRO 59	0.26
THR 59	SER 60	0.29
ARG 60	ARG 61	0.17
PHE 61	PHE 62	0.09
SER 62	SER 63	0.22
GLY 63	GLY 64	0.18
SER 64	SER 65	0.38
LYS 65	GLY 66	0.46
GLY 67	GLY 68	2.27

THR 68	THR 69	0.66
SER 69	ASP 70	0.74
ALA 70	TYR 71	0.49
SER 71	THR 72	0.90
LEU 72	PHE 73	0.39
ALA 73	THR 74	0.38
ILE 74	ILE 75	0.22
SER 75	SER 76	0.22
GLY 76	SER 77	0.65
LEU 77	LEU 78	0.96
GLU 78	GLN 79	1.15
ALA 79	PRO 80	1.71
GLU 80	GLU 81	1.20
ASP 81	ASP 82	1.22
GLU 82	ILE 83	1.35
SER 83	ALA 84	0.92
ASP 84	THR 85	0.25
TYR 85	TYR 86	0.25
TYR 86	TYR 87	0.24
CYS 87	CYS 88	0.52
ALA 88	GLN 89	0.74
SER 89	GLN 90	0.97
TRP 90	TYR 91	1.72
SER 96	LEU 94	1.26
SER 96	PRO 95	1.55
TYR 97	TYR 96	0.91
VAL 98	THR 97	1.44
PHE 99	PHE 98	0.78
GLY 100	GLY 99	0.89
THR 101	GLN 100	1.02
GLY 102	GLY 101	1.11
THR 103	THR 102	0.81
LYS 104	LYS 103	0.71
VAL 105	LEU 104	0.95
THR 106	GLN 105	1.40
VAL 107	ILE 106	1.53
LEU 108	THR 107	1.55

1FB4 Res	1REI Res	Dist
GLU 1	ASP 1	2.28
LEU 4	MET 4	0.81
THR 5	THR 5	0.43
GLN 6	GLN 6	0.58
PRO 7	SER 7	1.84
PRO 7	PRO 8	2.13
PRO 8	SER 9	0.65
SER 9	SER 10	1.45
ALA 10	LEU 11	2.08
GLY 12	ALA 13	1.84
THR 13	SER 14	1.54
PRO 14	VAL 15	1.09
GLY 15	GLY 16	0.83
GLN 16	ASP 17	1.11
ARG 17	ARG 18	0.52
VAL 18	VAL 19	0.42
THR 19	THR 20	0.49
ILE 20	ILE 21	0.48
SER 21	THR 22	0.28
CYS 22	CYS 23	0.25
THR 23	GLN 24	0.75
GLY 24	ALA 25	0.58
THR 25	SER 26	1.64
SER 26	GLN 27	2.25
SER 26	ASP 28	2.27
GLY 28	ASP 28	1.82
THR 31	TYR 32	1.41
VAL 32	LEU 33	0.93
ASN 33	ASN 34	0.61
TRP 34	TRP 35	0.29
TYR 35	TYR 36	0.23
GLN 36	GLN 37	0.18
GLN 37	GLN 38	0.48
ALA 42	ALA 43	0.77
PRO 43	PRO 44	0.38
LYS 44	LYS 45	0.42
LEU 45	LEU 46	0.28
LEU 46	LEU 47	0.59
ILE 47	ILE 48	0.56
TYR 48	TYR 49	0.55
ARG 49	GLU 50	1.06
ASP 50	ALA 51	0.88
ALA 51	SER 52	0.81
MET 52	ASN 53	0.81
ARG 53	LEU 54	1.05
PRO 54	GLN 55	1.31
SER 55	ALA 56	1.43
GLY 56	GLY 57	0.91
VAL 57	VAL 58	0.44
PRO 58	PRO 59	0.50
THR 59	SER 60	0.45
ARG 60	ARG 61	0.36
PHE 61	PHE 62	0.22
SER 62	SER 63	0.20
GLY 63	GLY 64	0.25
SER 64	SER 65	0.40
LYS 65	GLY 66	0.43
GLY 67	GLY 68	2.36
THR 68	THR 69	0.30
SER 69	ASP 70	0.60
ALA 70	TYR 71	0.52

SER 71	THR 72	0.69
LEU 72	PHE 73	0.31
ALA 73	THR 74	0.32
ILE 74	ILE 75	0.27
SER 75	SER 76	0.29
GLY 76	SER 77	0.47
LEU 77	LEU 78	0.87
GLU 78	GLN 79	1.21
ALA 79	PRO 80	1.36
GLU 80	GLU 81	1.15
ASP 81	ASP 82	0.93
GLU 82	ILE 83	0.90
SER 83	ALA 84	0.63
ASP 84	THR 85	0.14
TYR 85	TYR 86	0.26
TYR 86	TYR 87	0.21
CYS 87	CYS 88	0.50
ALA 88	GLN 89	0.70
SER 89	GLN 90	0.84
TRP 90	TYR 91	1.73
SER 96	LEU 94	1.25
SER 96	PRO 95	1.54
TYR 97	TYR 96	1.00
VAL 98	THR 97	1.48
PHE 99	PHE 98	0.82
GLY 100	GLY 99	0.87
THR 101	GLN 100	0.99
GLY 102	GLY 101	0.76
THR 103	THR 102	0.54
LYS 104	LYS 103	0.58
VAL 105	LEU 104	0.63
THR 106	GLN 105	1.34
VAL 107	ILE 106	1.73
LEU 108	THR 107	2.45

To Page No. 4

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Date _____

Recorded by _____

TITLE _____

From Page No. 4

From PDB files: lfb4.test 2hfl.test
 Maximum distance cutoff for CA-CA was 2.50
 NUMRES molecules 162 112 110

lfb4	2hfl	Dist			
Res	Res	Dist			
LEU 4	LEU 4	0.87	SER 71	SER 71	0.63
THR 5	THR 5	0.46	LEU 72	LEU 72	0.31
GLN 6	GLN 6	0.46	ALA 73	THR 73	0.42
PRO 7	SER 7	2.09	ILE 74	ILE 74	0.59
PRO 7	PRO 8	2.02	SER 75	SER 75	0.89
PRO 8	ALA 9	0.51	GLY 76	SER 76	0.42
SER 9	ILE 10	1.75	LEU 77	MET 77	0.44
ALA 10	MET 11	2.16	GLU 78	GLU 78	0.47
SER 11	SER 12	1.79	ALA 79	THR 79	0.47
GLY 12	ALA 13	1.27	GLU 80	GLU 80	0.21
THR 13	SER 14	0.96	ASP 81	ASP 81	0.80
PRO 14	PRO 15	0.69	GLU 82	ALA 82	0.68
GLY 15	GLY 16	0.38	SER 83	ALA 83	0.39
GLN 16	GLU 17	0.99	ASP 84	GLU 84	0.27
ARG 17	LYS 18	0.39	TYR 85	TYR 85	0.20
VAL 18	VAL 19	0.50	TYR 86	TYR 86	0.42
THR 19	THR 20	0.65	CYS 87	CYS 87	0.67
ILE 20	MET 21	0.32	ALA 88	GLN 88	0.56
SER 21	THR 22	0.40	SER 89	GLN 89	0.68
CYS 22	CYS 23	0.28	TRP 90	TRP 90	2.33
THR 23	SER 24	0.43	TRP 90	GLY 91	2.28
GLY 24	ALA 25	0.37	ASN 95	ARG 92	2.32
THR 25	SER 27	1.91	SER 96	ASN 93	0.38
SER 26	SER 28	2.31	TYR 97	PRO 94	0.40
GLY 28	SER 28	1.89	VAL 98	THR 95	0.55
THR 31	TYR 31	1.01	PHE 99	PHE 96	0.39
VAL 32	MET 32	0.39	GLY 100	GLY 97	0.85
ASN 33	TYR 33	0.39	THR 101	GLY 98	0.91
TRP 34	TRP 34	0.40	GLY 102	GLY 99	0.70
TYR 35	TYR 35	0.58	THR 103	THR 100	0.41
GLN 36	GLN 36	0.43	LYS 104	LYS 101	0.41
GLN 37	GLN 37	0.43	VAL 105	LEU 102	0.48
LEU 38	LYS 38	1.71	THR 106	GLU 103	1.08
ALA 42	SER 42	0.43	VAL 107	ILE 104	1.32
PRO 43	PRO 43	0.37	LEU 108	LYS 105	0.88
LYS 44	LYS 44	0.46	GLY 109	ARG 106	1.12
LEU 45	ARG 45	0.48			
LEU 46	TRP 46	0.57			
ILE 47	ILE 47	0.39			
TYR 48	TYR 48	0.51			
ARG 49	ASP 49	0.31			
ASP 50	THR 50	0.30			
ALA 51	SER 51	0.16			
MET 52	LYS 52	0.28			
ARG 53	LEU 53	1.24			
PRO 54	ALA 54	2.15			
GLY 56	GLY 56	1.19			
VAL 57	VAL 57	1.04			
PRO 58	PRO 58	0.81			
THR 59	VAL 59	0.34			
ARG 60	ARG 60	0.42			
PHE 61	PHE 61	0.42			
SER 62	SER 62	0.59			
GLY 63	GLY 63	0.33			
SER 64	SER 64	0.34			
LYS 65	GLY 65	1.11			
SER 66	SER 66	2.08			
GLY 67	GLY 67	2.25			
THR 68	THR 68	0.62			
SER 69	SER 69	0.72			
ALA 70	TYR 70	0.36			

