

BRIEF COMMUNICATION

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New alleles of human immunoglobulin κ J segments *IGKJ2* and *IGKJ4*

Received: 1 October 1999 / Revised: 30 December 1999

Key words Immunoglobulin · J segments · *IGKJ* genes · Alleles · Human

During the course of sequencing rearranged κ VJ regions from many individuals, we discovered one individual with an apparently new J-segment sequence polymorphism in *IGKJ2* and another individual with an apparently new *IGKJ4* allele. Since these changes were near the junction, we wished to confirm that the apparent polymorphisms were truly new alleles, and not due to N nucleotide addition, or somatic hypermutation. Primers were therefore designed to amplify the genomic unrearranged *IGKJ* genes from these two individuals. Amplified products were cloned and sequenced. The upstream primers were *J κ 2* (5'-AGT-CAAGCTTGAGAATTGATTGCAC) and *J κ 4* (5'-GAATAAGCTTGGTCACCCAGAAGT). These were used with the previously described primers AF80, which is complementary to the 3' half of *IGKJ1* and *IGKJ4* segments, and with the *J κ 2* primer, which is in

the identical location to AF80, but is an exact match to *IGKJ2* (Feeney et al. 1996, 1997). PCR conditions were as previously described (Feeney et al. 1996).

The *IGKJ4b* allele described here has one silent change from the published *IGKJ4* allele (called *IGKJ4a* here) (Hieter et al. 1982), as shown in Fig. 1. A total of 169 bp was sequenced, including 114 bp 5' of the RSS, the RSS, and 16 bp of the *IGKJ4* coding region up to the primer location, and all other positions were identical. A search of GenBank revealed only three entries which have this change (AF103571, Z85931, and L26899). Rearranged κ regions containing *IGKJ4* genes from 24 individuals have been sequenced, and only one individual has been encountered who ap-

Fig. 1 New alleles of *IGKJ2* (*IGKJ2c*, GenBank AF189007) and *IGKJ4* (*IGKJ4c*, GenBank AF189008) are compared to the published alleles, and to another newly described allele *IGKJ2b* (Fischer et al. 1997)

	Nonamer	Spacer	Heptamer	<i>IGKJ</i> coding region					
<i>IGKJ4a</i>	GGTTTTTGT	TGAGGGGAAAGGGTGAGATCCCT	CACTGTG	G	CTC	ACT	TTC	GGC	GGA
<i>IGKJ4b</i>	-----	-----	-----	-	-	-	-	-	-
<i>IGKJ2a</i>	AGTTTTTGT	ATAGGAGGAAGTTAAGAGGAAC	CATTGTG	TG	TAC	ACT	TTT	GGC	CAG
<i>IGKJ2b</i>	-----	-----	-----	-	-	-	-	-	-
<i>IGKJ2c</i>	-----	-----	-----	-	-	-	-	-	-

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parently has this allele. Since the RSS has been sequenced, and it is identical to that of the published *IGKJ4*, the low frequency of this allele in the analysis of rearranged sequences and in GenBank is not directly attributable to an atypical RSS, but is more likely to be due to the paucity of the allele in the general population.

The *IGKJ2c* allele has two changes from the published *IGKJ2* allele (called *IGKJ2a* here) (Hieter et al. 1982), and one change from a recently published allele of *IGKJ2* (called *IGKJ2b*) (Fischer et al. 1997), from a total of 167 bp of coding and flanking sequence (Fig. 1). The change shared with the previously published *IGKJ2b* allele is a C to G change in the second codon resulting in a Thr to Ser coding region change. The additional unique change in *IGKJ2c*, absent from *IGKJ2a* or *IGKJ2b*, is in the first codon, and is an A to C substitution, resulting in a Tyr to Cys change. A search of GenBank showed eight independent sequences with this allele (HUMIKCCR, HSG21KAP, AF103434, HSA223701, HSU95246, HSIKGLV52, HUMFRAJ, AF044457), and all were derived from mRNA or were productive rearrangements from DNA. Thus, the cysteine encoded here apparently seems compatible with expression of a functional κ protein. Rearranged *IGKJ2* genes from 12 individuals have been sequenced, and this allele has been found in only one individual.

Thus, these data document one new allele each of the human immunoglobulin J segments *IGKJ2* and

IGKJ4, each of which is present at low frequency in the general population.

Acknowledgements This work was supported by NIH grant AI37098. DNA samples came from the Scripps General Clinical Research Center, which is supported by NIH grant M01RR00833. This is manuscript number 12727-IMM from The Scripps Research Institute. Guia Escuro's excellent technical support is gratefully acknowledged.

References

- Feeney AJ, Atkinson MJ, Cowan MJ, Escuro G, Lugo G (1996) A defective $V_{\kappa}A2$ allele in Navajos which may play a role in increased susceptibility to *Haemophilus influenzae* type b disease. *J Clin Invest* 97:2277-2282
- Feeney AJ, Lugo G, Escuro G (1997) Human cord blood κ repertoire. *J Immunol* 58:3761-3768
- Fischer M, Klein U, Kuppers R (1997) Molecular single-cell analysis reveals that CD5-positive peripheral blood B cells in healthy humans are characterized by rearranged V_{κ} genes lacking somatic mutation. *J Clin Invest* 100:1667-1676
- Hieter PA, Maizel JJV, Leder P (1982) Evolution of human immunoglobulin κ J region genes. *J Biol Chem* 257:1516-1522