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(54) Title: POLYPEPTIDE CONSTRUCTS BINDING TO CD3

(57) Abstract: The invention relates to a polypeptide or polypeptide construct comprising: a binding domain binding to an extracellular epitope of the human CD3s chain comprising or consisting of a VH region and a VL region, wherein i) the VH region comprises: a CDR-H1 sequence of X_1YAX_2N , where X_1 is K, V, S, G, R, T, or I; and X_2 is M or I; a CDR-H2 sequence of $RIRSKYNNYATYYADX_1VKX_2$, where X_1 is S or Q; and X_2 is D, G, K, S, or E; and a CDR-H3 sequence of $HX_1NFGNSYX_2SX_3X_4AY$, where X_1 is G, R, or A; X_2 is I, L, V, or T; X_3 is Y, W or F; and X_4 is W, F or Y; and ii) wherein the VL region comprises: a CDR-L1 sequence of $X_1SSTGAVTX_2X_3X_4YX_5N$, where X_1 is G, R, or A; X_2 is S or T; X_3 is G or S; X_4 is N or Y; and X_5 is P or A; a CDR-L2 sequence of $X_1TX_2X_3X_4X_5X_6$, where X_1 is G or A; X_2 is K, D, or N; X_3 is F, M or K; X_4 is L or R; X_5 is A, P, or V; and X_6 is P or S; and a CDR-L3 sequence of $X_1LWYSNX_2VW$, where X_1 is V, A, or T; and X_2 is R or L; and iii) wherein one or more of CDR sequences of the VH region of i) and/or of the VL region of ii) comprise one amino acid substitution or a combination thereof selected from X_24V and X_24F in CDR-H1; D15, and X_116A in CDR-H2; H1, X_12E , F4, and N6 in CDR-H3; and X_11L and W3 in CDR-L3. The invention also relates to a polynucleotide encoding the polypeptide or polypeptide construct of the invention, a vector comprising said polynucleotide and a host cell transformed or transfected with said polynucleotide or with said vector. Moreover, the invention also provides for a process for the production of said polypeptide or polypeptide construct and a pharmaceutical composition comprising said polypeptide or polypeptide construct of the invention. Furthermore, the invention relates to medical uses of said polypeptide or polypeptide construct and kits comprising said polypeptide or polypeptide construct.

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