To Page No. 6

Witnessed & Understood by me, _____

Date _____

Invented by _____

Date _____

Recorded by _____

From Page No. 5

From PDB files: lfbj.test
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 111 118

lfbj	2mcp	Dist
Res	Res	
GLU 1	ASP 1	1.67
ILE 2	ILE 2	0.48
VAL 3	VAL 3	0.84
LEU 4	MET 4	1.32
THR 5	THR 5	0.61
GLN 6	GLN 6	0.31
SER 7	SER 7	0.50
PRO 8	PRO 8	0.28
ALA 9	SER 9	0.60
ILE 10	SER 10	0.81
THR 11	LEU 11	1.00
ALA 12	SER 12	1.10
ALA 13	VAL 13	1.35
SER 14	SER 14	1.71
LEU 15	ALA 15	1.62
GLY 16	GLY 16	1.13
GLN 17	GLU 17	1.05
LYS 18	ARG 18	1.15
VAL 19	VAL 19	0.52
THR 20	THR 20	0.45
ILE 21	MET 21	0.34
THR 22	SER 22	0.55
CYS 23	CYS 23	0.32
SER 24	LYS 24	0.42
ALA 25	SER 25	0.60
SER 26	SER 26	0.41
SER 27	GLN 27	1.57
SER 28	SER 28	1.94
VAL 29	LEU 29	0.75
SER 31	PHE 31	1.43
LEU 32	LEU 32	0.67
HIS 33	ALA 33	0.71
TRP 34	TRP 34	0.30
TYR 35	TYR 35	0.38
GLN 36	GLN 36	0.48
GLN 37	GLN 37	0.54
LYS 38	LYS 38	0.66
SER 39	PRO 39	2.07
GLY 40	GLY 40	0.52
THR 41	GLN 41	0.74
SER 42	PRO 42	0.36
PRO 43	PRO 43	0.76
LYS 44	LYS 44	0.77
PRO 45	LEU 45	0.73
TRP 46	LEU 46	0.67
ILE 47	ILE 47	0.62
TYR 48	TYR 48	0.89
GLU 49	GLY 49	1.57
ILE 50	ALA 50	0.96
SER 51	SER 51	0.80
LYS 52	THR 52	1.15
LEU 53	ARG 53	1.20
ALA 54	GLU 54	1.34
SER 55	SER 55	1.89
GLY 56	GLY 56	1.17
VAL 57	VAL 57	1.01
PRO 58	PRO 58	1.00
ALA 59	ASP 59	0.60
ARG 60	ARG 60	0.64
PHE 61	PHE 61	0.66
SER 62	THR 62	0.11

GLY 63	GLY 63	0.23
SER 64	SER 64	0.70
GLY 65	GLY 65	0.58
SER 66	SER 66	0.87
GLY 67	GLY 67	0.54
THR 68	THR 68	0.32
SER 69	ASP 69	0.66
TYR 70	PHE 70	0.15
SER 71	THR 71	0.15
LEU 72	LEU 72	0.22
THR 73	THR 73	0.36
ILE 74	ILE 74	0.76
ASN 75	SER 75	1.02
THR 76	SER 76	0.91
MET 77	VAL 77	1.36
GLU 78	GLN 78	1.38
ALA 79	ALA 79	1.83
GLU 80	GLU 80	1.38
ASP 81	ASP 81	0.70
ALA 82	LEU 82	1.87
ALA 83	ALA 83	0.62
ILE 84	VAL 84	0.26
TYR 85	TYR 85	0.39
TYR 86	TYR 86	0.34
CYS 87	CYS 87	0.22
GLN 88	GLN 88	0.40
GLN 89	ASN 89	1.12
TRP 90	ASP 90	1.75
TRP 91	HIS 91	2.05
THR 92	HIS 92	1.90
LEU 93	TYR 93	1.12
ILE 94	LEU 94	1.63
THR 95	THR 95	1.28
PHE 96	PHE 96	1.19
GLY 97	GLY 97	1.57
ALA 98	ALA 98	1.56
GLY 99	GLY 99	0.62
THR 100	THR 100	0.73
LYS 101	LYS 101	0.74
LEU 102	LEU 102	1.00
GLU 103	GLU 103	0.80
LEU 104	LEU 104	1.12
LYS 105	LYS 105	1.25
ARG 106	ARG 106	1.20
ARG 107	ARG 107	1.20

From PDB files: lfbj.test
Maximum distance cutoff for CA-CA was 2.50
NUMRES molecules 1&2 111 110

lfbj	2hfl	Dist
Res	Res	
GLU 1	ASP 1	1.34
ILE 2	ILE 2	0.24
VAL 3	VAL 3	0.48
LEU 4	LEU 4	0.51
THR 5	THR 5	0.81
GLN 6	GLN 6	0.20
SER 7	SER 7	0.93
PRO 8	PRO 8	0.48
ALA 9	ALA 9	0.19
ILE 10	ILE 10	0.88
THR 11	MET 11	0.41
ALA 12	SER 12	0.48
ALA 13	ALA 13	0.65
SER 14	SER 14	0.74
LEU 15	PRO 15	1.17
GLY 16	GLY 16	0.52
GLN 17	GLU 17	0.93
LYS 18	LYS 18	0.55
VAL 19	VAL 19	0.23
THR 20	THR 20	0.25
ILE 21	MET 21	0.44
THR 22	THR 22	0.55
CYS 23	CYS 23	0.12
SER 24	SER 24	0.88
ALA 25	ALA 25	0.40
SER 26	SER 26	0.72
SER 27	SER 27	0.85
SER 28	SER 28	2.20
VAL 29	VAL 29	1.20
SER 31	TYR 31	2.06
LEU 32	MET 32	0.74
HIS 33	TYR 33	0.26
TRP 34	TRP 34	0.19
TYR 35	TYR 35	0.30
GLN 36	GLN 36	0.08
GLN 37	GLN 37	0.49
LYS 38	LYS 38	0.49
SER 39	SER 39	1.20
GLY 40	GLY 40	0.97
THR 41	THR 41	0.50
SER 42	SER 42	0.37
PRO 43	PRO 43	0.83
LYS 44	LYS 44	0.34
PRO 45	ARG 45	0.50
TRP 46	TRP 46	0.54
ILE 47	ILE 47	0.29
TYR 48	TYR 48	0.08
GLU 49	ASP 49	1.48
ILE 50	THR 50	1.18
SER 51	SER 51	0.33
LYS 52	LYS 52	0.50
LEU 53	LEU 53	0.71
ALA 54	ALA 54	0.78
SER 55	SER 55	0.84
GLY 56	GLY 56	1.23
VAL 57	VAL 57	0.18
PRO 58	PRO 58	0.19
ALA 59	VAL 59	0.74
ARG 60	ARG 60	0.51
PHE 61	PHE 61	0.14
SER 62	SER 62	0.27

GLY 63	GLY 63	0.64
SER 64	SER 64	0.26
GLY 65	GLY 65	0.27
SER 66	SER 66	0.36
GLY 67	GLY 67	0.69
THR 68	THR 68	0.34
SER 69	SER 69	0.40
TYR 70	TYR 70	0.07
SER 71	SER 71	0.43
LEU 72	LEU 72	0.37
THR 73	THR 73	0.05
ILE 74	ILE 74	0.20
ASN 75	SER 75	0.25
THR 76	SER 76	0.19
MET 77	MET 77	0.29
GLU 78	GLU 78	0.26
ALA 79	THR 79	0.52
GLU 80	GLU 80	0.47
ASP 81	ASP 81	0.48
ALA 82	ALA 82	0.78
ALA 83	ALA 83	0.34
ILE 84	GLU 84	0.33
TYR 85	TYR 85	0.15
TYR 86	TYR 86	0.52
CYS 87	CYS 87	0.15
GLN 88	GLN 88	0.28
GLN 89	GLN 89	0.19
TRP 90	TRP 90	1.00
THR 91	GLY 91	1.87
TYR 92	ARG 92	2.33
PRO 93	ARG 93	1.84
LEU 94	ASN 94	1.23
ILE 95	PRO 95	0.45
THR 96	THR 96	0.26
PHE 97	PHE 97	0.33
GLY 98	GLY 98	0.62
ALA 99	GLY 99	0.72
GLY 100	GLY 100	0.16
THR 101	THR 101	0.38
LYS 102	LYS 102	0.43
LEU 103	LEU 103	0.32
GLU 104	GLU 104	0.46
LEU 105	ILE 105	0.97
LYS 106	LYS 106	0.66
ARG 107	ARG 107	1.59

