Abstract

Single domain human immunoglobulin fold-based biomolecules

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We have developed human immunoglobulin fold containing proteins as alternative binding ligands to antibodies. Firstly, we have evaluated cytotoxic T lymphocyte associated antigen 4 (CTLA-4) as a protein scaffold. CTLA-4 is an important regulator of cellular immunity and is transiently expressed on the surface of T cells. To have a suitable library selection system we have displayed the extracellular domain of CTLA-4 in

a functional form on the surface of filamentous phage. We have generated both engineered CTLA-4 variants and repertoires of CTLA-4 variants from which binding ligands to somatostatin receptors and $\alpha v \beta 3$ integrin have been isolated.

We have also investigated the potential of single VL domains as binding ligands. From a naïve repertoire, single VL domains were isolated which were able to bind to B7-1 and B7-2 which are important costimulatory molecules on antigen presenting cells.

We believe that these monomeric immunoglobulins may present certain advantages over classical antibodies for certain applications.

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