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Exceptionally long CDR3H of bovine scFv antigenized with BoHV-1 B-epitope generates specific immune response against the targeted epitope

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Some bovine antibodies are the largest known to exist in a species because of an exceptionally long CDR3H (up to 61 amino acids). The exceptionally long CDR3H is encoded by an unusually long germline *IGHD* genes together with insertion of “a” nucleotide rich conserved short nucleotide sequence at the *IGHV-IGHD* junction. The atypical CDR3H confers unique “knob and stalk” structural architecture where configurational diversity of the knob is generated by variable intra-CDR3H disulfide bridges. The knob is separated by solvent exposed stalk formed by anti-parallel beta strands. Structural features of the bovine antibody with an exceptionally long CDR3H can be exploited for the development of new therapeutics, vaccines and drugs. In this context, I will discuss structural optimization of bovine scFvs to enhance viral neutralization potency. An evidence for subtle influence of framework residues on viral neutralization functions will be presented. I will discuss our recent data on bovine scFv with exceptionally long CDR3H antigenized with B-epitope that induces specific immune response. To this end, we first developed functional scFv with an exceptionally long CDR3H followed by grafting of a B-epitope (gC156) from bovine herpes virus-1 into the CDR3H. The grafted B-epitope in bovine scFv with an exceptionally long CDR3H sustained configuration similar to the native epitope. The antigenized scFv (gC156scFv1H12) induced higher antibody response as compared to free recombinant gC156 fragment in the calves. To conclude, antigenization of bovine scFv with an exceptionally long CDR3H provides a novel approach to developing new vaccines for humoral protection against infectious agents.

Biography

Azad K Kaushik has published over 87 research articles and book chapters, and co-edited two books [Molecular Immunobiology of Self-Reactivity (1992) and Comparative Immunoglobulin genetics (2014)]. He is on the editorial boards of several immunology journals and is a Consultant to various international organizations. He was recognized as The Esther Z. Greenberg Honors Chair in Biomedical Research, and Visiting Professor, Oklahoma Medical Research Foundation, USA, in 1998. He received BVSc&AH (Honors) in 1976 and MVSc (1978) from the Faculty of Veterinary Science, Hisar, Haryana, India; followed by Docteur es Science (DSc) in Immunology (1987) from the Pasteur Institute (University of Paris VII), Paris, France. He has been teaching Immunology at the University of Guelph since 1991.

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