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Date

Invented by

Date

Recorded by

TITLE _____

From Page No. 6

From PDB files: lfbj.test lrei.testa
 Maximum distance cutoff for CA-CA was 2.50
 NUMRES molecules l&2 l11 107

lfbj Res	lrei Res	Dist			
GLU 1	ASP 1	2.29			
ILE 2	ILE 2	0.44			
VAL 3	GLN 3	0.64	GLY 63	GLY 64	0.39
LEU 4	MET 4	0.68	SER 64	SER 65	0.33
THR 5	THR 5	0.48	GLY 65	GLY 66	0.76
GLN 6	GLN 6	0.15	SER 66	SER 67	0.85
SER 7	SER 7	0.69	GLY 67	GLY 68	0.80
PRO 8	PRO 8	0.42	THR 68	THR 69	0.70
ALA 9	SER 9	0.76	SER 69	ASP 70	0.24
ILE 10	SER 10	0.67	TYR 70	TYR 71	0.22
THR 11	LEU 11	0.87	SER 71	THR 72	0.61
ALA 12	SER 12	1.04	LEU 72	PHE 73	0.20
ALA 13	ALA 13	1.23	THR 73	THR 74	0.18
SER 14	SER 14	1.97	ILE 74	ILE 75	0.68
LEU 15	VAL 15	1.58	ASN 75	SER 76	0.85
GLY 16	GLY 16	0.51	THR 76	SER 77	0.73
GLN 17	ASP 17	0.90	MET 77	LEU 78	1.52
LYS 18	ARG 18	0.79	GLU 78	LEU 78	2.47
VAL 19	VAL 19	0.98	GLU 78	GLN 79	1.61
THR 20	THR 20	0.68	GLU 80	GLU 81	1.84
ILE 21	ILE 21	0.41	ASP 81	ASP 82	0.64
THR 22	THR 22	0.41	ALA 82	ILE 83	1.82
CYS 23	CYS 23	0.45	ALA 83	ALA 84	0.83
SER 24	GLN 24	0.66	ILE 84	THR 85	0.26
ALA 25	ALA 25	0.41	TYR 85	TYR 86	0.34
SER 26	SER 26	0.43	TYR 86	TYR 87	0.47
SER 27	GLN 27	0.70	CYS 87	CYS 88	0.03
SER 28	ASP 28	2.20	GLN 88	GLN 89	0.31
VAL 29	ILE 29	0.84	GLN 89	GLN 90	0.50
SER 31	TYR 32	0.25	TRP 90	TYR 91	0.71
LEU 32	LEU 33	0.13	THR 91	GLN 92	1.37
HIS 33	ASN 34	0.68	THR 91	SER 93	2.46
TRP 34	TRP 35	0.41	LEU 94	LEU 94	0.69
TYR 35	TYR 36	0.55	ILE 95	TYR 96	1.39
GLN 36	GLN 37	0.37	THR 96	THR 97	1.28
GLN 37	GLN 38	0.72	PHE 97	PHE 98	1.24
LYS 38	THR 39	0.63	GLY 98	GLY 99	1.39
SER 39	PRO 40	1.55	ALA 99	GLN 100	1.13
GLY 40	GLY 41	0.93	GLY 100	GLY 101	0.83
THR 41	LYS 42	0.86	THR 101	THR 102	0.86
SER 42	ALA 43	1.14	LYS 102	LYS 103	0.77
PRO 43	PRO 44	0.99	LEU 103	LEU 104	1.29
LYS 44	LYS 45	0.88	GLU 104	GLN 105	1.19
PRO 45	LEU 46	0.90	LEU 105	ILE 106	1.68
TRP 46	LEU 47	0.66	LYS 106	THR 107	0.97
ILE 47	ILE 48	0.55			
TYR 48	TYR 49	0.65			
GLU 49	GLU 50	1.36			
ILE 50	ALA 51	1.28			
SER 51	SER 52	0.96			
LYS 52	ASN 53	1.20			
LEU 53	LEU 54	1.09			
ALA 54	GLN 55	1.54			
SER 55	ALA 56	1.37			
GLY 56	GLY 57	1.12			
VAL 57	VAL 58	1.16			
PRO 58	PRO 59	1.11			
ALA 59	SER 60	0.33			
ARG 60	ARG 61	0.58			
PHE 61	PHE 62	0.56			
SER 62	SER 63	0.51			

From PDB files: lfbj.test lrei.testb
 Maximum distance cutoff for CA-CA was 2.50
 NUMRES molecules l&2 l11 107

lfbj Res	lrei Res	Dist			
GLU 1	ASP 1	2.35			
ILE 2	ILE 2	0.49			
VAL 3	GLN 3	0.51	SER 62	SER 63	0.25
LEU 4	MET 4	0.50	GLY 63	GLY 64	0.33
THR 5	THR 5	0.87	SER 64	SER 65	0.16
GLN 6	GLN 6	0.19	GLY 65	GLY 66	0.63
SER 7	SER 7	0.69	SER 66	SER 67	0.85
PRO 8	PRO 8	0.24	GLY 67	GLY 68	0.61
ALA 9	SER 9	0.58	THR 68	THR 69	0.58
ILE 10	SER 10	0.41	SER 69	ASP 70	0.41
THR 11	LEU 11	0.39	TYR 70	TYR 71	0.23
ALA 12	SER 12	1.25	SER 71	THR 72	0.32
ALA 13	ALA 13	1.51	LEU 72	PHE 73	0.16
SER 14	SER 14	1.41	THR 73	THR 74	0.18
LEU 15	VAL 15	1.31	ILE 74	ILE 75	0.71
GLY 16	GLY 16	0.95	ASN 75	SER 76	0.78
GLN 17	ASP 17	0.96	THR 76	SER 77	0.64
LYS 18	ARG 18	0.71	MET 77	LEU 78	1.43
VAL 19	VAL 19	0.88	GLU 78	LEU 78	2.48
THR 20	THR 20	0.65	GLU 78	GLN 79	1.57
ILE 21	ILE 21	0.42	ALA 79	PRO 80	2.14
THR 22	THR 22	0.41	GLU 80	PRO 80	2.44
CYS 23	CYS 23	0.26	GLU 80	GLU 81	1.79
SER 24	GLN 24	0.56	ASP 81	ASP 82	0.76
ALA 25	ALA 25	0.36	ALA 82	ILE 83	1.68
SER 26	SER 26	0.32	ALA 83	ALA 84	0.54
SER 27	GLN 27	1.04	ILE 84	THR 85	0.08
SER 28	ASP 28	2.36	TYR 85	TYR 86	0.31
VAL 29	ILE 29	0.73	TYR 86	TYR 87	0.47
SER 31	TYR 32	0.31	CYS 87	CYS 88	0.08
LEU 32	LEU 33	0.08	GLN 88	GLN 89	0.29
HIS 33	ASN 34	0.57	GLN 89	GLN 90	0.38
TRP 34	TRP 35	0.40	TRP 90	TYR 91	0.71
TYR 35	TYR 36	0.60	THR 91	GLN 92	1.31
GLN 36	GLN 37	0.38	LEU 94	LEU 94	0.61
GLN 37	GLN 38	0.60	ILE 95	TYR 96	1.47
LYS 38	THR 39	0.76	THR 96	THR 97	1.35
SER 39	PRO 40	1.94	PHE 97	PHE 98	1.20
GLY 40	GLY 41	0.84	GLY 98	GLY 99	1.32
THR 41	LYS 42	0.93	ALA 99	GLN 100	1.01
SER 42	ALA 43	0.76	GLY 100	GLY 101	0.67
PRO 43	PRO 44	1.16	THR 101	THR 102	0.65
LYS 44	LYS 45	1.04	LYS 102	LYS 103	0.52
PRO 45	LEU 46	0.92	LEU 103	LEU 104	0.96
TRP 46	LEU 47	0.75	GLU 104	GLN 105	1.00
ILE 47	ILE 48	0.67	LEU 105	ILE 106	1.62
TYR 48	TYR 49	0.74	LYS 106	THR 107	1.90
GLU 49	GLU 50	1.28			
ILE 50	ALA 51	1.22			
SER 51	SER 52	1.18			
LYS 52	ASN 53	1.43			
LYS 52	LEU 54	2.42			
LEU 53	LEU 54	1.51			
ALA 54	GLN 55	1.62			
SER 55	ALA 56	1.41			
GLY 56	GLY 57	1.37			
VAL 57	VAL 58	1.12			
PRO 58	PRO 59	0.97			
ALA 59	SER 60	0.11			
ARG 60	ARG 61	0.32			
PHE 61	PHE 62	0.36			

