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(57) **ABSTRACT**

An altered antibody chain is produced in which the CDR's of the variable domain of the chain are derived from a first mammalian species. The framework-encoding regions of DNA encoding the variable domain of the first species are mutated so that the mutated framework-encoding regions encode a framework derived from a second different mammalian species. The or each constant domain of the antibody chain, if present, are also derived from the second mammalian species.

11 Claims, 33 Drawing Sheets

Fig. 1

*Hind*III

1 AAGCTTATGAATATGCAAATCCTCTGAATCTACATGGTAAATATAGGTTTGTCTA
60 ACAAACAGAAAAACATGAGATCACAGTTCTCTCTACAGTTACTGAGCACACAGGAC
-19 M G W S C I I L F L V A T A T
120 CCATGGGATGGAGCTGTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTAAGGGG
180 CAGTAGCAGGCTTGAGGTCTGGACATATATATGGGTGACAATGACATCCACTTTGC
-4 G V H S D I Q L T Q S P V S L S
240 CTCTCCACAGGTGTCCACTCCGACATCCAGCTGACCCAGTCTCCAGTTTCCCTGTC
CDR1
14 S L G E T V N I E C L A S E D I Y S D
300 TCTCTGGGAGAAACTGTCAACATCGAATGTCTAGCAAGTGAGGACATTTACAGTGA

Fig. 1A

34 A W Y Q Q K P G K S P Q L L I Y N T D CDR 2
360 GCATGGTATCAGCAGAAGCCAGGGAAATCTCCTCAACTCCTGATCTATAATACAGAT

54 L Q N G V P S R F S G S G S G T Q Y S
420 TTGCAAAATGGGGTCCCTTCACGGTTTAGTGGCAGTGGATCTGGCACACAGTATTCT

74 K I N S L Q S E D V A T Y F C Q Q Y N CDR 3
480 AAAATAAACAGCCTGCAATCTGAAGATGTCGCGACTTATTTCTGTCAACAATATAAC

94 Y P W T F G G G T K L E I K R
540 TATCCGTGGACGTTCCGGTGGAGGGACCAAGCTGGAGATCAAACGTGAGTAGAATTTA

*Bam*HI

600 TTTGCTTCCTCAGTTGGATCC

Fig. 2

-19 *Hind*III M G W S C
1 AAGCTTGGCTCTACAGTTACTGAGCACACAGGACCTCACCATGGGATGGAGCTC

-13 I L F L V A T A T G V H S D I Q M T C
59 ATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACTCCGACATCCAGATGACCCA
CD

8 P S S L S A S V G D R V T I T C K A S
119 CCAAGCAGCCTGAGCGCCAGCGTGGGTGACAGAGTGACCATCACCTGTAAAGCAA

28 N I D K Y L N W Y Q Q K P G K A P K I
179 AATATTGACAAATACTTAAACTGGTACCAGCAGAAGCCAGGTAAGGCTCCAAAGCT

CDR 2

48 I Y N T N N L Q T G V P S R F S G S C
239 ATCTACAATACAAACAATTTGCAAACGGGTGTGCCAAGCAGATTCAGCGGTAGCGC

68 G T D F T F T I S S L Q P E D I A T Y
299 GGTACCGACTTCACCTTCACCATCAGCAGCCTCCAGCCAGAGGACATCGCCACCTA

CDR 3

Fig. 2A

88 C L Q H I S R P R T F G Q G T K V E I K
359 TGCTTGCAGCATATAAGTAGGCCGCGCACGTTCCGGCCAAGGGACCAAGGTGGAAATCAA

108 R T V A A P S V F I F P P S D E Q L K S
419 CGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATC

128 G T A S V V C L L N N F Y P R E A K V Q
479 GGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACA

148 W K V D N A L Q S G N S Q E S V T E Q D
539 TGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGGA

168 S K D S T Y S L S S T L T L S K A D Y E
599 AGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGA

188 K H K V Y A C E V T H Q G L S S P V T K
659 AAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAA

208 S F N R G E C Trm *HindIII*
719 AGCTTCAACAGGGGAGAGTGTTAGAAGCTT

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