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Duplication of primate and rodent B7-H3 immunoglobulin V- and C-like domains: divergent history of functional redundancy and exon loss

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Abstract

B7-H3 is a novel protein structurally related to the B7 family of ligands by the presence of a single set of immunoglobulin-V-like and immunoglobulin-C-like (VC) domains. By multiplex PCR, the dominantly expressed form of human B7-H3 was found to be a splice variant containing tandemly duplicated VC domains (VCVC). In contrast, mouse B7-H3 cDNA contained only one single VC form due to an exon structure corresponding to Vâ€“(pseudoexon C)â€“(pseudoexon V)â€“C. Comparisons of human, monkey, mouse, and hamster genomic *B7-H3* reveal that primates, but not rodents, exhibited a higher

degree of intramolecular sequence similarity between VC duplications than between molecules. Both VC and VCVC forms of human B7-H3 inhibited $CD4^+$ T cell proliferation and downregulated cytokine production upon TCR activation. These results suggest independent, but convergent, paths of B7-H3 active domain duplication followed by divergent histories of exon degeneration in rodents and exon maintenance by humans.

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Keywords

B7; Costimulation; Immune modulation; Immunoglobulin variable domain

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