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Date _____

Invented by _____

Date _____

Recorded by _____

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 FB4L, 3FAB and RHE are lambda-type REI, MCPL, FBJL AND 2HFL are kappa-type

 a) residues between parentheses are included in beta-sheet based on backbone dihedral angles and hydrogen-bonding patterns
 b) letter repeats above sequences correspond to beta-sheet strands
 c) L1, L2, L3 correspond to hypervariable loops
 d) @ first residue is PCA - pyrroglutamyl
 e) small letter in sequence - Ca-Ca distance between proteins > 1.0 A

```

  AAAAAAAAAA  A'A'A'A'A'A'  BBBBBBBBBBBBBBBB  L1-----
  FB4L  E S V [L T Q] P)P(S A S G T)P)G(Q R V T I S C T G)T)S S N I G
  3FAB  @ s v [L T Q] P P S V S G A p g q R V T I S C T G S S S N I G a
  RHE  e s v [L T Q] P)P(S A S G T)P)G(Q R V T I S C T G)S)A T D I G
  REI  d(i(q [M T Q] s p)S(s l s a s v)G(Q R V T I T C Q A)s q d i i
  MCPL (d i(v [M T Q] s p)S(s l s v)s a g(e(R V T M S C k S)s q s l l n s g n q
  FBJL (e i(v [L T Q] s p)A(i t a A S)L)G(Q K V T I T C S A)s s s v
  2HFL d i v [L T Q] s p A i m s a S P G E K V T M T C S A s s s v
  1 10 20 23 27 a b 29
  
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  *****
  -L1--CCCCCCCCCCCCC C'C'C'C'C'C'C'--L2--C"C"C"
  FB4L S(I [V N W Y Q Q] L)P)G(M [P K L]L(I Y)R D A(M R)P S)G V P
  3FAB g N H V K W Y Q Q l p g t a P K L l i f h n n
  RHE S(N S[V I W Y Q Q] v p)g(k a [P K L]L(I Y)Y N D(L L)P S)G V S
  REI k(y [L N W Y Q Q] t)p)g(k a [P K L]L(I Y)E A S(N L q)a)G V P
  MCPL (x n(f [L A W Y Q Q] k)p)g(q [P K L]L(I Y)G A S(T r e)s)g V P
  FBJL S(s [L H W Y Q Q] k)s)g(t s [P K P]W(I Y)e i(S(K l a)s)g V P
  2HFL n Y [M Y W Y Q Q] k s g t S [P K R W I Y D T S K] l a s g V P
  30 35 40 50 55
  
```

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  *****
  DDDDDDDDDDD EEEEEEEEEEE FFFFFFFFFFFFFF
  FB4L T R(F S G S)k S)G T(S A S L A I S)G L E A E D(E(S D Y Y C A S
  3FAB a R(F S V S)k S)G S S A T L A I T g l Q A E D E A D Y Y C Q S
  RHE D R(F S A S)k S)G T(S A S L A I S)G L E S E D E A D Y Y C A A
  REI S R(F S G S)g s)g T(D Y T F T I)S S L q p e d(i(A T Y Y C Q Q)
  MCPL D R(F T G S)g s)g t(D F T L T I)S S V Q A E D(l(A V Y Y C Q n)
  FBJL A R(F S G S)g s)g T(S Y S L T I)N T M E A E d(a A I Y Y C Q Q
  2HFL V R F S G S g s g T S Y S L T I S S M E T E D A A E Y Y C Q Q
  60 70 80 90
  
```

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  *****
  -L3--GGGGGGGGG HHHHHHHHHH -J1- LIGHT CONSTANT->
  FB4L W N)S S D N(S [Y V F G] T G(T K V)T V L) G Q(P(K A N P T V T
  3FAB Y D r s L R V F G g g T K L T V L r q
  RHE W N)d s l D(e P C F G)G G(T K L T V L) g
  REI y q (s l p Y(t F G)q g(T K L q i t) r
  MCPL d)h (s y p l(t F g)a G(T K L E i k) r
  FBJL w t y) p(l I T F G)a G(T K L E L K) r
  2HFL w g r N [P T F G] G G(T K L) e i K r
  91 97 100 110
  *****
  
```

residues included in average coordinates

Allouf of Avgard or KAPLAN. Avgard

To Page No. _____

Witnessed & Understood by me,	Date	Invented by	Date
		Recorded by	

From Page No. _____

 FB4L, 3FAB and RHE are lambda-type

- a) residues between parentheses are included in beta-sheet based on backbone dihedral angles and hydrogen-bonding patterns
- b) letter repeats above sequences correspond to beta-sheet strands
- c) L1, L2, L3 correspond to hypervariable loops
- d) @ first residue is PCA - pyrroglutanyl
- e) small letter in sequence = Ca-Ca distance between proteins > 1.0 A

LAMBDA. Avgord

```

*****
AAAAAAAAA A'A'A'A'A' BBBBBBBBBBBBBBBB -----L1-----
FB4L E S V(L T Q)P(P(S A S G T)P)G(Q R V T I S C T G)T)S S N I G
3FAB @ s v L T Q P P S V S G A p g q R V T I S C T G S S S N I G a
RHE e s v(L T Q)P(P(S A S G T)P)G(Q R V T I S C T G)S)A T D I G
1 10 20 23 27 a b 29
*****
-L1-CCCCCCCCCCCC C'C'C'C'C'C'C'C' --L2--C"C"C"C"
FB4L S(I T V N W Y Q Q)L)P)G(M A(P K L)L(I Y)R D A(M R)P S)G V P
3FAB g N H V K W Y Q Q l p g t a P K L l i f h n n
RHE S(N S V I W Y Q Q)v p)g(k a(P K L)L(I Y)Y N D(L L)P S)G V S
30 35 40 50 59
*****
DDDDDDDDDD EEEEEEEEEEEE FFFFFFFFFFFFFFFF
FB4L T R(F S G S K S)G T(S A S L A I S)G L E A E D(E S D Y Y C A S
3FAB a R F S V S K S G S S A T L A I T g l Q A E D E A D Y Y C Q S
RHE D R(F S A S K S)G T(S A S L A I S)G L E S E D(E A D Y Y C A A
60 70 80 90
*****
L3-----GGGGGGGG HHHHHHHHHH -J1- LIGHT CONSTANT->
FB4L W N)S S D N(S Y V F G)T G(T K V T V L) G Q(P(K A N P T V T
3FAB Y D r s L R V F G g g T K L T V L r q
RHE W N)S l D(e P G F G)G G(T K L T V L) g
91 97 100 110
*****
    
```

residues included in average coordinates

 REI, MCPL, FBJL AND 2HFL are kappa-type

- a) residues between parentheses are included in beta-sheet based on backbone dihedral angles and hydrogen-bonding patterns
- b) letter repeats above sequences correspond to beta-sheet strands
- c) L1, L2, L3 correspond to hypervariable loops
- d) small letter in sequence = Ca-Ca distance between proteins > 1.0 A

KAPPA. Avgord

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*****
AAAAAAAAA A'A'A'A'A' BBBBBBBBBBBBBBBB -----L1-----
FBJL (E I V L T O S P)A(I T A A S)L)G(Q K V T I T C S A)S S V
REI d(I Q M T O S P)S(S L s a s)v)G(D R V T I T C Q A)S Q d I i
MCPL (d I V m T O S P)S(S L s v)s a g(e r V T M S C K S)S q s l l n s g n q
2HFL d I V L T Q S P A I M S A S p G E K V T M T C S A S S v
1 10 20 23 27 a b c d e f 29
*****
L1-CCCCCCCCCCCC C'C'C'C'C'C'C'C' --L2--C"C"C"C"
FBJL S(S L H W Y Q Q K)S)G(T S(P K P)W(I Y)E I(S K L A)S G V P
REI k(Y L N W Y Q Q T)p)G(K A P(K L)L(I Y)e a S(n l q)a)g v p
MCPL (k n(f L A W Y Q Q K)p)G(Q P(P K L L I Y)g A S(t r e)s)g v p
2HFL n y M Y W Y Q Q K s G T S P K R W I Y d t S K L A S g v P
30 35 40 50
*****
DDDDDDDDDD EEEEEEEEEEEE FFFFFFFFFFFFFFFF
FBJL A R(F S G S)G S)G T(S Y S L T I)N T M E A E D(A A I Y Y C Q Q
REI S R(F S G S)G S G T(D Y T F T I)S S l q p e D(i A T Y Y C Q Q)
MCPL D R(F T G S)G S G T(D F T L T I)S S v q a e D(l A V Y Y C Q n)
2HFL V R F S G S G S G T S Y S L T I S S M E T E D A A E Y Y C Q O
60 70 80 90
*****
L3-----GGGGGGGG HHHHHHHHHH -J1- LIGHT CONSTANT->
FBJL W T Y) P(l I T F G)A)G(T K L E L K) R
REI Y q (s l p y(t f g)q)G(T K l q i T)
MCPL d h (s y p l(t f g)a)G(T K L E l k) r
2HFL W g r n P T F G G G T K L E I K r
91 97 100 110
*****
    
