

First genomic sequence of a human Ig variable lambda gene belonging to subgroup III

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Submitted October 31, 1990

EMBL accession no. X56178

A cosmid clone C40.2 was isolated by screening the genomic Colo320HSR library (1), with a 375 base pair (bp) fragment (probe pVλ3RST0.36) from the p3C4λ5 cDNA clone (2). The C40.2 clone contains an immunoglobulin variable lambda gene, which was shown by sequencing to belong to subgroup III according to Chuchana *et al.* (3). This gene was designated as Vλ3.1, or IGLV3S1, since it represents the first genomic sequence of a VλIII subgroup gene. ('IGLV3' stands for 'human immunoglobulin lambda variable gene belonging to subgroup III'. 'IGLV3S1' stands for Vλ3.1 following the Human Gene Mapping recommendation (HGM9).) There are nine nucleotide differences, resulting in eight aminoacid changes, between the 3C4 and IGLV3S1 variable regions. Five of these aminoacid changes are located in the complementary determining regions. These differences most probably represent somatic mutations. Comparison of the IGLV3S1 sequence with those of the published lambda protein or cDNAs (for review, see ref. 3) shows that

the variable regions of 3C4 (2), SH (4) and BAK (5) proteins are encoded by the IGLV3S1 gene. Interestingly, it should be noted that the first serine residue of these VλIII mature proteins was missed, probably for technical reasons, in these previous sequences.

ACKNOWLEDGEMENT

We thank Dr. T.Watanabe for kindly providing the p3C4λ5 cDNA clone.

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ATG GCC TGG ACC CCT CTC TGG CTC ACT CTC CTC ACT CTT TGC ATA G|GTGCTGCCTCCAGGCTCAACCCATATATCATGCTAGCTGTGCCAACCTGGCCCTGAG 104
M A W T P L W L T L L T L C I

CTTCGGCTCAACACAGGGAGTAGTGTAGGGTGTGGACTCTAGCGTGAAACCCCTATCTCACTCTCTGTCTCTTTGCA|GT TCT GTG GTT TCT TCT GAG CTG ACT 215
G S V V S S E L T

CAG GAC CCT GCT GTG TCT GTG GCC TTG GGA CAG ACA GTC AGG ATC ACA TGC CAA GGA GAC AGC CTC AGA AGC TAT TAT GCA AGC TGG TACKpnI 305
Q D P A V S V A L G Q T V R I T C Q G D S L R S Y Y A S W Y

CAG CAG AAG CCA GGA CAG GCC CCT GTA CTT GTC ATC TAT GGT AAA AAC AAC CGG CCC TCA GGG ATC CCA GAC CGA TTC TCT GGC TCC AGCBamHI 395
Q Q K P G Q A P V L V I Y G K N N R P S G I P D R F S G S S

TCA GGA AAC ACA GCT TCC TTG ACC ATC ACT GGG GCT CAG GCG GAA GAT GAG GCT GAC TAT TAC TGT AAC TCC CGG GAC AGC AGT GGT AAC 485
S G N T A S L T I T G A Q A E D E A D Y Y C N S R D S S G N

CAT CTACAGTGCACAGACAGATGGGAAGTGAGACAGAAACCCTTCACTATCTGTGTCATCCTCTCTCCAGGCCAGGACTGTGAACAAAGCCATAAACAGGGTGGCC 603
H

AGTTCACTGCATCTGAGACCTCCAGGTGCCTTT 637

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Figure 1. Sequence of the IGLV3S1 gene. Splicing sites are indicated by arrows. The heptamer-nonamer recombination signal sequences are boxed and the cysteines, involved in the intrachain disulfide bond, are circled. A vertical line locates the end of the peptide leader and the beginning of the mature protein.

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