```

residues included in average coordinates

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From Page No. 9AVB
SD
#100

Bond Lengths & Angles for KAPPA variable light

N-Ca	Ca-C	C=O	C-N	Ca-Cb	C-N-Ca	N-Ca-C	Ca-C=O	Ca-C-N	O=C-N	N-Ca-Cb	Cb-Ca
1.459	1.515	1.208	1.288	1.508	123.5	110.0	120.5	116.6	123.1	110.3	111.4
0.012	0.012	0.062	0.049	0.026	4.2	4.0	1.9	4.0	4.1	2.1	2.4
72	72	72	65	66	65	72	72	65	65	66	66

Bond Lengths & Angles for LAMBDA variable light

N-Ca	Ca-C	C=O	C-N	Ca-Cb	C-N-Ca	N-Ca-C	Ca-C=O	Ca-C-N	O=C-N	N-Ca-Cb	Cb-Ca
1.453	1.514	1.217	1.298	1.522	124.4	111.4	120.1	117.0	122.7	110.4	109.9
0.017	0.018	0.063	0.061	0.031	6.0	2.4	1.9	4.8	4.9	2.7	2.4
97	97	97	92	87	92	97	97	92	92	87	87

Bond Lengths & Angles for KAPPA & LAMBDA variable light

N-Ca	Ca-C	C=O	C-N	Ca-Cb	C-N-Ca	N-Ca-C	Ca-C=O	Ca-C-N	O=C-N	N-Ca-Cb	Cb-Ca
1.452	1.510	1.190	1.288	1.510	124.3	110.7	120.6	117.5	121.9	110.4	110.8
0.014	0.016	0.129	0.081	0.029	6.7	3.1	2.5	7.6	9.6	2.1	2.2
62	62	62	52	60	52	62	62	52	52	60	60

Average geom. for average coordinate files

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 FB4L, 3FAB and RHE are lambda-type REI, MCPL, FBJL AND 2HFL are kappa-type
 hll = human lambda light
 hkl = human kappa light

- a) residues between parentheses are included in beta-sheet based on backbone dihedral angles and hydrogen-bonding patterns
- b) letter repeats above sequences correspond to beta-sheet strands
- c) L1, L2, L3 correspond to hypervariable loops
- d) @ first residue is PCA = pyroglutamyl
- e) small letter in sequence = Ca-Ca distance between proteins > 1.0 A

 AAAAAAAAAA A'A'A'A'A'A'BBBBBBBBBBBBBBBBB -----L1-----
 FB4L E S V(L T Q) P)P(S A S G T)P)G(Q R V T I S C T G)T)S S N I G
 3FAB @ s v L T Q P P S V S G A p g q R V T I S C T G S S N I G a
 RHE e s v(L T Q) P)P(S A S G T)P)G(Q R V T I S C T G)S)A T D I G
 REI d(i(q M T Q s p)S(s l s a s)v)G(d R V T I T C Q A)s q d i i
 MCPL (d i(v M T Q s p)S(s l s v)s a g(e(R V T M S C k S)s q s l l n s g n q
 FBJL (e i(v l T Q s p)A(i t a A S)L)G(Q K V T I T C S A)s s s v
 2HFL d i v L T Q s p A i m s a S P G E K V T M T C S A s s s v
 1 10 20 23 27 a b 29
 con D I V M T Q S P S S L S V S P G E R V T I S C R A S Q S LLSSV D G
 hllI @ S V L T Q - P P S A S G T P G Q R V T I S C S G S S S N I I G
 hllII @ S A L T Q - P A S V S G S P G Q S I T I S C T G T S S D V G G
 hllIII S Y E L T Q - P P S V S V S P G Q T A R I T C S G D A L G
 hllVI N F M L T Q - P H S V S E S P G K T V T I S C T x s x G S D S I A
 hklI D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q S V xxS D I
 S
 hklII D I V M T Q S P L S L P V T P G E P A S I S C R S S Q LLHS x D G
 hklIII E I V L T Q S P G T L S L S P G E R A T L S C R A S Q S V S
 hklIV D I V M T Q S P D S L A V S L G E R A T I N C K S S Q SVLYS S N N

-----L1-----CCCCCCCCCCCCCCCC C'C'C'C'C'C'C'C'-----L2-----C"C"C"C"
 FB4L S(I T(V N W Y Q Q L)P)G(M A(P K L)L(I Y)R D A(M R)P S)G V P
 3FAB g N H V K W Y Q Q l p g t a P K L l i f h n n
 RHE S(N S(V I W Y Q q)v p)g(k a(p K L)L(I Y)Y N D(L L)P S)G V S
 REI k(y L N W Y Q Q t)p)g(k A P(K L)L(I Y)E A S(N L q)a)G V P
 MCPL (k n(f l A W Y Q Q k)p)g(q P(P K L L I Y)G A S(T r e)s)g V P
 FBJL S(s L H W Y Q Q k)s)g(t s(P K P)W(I)Y)e i(S(K l a)s g v P
 2HFL n Y M Y W Y Q Q k s g t S P K R W I Y D T S K l a s g V P
 30 35 40 50 59
 con S N Y L A W Y Q Q K P G Q S P K L L I Y G A S N L A S G V P
 S
 hllI S N Y V x W Y Q Q L P G T A P K L L I Y S N N Q R P S G V P
 hllII Y N Y V S W Y Q Q H P G K A P K L x I Y D V S x R P S G V x
 hllIII EK Y V Y W Y Q Q K P G Q A P V L V I Y E D S K R P S G I P
 hllVI S x Y V Q W Y Q Q R P G S A P T T V I Y E D N Q R P S G V P
 hklI S S Y L N W Y Q Q K P G K A P K L L I Y x A S S L E S G V P
 A
 hklII N N Y L N W Y L Q K P G Q S P Q L L I Y L G S N R A S G V P
 D
 hklIII S S Y L A W Y Q Q K P G Q A P R L L I Y G A S S R A T G I P
 hklIV K N Y L A W Y Q Q K P G Q P P K L L I Y W A S T R E S G V P

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Witnessed & Understood by me,	Date	Invented by	Date
		Recorded by	

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```

          DDDDDDDDDDD      EEEEEEEEEEEEE      FFFFFFFFFFFFFFFF
FB4L    T R(F S G S K S)G T(S A S L A I S)G L E A E D(E S D Y Y C A S
3FAB    a R F S V S K S G S S A T L A I T g l Q A E D E A D Y Y C Q S
RHE     D R(F S A S K S)G T(S A S L A I S)G L E S E D(E A D Y Y C A A
REI     S R(F S G S)G s g T(D Y T F T I)S S L q p e d(i(A T Y Y C Q Q)
MCPL    D R(F T G S)g s g t(D F T L T I)S S V Q A E D(l(A V Y Y C Q n)
FBJL    A R(F S G S)G s)g T(S Y S L T I)N T M E A E d(a A I Y Y C Q Q
2HFL    V R F S G S g s g T S Y S L T I S S M E T E D A A E Y Y C Q Q
        60                70                80                90
con     A R F S G S G S G T D F T L T I S S V E A E D A A T Y Y C Q Q
hllI    D R F S G S K S G T S A S L A I S G L Q S E D E A D Y Y C A T
hllIII  D R F S G S K S G N T A S L T I S G L Q A E D E A D Y Y C S S

```

```

hllIIII E R F S G S N S G T T A T L T I S G V Q A x D E A D Y Y C Q A
hllVI   D R F S G S S S N S A S L T I S G L K T E D E Q D Y Y C Q S Y
hklI    S R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q
hklII   D R F S G S G S G T D F T L T I S R V E A E D V G V Y Y C M Q
hklIIII D R F S G S G S G T D F T L T I S R L E P E D F A V Y Y C Q Q
hklIV   D R F S G S G S G T D F T L T I S S L Q A E D V A V Y Y C Q Q

```

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*****
-----L3-----GGGGGGGG      HHHHHHHHHHH      -J1- LIGHT CONSTANT->
FB4L    W N)S S D N(S Y V F G)T G(T K V T V L)      G Q(P(K A N P T V T
3FAB    Y D      r s L R V F G g g T K L T V L      r q
RHE     W N)d s l D(e P G F G)G G(T K L T V L)      g
REI     y q      (s l p Y(t F G)q g(T K L q i t)
MCPL    d)h      (s y p l(t F g)a G(T K L E i k)      r
FBJL    w t y)   p(l I T F G)a G(T K L E L K)      r
2HFL    w        g r N P T F G G G T K L e i K      r

```

```

        91                97                100                110
con     W N S N P S G D S W T F G G G T K L E I L      K R P
        S
hllI    W D D S L D G P V F G G G T K x T V L      G Q P
hllIII  Y A G S x x x V V F G G G T K L T V L      G Q P
hllIIII W D S x T x x V V F G G G T K L T V L      G Q P
hllVI   D S N N x      W V F G G G T K L T V L      G Q P
hklI    Y N S L P x x Y D Y T F G Q G T K V E I K      R T
hklIII  A L Q x P      Y T F G Q G T K x E I K      R T
hklIIII Y G S S P P      Y T F G Q G T K V E I K      R T
hklIV   Y Y S T P      x T F G Q G T K x E I K      R T

```

hllI = human lambda light subgroup I
hklI = human kappa light subgroup I

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Loop 12-15 Superimpose NC&C on KAPPA. Avoided
 using Res 10, 11, 16, 17

	RMC NC&C	
2HFL	0.307	Use HFL
1FBJ	0.282	
2MCP	0.283	
1REI(A)	0.201	

Loop 39 Res 37, 38, 40, 41 NC&C

	RMS	
2HFL	0.373	
1FBJ	0.209	
2MCP	0.151	(44, 45, 47, 48) Use MCP
1REI(A)	0.171	(38, 39, 41, 42)

Loop 77-80 Res 75, 76, 81, 82 NC&C

	RMS	
1FBJ	0.168	(75, 76, 81, 82)
2MCP	0.386	(82, 83, 88, 89)
2HFL	0.334	(75, 76, 81, 82)
1REI(A)	0.359	(A76, A77, A82, A83) Use REI(A)
1F19	0.486	(76, 77, 82, 83)

Res 105-110

Use REI

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Leonard Preita

Date

1-20-90

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CDR1 res 25-33 Kabat 24-34 Chothia/Lesk 26-32

res 23, 24, 35, 36 NCaC

	RMS	#AA
1F19	0.317	11
2HFM	0.169	11
1REI(A)	0.123	11

use REI(A)

68/72 Kabat seqs.
have CDR1 = 11 res
for subgroup I
human

2HFL	10
1FBJ	10

file: kappa.pdbcdr1

CDR2 res 49-57 Kabat 50-56 Chothia/Lesk 50-52

res 48, 49, 58, 60 NCaC

	RMS	
1FBJ	0.170	47, 48, 58, 59
2HFL	0.209	
1REI(A)	0.238	(A48, A49, A59, A60)
1F19	0.343	(48, 49, 59, 60)
2MCP	0.187	(54, 55, 65, 66)

use HFL

All Kabat seqs.
human hobe
CDR2 = 7 res

file: kappa.pdbcdr12

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Leonard Presta

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CDR3 res 91-98 Kabat 89-97 Chothia/Lesk 91-96

res ~~89,90,99,100~~ NCAC
90,91,101,102

	RMS		
1FI9	0.294	(90,91,101,102)	
1FBT	0.225	(89,90,100,101)	
2MCP	0.501	(96,97,107,108)	0.242 (96,107,108)
3HFM	0.285	(90,91,101,102)	
1REI(A)	0.154	(A90,A91,A101,A102)	use REI(A)
2HFL	0.239	(89,90,99,100)	

file : kappa.pdbcdr123

Human Subgroup	#res in CDR3 (Kabat)	89-97
I	9	30/32
II	9	7/7
III	9	18/20
IV	9	2/3

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Consensus kappa and VH

Oriented VL-VH domains on those of 1FB4

	1FB4	1FBJ	2HFL	2MCP	3FAB	3HFM	1F19
VH	18-25	S	S	18-25	18-25	18-25	S
	34-39	A	A	34-39	34-39	34-39	A
	46-52	M	M	46-52	46-52	46-52	M
	57-61	E	E	59-63	56-60	56-60	E
	68-71	F	F	70-73	67-70	67-70	F
	78-84	B	B	80-86	77-83	77-83	B
	92-99	4	4	94-101	91-98	91-98	4
VL	18-24	19-25	S	19-25	18-24	19-25	S
	32-37	32-37	A	39-44	32-37	33-38	A
	60-66	60-66	M	67-73	53-66	61-67	M
	69-74	69-74	F	76-81	69-74	70-75	F
	84-88	84-88	J	91-95	84-88	85-89	J
RMS Ca	0.729	1.01	0.834	0.944	0.868	1.180	

3HFM on 1FB4 VH 135 atoms
 Rms 0.72 Å

VL-VH 228 atoms
 Rms 0.853

Hfm on Hfl VL-VH 0.853 228 atoms
 VL 0.47 93
 VH 0.94

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Kabat #A	FB4	HFL	res #A		() long distance or poor geom.					
			FBJ	MCP	HFM	FI9	REI	RHE	FAB	
Q6NEZ	081T10Z	6,103	-	(6,101)	(6,108)	-	-	6,86	6,105	6,103
Q6NEZ	0 Y86	6,85	(6,85)	6,85	6,92	6,86	-	6,86	6,87	6,85
R61Nx	08x DP2	60,81	60,81	60,81	67,88	61,82	61,82	61,82	62,83	-
R61Nx	08x E81	60,80	60,80	60,80	67,87	-	-	-	-	-
C88N	0E1 Q6	87,6	87,6	(87,6)	94,6	-	-	(88,6)	(89,6)	(87,6)
G101N	0E1 Q6	(102,6)	99,6	100,6	(107,6)	101,6	-	-	(104,6)	-
T10Z081	0 P8	-	100,8	101,8	108,8	102,8	102,8	102,8	105,7	103,7
S708	081T22		(7,22)		7,22					
T14081	0E1 Q17	13,16			(14,17)			14,17	13,16	
T20081	0 V19		(20,19)	20,19	20,19			(20,19)		
Y360H	081 N34	35,33								
Y360H	0E1 Q89		35,88			36,89	36,89			
Q38NEZ	0 Q42				44,48	38,42			39,43	
K39NZ	0 E81			38,80	45,87	39,81				
R54NE	0 F82	(53,61)			60,68					
E79N	S8 m78		(78,77)	78,77						
E81N	081 T80		(80,79)			(81,80)				
@ Y860H	0E1 Q37		85,36	85,36	92,43		86,37			
Y860H	0 D82					86,82	(86,82)	86,82	87,83	85,81
* Q37NEZ	0H Y86	36,85						(37,86)	38,87	36,85
Q89NEZ	0H Y36			(88,35)	95,42			89,36		88,35
T97081	0E1 Q90			96,89	103,96	97,90	97,90			
T97081	0 I2				103,2	97,2		97,2		
Q90NEZ	081 T97							90,97		

* kappa only
@ lambda only

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<sequence of HuLys, unpublished, Foote and Winter>
 DIQMTQSPSSLSASVGDVRTITCRASGNIHNYLAWYQOKPGKAPKLLIYYTTTLADGVPS
 RFSGSGSGTDFTFITISSLQPEDATYYCQHFWSPTPRTFGQGTKVEIKR

<Fri Feb 16 08:54:28 1990
 <first sequence: /va/Biocat/presta/igg/pl.HuLys (length = 108)
 <second sequence: /va/Biocat/presta/igg/pl.humki (length = 109)
 <90 matches in an overlap of 108: 83.33 percent similarity
 <gaps in first sequence: 0, gaps in second sequence: 0
 <score: 455 (Dayhoff PAM 250 matrix, gap penalty = 8 + 4 per residue)
 <endgaps not penalized

	10	20	30	40	50
HuLys	DIQMTQSPSSLSASVGDVRTITCRASGNIHNYLAWYQOKPGKAPKLLIYY				
	***** * ** *****				
humki	DIQMTQSPSSLSASVGDVRTITCRASQDISSYLNWYQOKPGKAPKLLIYA				
	10	20	30	40	50
	60	70	80	90	100
HuLys	TTTLADGVPSRFSGSGSGTDFTFITISSLQPEDATYYCQHFWSPTPRTFGQ				
	... * ***** * ** *****				
humki	ASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQYNSLPYTFGQ				
	60	70	80	90	100

HuLys GTKVEIKR

 humki GTKVEIKRT

50 iterations:

12	17	27	21	23	13	12	12	21	18
16	20	12	8	11	16	12	16	14	7
21	6	31	26	11	19	19	17	26	16
17	23	24	36	13	32	12	20	18	8
16	25	14	18	14	9	26	12	18	25

 mean = 17.60, std dev = 6.69, z-score = 65.40

Residues in Kappahum I altered for HuLys

CDR1	Q27 Y		
	D28 N	Asn conf	-158,3 (1REI)
	S30 H	His conf	-69,69
	S31 N		
	N34 A		
CDR2	A50 Y	Tyr conf	-167, -86 (1FI9)
	AS1 T	Thr conf	-57
	S52 T	" "	-169
	S53 T	" "	-61

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CDR3	E55A	
	S56D	altered conf K45 to hbond to D56
	L73F	
	F83I	the conf -55, -174 (IREI)
	Q90H	
	Y91F	
	N92W	
	L94T	
Y96R		

Files: NULYS. PDBN1590 backbone = KappahumI H90
 NULYS. PDBG1N90 " " Q90
 NULYS. PDBMCPDR3 CDR3 backbone taken from 2MCP where res 90 is Asn

For purposes of creating a framework human kappa I Va for general use as a construct for inserting new CDRs, the following NULYS residues should be altered:

G27Q	Gln in human kappa subgroups I-IV
F73L	Leu " " " "
I83F	Phe in human kappa subgroups I & III
	Val " " " " II & IV
H90Q	Gln in " " " " I-IV

ASSE } may not be necessary
 D56S }

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Kappahum I. PDB converted to 4DS VL (kappa)

Residues Changed

Q 3 V	CDR3	S 93 T
P 8 H		L 94 T
S 9 K		Y 96 P
S 10 F		Q 100 H
L 11 M		

A 13 T

T 20 S

R 24 K

I 29 V

CDR1 S 30 N

S 31 T

Y 32 A

W 33 V

K 42 H

A 43 S

A 50 S

S 53 F

L 54 R

CDR2 E 55 Y

S 56 T

S 60 D

S 63 T

S 65 N

Y 66 R

L 73 F

L 78 V

P 80 A

F 83 L

T 85 V

Y 91 H

N 92 Y

HER2.KAP1

R54-P59 from 2MCP (kappa)
R66-F71 from 2FB4 (λ)

HER2.KAP2

R54-P59 from 2MCP (kappa)
~~CDR1~~ R66-F71 from 2FB4 (λ)

CDR1 moved to accommodate R66

HER2.KAP3

• KAP2 + new conf for residues Y49, F53, Y55

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2-19-90

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In kappa structures 1REI, 2MCP, 1FBJ, 2HFL & 3HFM the peptide bond between S7-P8 is cis. In 1F19 and 4D5 res 8 is T or H (not P). Therefore the backbone of 1F19 from residues 7-~~19~~¹⁹ was taken from 1F19.

Formation of VL-VH dimer

VL file	VH file	filename	Comments
NER2LV.KAP2	NER2HV.MCP	Dimer.kap2mcp	
NER2LV.KAP2	NER2HV.MCP	Dimer.kap2mcpnew	bone 7-10 altered
"	"	Dimer.kap2mcpnew2	bone 7-10 altered & His 91 @ -60°
NER2LV.KAP3	NER2HV.MCP	Dimer.kap3mcp	
NER2LV.KAP2	NER2HV.PRC2	Dimer.kap2prc	
NER2LV.KAP2	NER2HV.model	Dimer.kap2mod	
NER2LV.KAP3	NER2HV.model	Dimer.kap3mod	

⊕ Protonation states of His residues

VL His 8 ⊕
 His 42 ⊕
 His 91 ~~NEH~~ NEH
 VH His 35 NEH

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2-20-90

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Dennis and Paul,
here are the human consensus sequences and the proposed
humanized 4D5 sequences.

VARIABLE LIGHT
HuLys has 83% similarity to human kappa subgroup I even when the
CDR sequences are included. The sequences inside the CDR boxes
(Chothia/Lesk definition) can be taken from HuLys or humkapI --
those outside the boxes should be taken from humkapI.

(Kabat/Wu CDR in capital letters; Chothia/Lesk CDR in boxes)

1 10
humkapI asp ile gln met thr gln ser pro ser ser leu ser ala ser val gly
HuLys

20 30
humkapI asp arg val thr ile thr cys ARG ALA SER GLN ASP ILE SER SER TYR
HuLys GLY ASN HIS ASN

40
humkapI LEU ASN trp tyr gln gln lys pro gly lys ala pro lys leu leu ile
HuLys ALA

50 60
humkapI tyr ALA ALA SER SER LEU GLU SER gly val pro ser arg phe ser gly
HuLys TYR THR THR THR ALA ASP

70 80
humkapI ser gly ser gly thr asp phe thr leu thr ile ser ser leu gln pro
HuLys phe

90
humkapI glu asp phe ala thr tyr tyr cys GLN GLN TYR ASN SER LEU PRO TYR
HuLys ile HIS PHE TRP THR ARG

100
humkapI THR phe gly gln gly thr lys val glu ile lys arg thr
HuLys

VARIABLE HEAVY
The sequences inside the CDR boxes (Chothia/Lesk definition) can be taken
from KOL or humIII -- those outside the boxes should be taken from humIII.

(Kabat/Wu CDR in capital letters; Chothia/Lesk CDR between bars)

1 10
humiii glu val gln leu val glu ser gly gly gly leu val gln pro gly gly
kol gln val arg

20 30
humiii ser leu arg leu ser cys ala ala ser GLY PHE THR PHE SER ASP TYR
kol ser ser ILE SER

40
humiii ALA MET SER trp val arg gln ala pro gly lys gly leu glu trp val
kol TYR

50 52 52a 53 60
humiii ala VAL ILE SER GLU ASN GLY SER ASP THR TYR TYR ALA ASP SER VAL
kol ILE TRP ASP ASP GLN HIS

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humiii LYS GLY arg phe thr ile ser arg asp asp ser lys asn thr leu tyr
kol asn phe

80 82 82a 82b 82c 83 90
humiii leu gln met asn ser leu arg ala glu asp thr ala val tyr tyr cys
kol asp pro gly phe

humiii	ala arg ASP	ARG GLY GLY ALA VAL SER TYR GLY PHE PHE GLY TYR GLY	100 a b c d e f g h
kol		GLY HIS GLY PHE CYS SER SER ALA SER CYS PHE GLY	

humiii	i j k 101	VAL trp gly gln gly thr leu val thr val ser ser	110
kol	GLY PHE PHE ASP	TYR	pro

The following are proposed humanized 4D5 sequences; changes in Hum4D5b and Hum4D5c from Hum4D5a are followed by an asterisk

V_L

humkapI	1	asp ile gln met thr gln ser pro ser ser leu ser ala ser val gly	10
Hum4D5a			
Hum4D5b			
Hum4D5c			

humkapI	20	asp arg val thr ile thr cys ARG ALA	SER GLN ASP ILE SER SER TYR	30
Hum4D5a			VAL ASN THR ALA	
Hum4D5b			VAL ASN THR ALA	
Hum4D5c			VAL ASN THR ALA	

humkapI	40	LEU ASN trp tyr gln gln lys pro gly lys ala pro lys leu leu ile
Hum4D5a		VAL ALA
Hum4D5b		VAL ALA
Hum4D5c		VAL ALA

humkapI	50	tyr ALA ALA SER	SER LEU GLU SER gly val pro ser arg phe ser gly	60
Hum4D5a		SER	PHE	
Hum4D5b		SER	PHE	
Hum4D5c		SER	PHE TYR*	

humkapI	70	ser gly ser gly thr asp phe thr leu thr ile ser ser leu gln pro	80
Hum4D5a		arg	
Hum4D5b		gly*	
Hum4D5c		arg	

humkapI	90	glu asp phe ala thr tyr tyr cys GLN GLN	TYR ASN SER LEU PRO TYR
Hum4D5a			HIS TYR THR THR PRO
Hum4D5b			HIS TYR THR THR PRO
Hum4D5c			HIS TYR THR THR PRO

humkapI	100	THR phe gly gln gly thr lys val glu ile lys arg thr
Hum4D5a		
Hum4D5b		
Hum4D5c		

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VH

humiii	1	glu val gln leu val glu ser gly gly gly leu val gln pro gly gly	10
Hum4D5a			
Hum4D5b			
Hum4D5c			
humiii	20	ser leu arg leu ser cys ala ala ser	30
Hum4D5a			GLY PHE THR PHE SER ASP TYR
Hum4D5b			ASN ILE LYS THR
Hum4D5c			ASN ILE LYS THR
humiii	40	ALA MET SER trp val arg gln ala pro gly lys gly leu glu trp val	
Hum4D5a		TYR ILE HIS	
Hum4D5b		TYR ILE HIS	
Hum4D5c		TYR ILE HIS	
humiii	50	ala VAL ILE SER GLU ASN GLY SER	60
Hum4D5a		ARG TRP TYR PRO THR ASN GLY TYR	ASP THR TYR TYR ALA ASP SER VAL
Hum4D5b		ARG TYR PRO THR ASN GLY TYR	ARG
Hum4D5c		ARG TYR PRO THR ASN GLY TYR	ARG
humiii	70	LYS GLY arg phe thr ile ser arg asp asp ser lys asn thr leu tyr	
Hum4D5a			ala thr ala
Hum4D5b			ala thr leu*
Hum4D5c			ala thr ala
humiii	80	leu gln met asn ser leu arg ala glu asp thr ala val tyr tyr cys	90
Hum4D5a			
Hum4D5b			
Hum4D5c			
humiii	100	ala arg ASP ARG GLY GLY ALA VAL SER TYR GLY ASP VAL trp gly gln	
Hum4D5a		ser TRP GLY GLY ASP GLY PHE TYR ALA MET ASP	
Hum4D5b		ser TRP GLY GLY ASP GLY PHE TYR ALA MET ASP	
Hum4D5c		ser TRP GLY GLY ASP GLY PHE TYR ALA MET ASP TYR*	
humiii		gly thr leu val thr val ser ser	
Hum4D5a			
Hum4D5b			
Hum4D5c			

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V_L 4D5

- (1) Res 66 is Gly in human and mouse kappa sequences but is non-Gly in lambda sequences. Mouse 4D5 has an Arg at 66 though it is otherwise a kappa sequence. The sidechain at 66 should affect the conformations of CDR1, CDR2 and the hairpin turn at 68-69. Since kappa CDR1 should have a different canonical backbone conformation than lambda CDR1, the exact effect of Arg 66 cannot be deduced from available crystal structures. Hence the only difference between Hum 4D5a and Hum 4D5b V_L humanized sequences is Arg 66 versus Gly 66, respectively.
- (2) Although res 55 is part of the Kabat/Wu CDR2, it is not included in the Chothia/Lesk CDR2. From model-building, the 4D5 Tyr 55 sidechain may play one of two roles: stabilizing the conformation of V_H CDR3 or providing an interaction in the V_L-V_H interface. The latter function may be dependent on the presence of V_H Tyr 102.
- (3) Note that 4D5 Val 29 & Val 33 are smaller than consensus sequences of human kappa I and mouse kappa V where I 29 & L 33 provide buried interaction. Hence V_L CDR1 in 4D5 may have a CDR1 conformation different from those canonical conformations of Chothia/Lesk.

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From Page No. 25 V_H

- (1) Tyr 102 in 4D5 may function to stabilize V_H CDR3 or provide a V_L - V_H interface interaction in concert with V_L Tyr 55
- (2) The conformation of V_H CDR1 is dependent on interactions between CDR1 res 29 and sidechains of res 34, 71, 78 & 94.

	29	34	71	78	94
Hum III	F	M	R	L	R
mouse IIc	I	M	A	A	R
4D5	I	I	A	A	R

The presence of Ile at 29 & 34 as well as Ala at res 71 & 78 may affect the structure of CDR1. However in previous studies of Chothia/Lesk res 78 has not been considered. As a test of the importance of this residue on the conformation of V_H CDR1, sequence Hum 4D5b differs from Hum 4D5a by Leu 78 only (see page 24).

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Model	Energy 6000 cycles	Phelo	CDR3H	R66		
				NE	NH1	NH2
A4DSK2L	-1402	out	modeled	N300'	g680' N300'	T310Y1
A4DSK2LNE ^w * *	-1379	out	modeled	g680'	g680'	
A4DSK2M	-1404	in in	2MCP	g680'	g680' N300'	
A4DSK3M ©	-1398	out	2MCP	g680' N300'	g680' N300'	
A4DSK2P	-1381	out	2PRC	g680' N300'	g680' N300'	
A4DSK2MODA	-1413	in	2MCP	S500'	S520Y	T310' S500Y S500'
A4DSK2MODB	-1420	in	2MCP	T310Y1	S520Y	A510' S520Y S500'
A4DSK2MODC	-1419	in	2MCP	S520Y S500'	S520Y	N300' T310Y1
A4DSK2MODD	-1420	in	2MCP		T310Y1	S500' S520Y T310Y1
A4DSK2MODE	-1424	in	2MCP	S500'		N300' T310Y1

* A4DSK2LNEW = A4DSK2L after 3000 cycles + alter conformation F53-V58, Y49, F600 to restack

© A4DSK3M = A4DSK2M + new conformation for Y49, F53, Y55

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7-10-91

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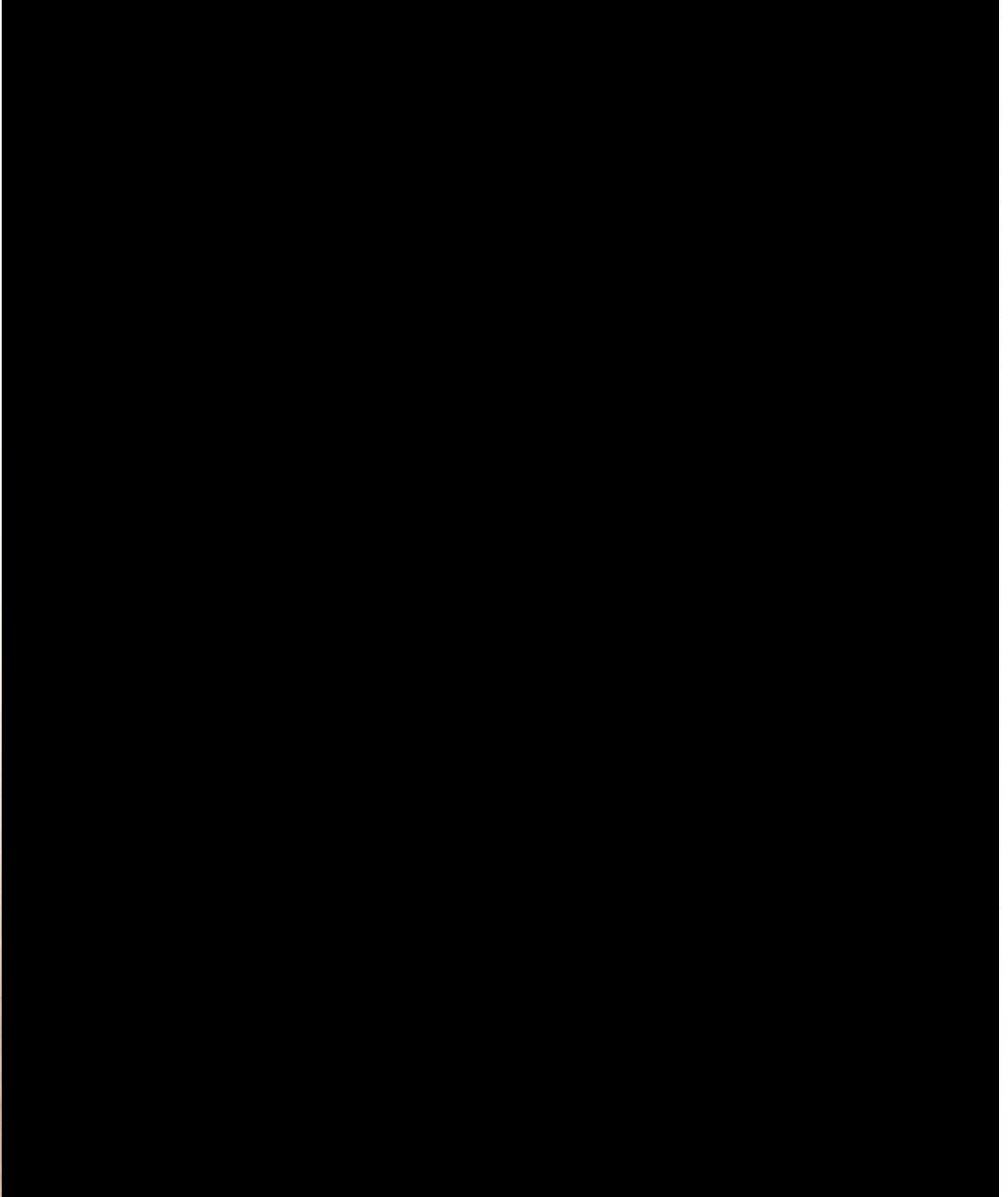
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8-13-91

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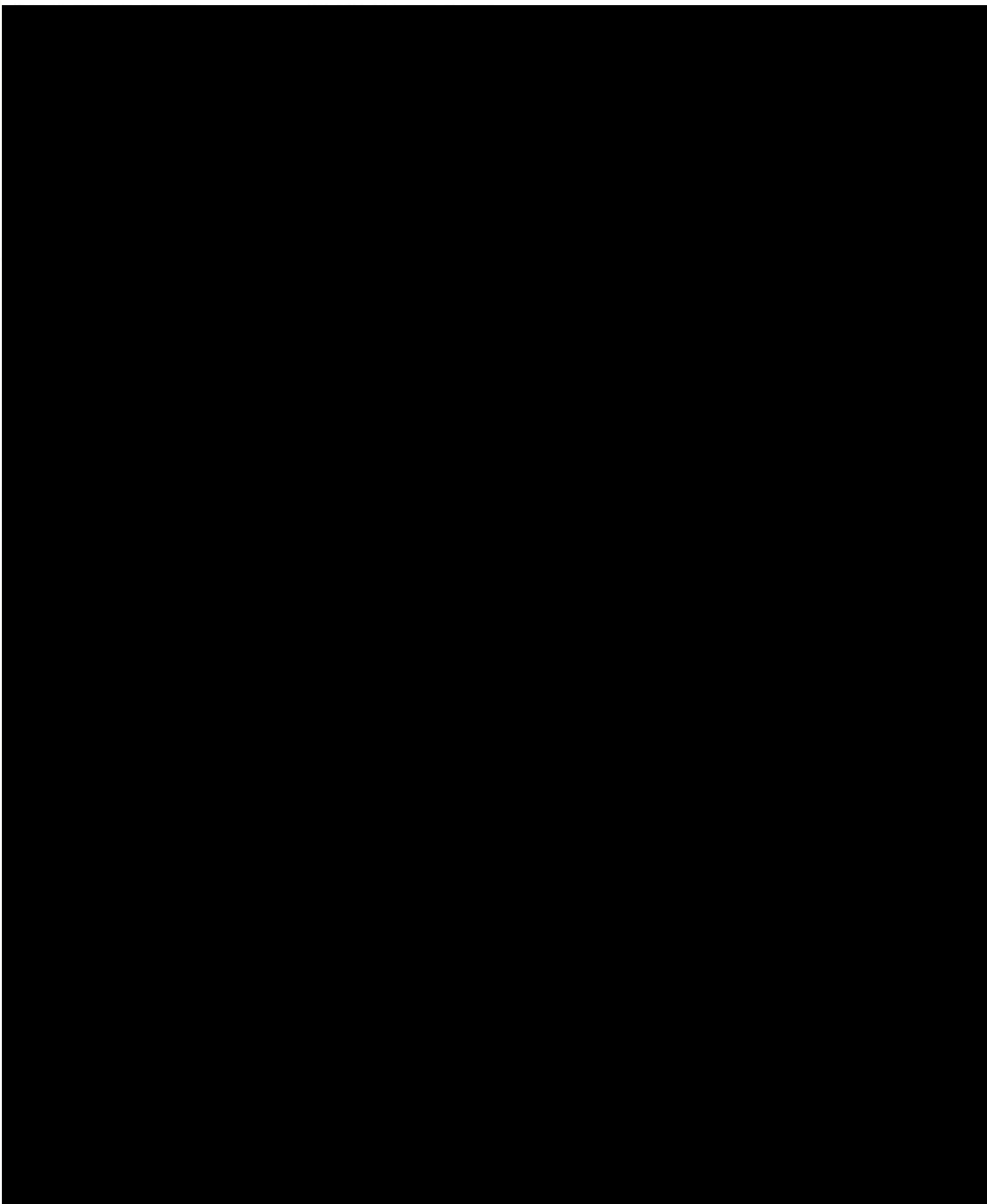
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