

C L A I M S

1. Amino acid sequence that is an immunoglobulin single variable domain capable of binding to human serum albumin that has:

- a CDR1 according to Abm that is the amino acid sequence GLTFSSYAMG (SEQ ID NO: 12) ~~or an amino acid sequence that has 2 or 1 amino acid difference(s) with the amino acid sequence of SEQ ID NO: 12;~~ and
- a CDR2 according to Abm that is the amino acid sequence SISRGGGYTY (SEQ ID NO: 13) ~~or an amino acid sequence that has 3, 2 or 1 amino acid difference(s) with the amino acid sequence of SEQ ID NO: 13;~~ and
- a CDR3 according to Abm that is the amino acid sequence ARYWATGSEYEFDY (SEQ ID NO: 14) ~~or an amino acid sequence that has 3, 2 or 1 amino acid difference(s) with the amino acid sequence of SEQ ID NO: 14.~~

~~2. Amino acid sequence according to claim 1, that has:~~

- ~~— a CDR1 according to Abm that is the amino acid sequence GLTFSSYAMG (SEQ ID NO: 12); and~~
- ~~— a CDR2 according to Abm that is the amino acid sequence SISRGGGYTY (SEQ ID NO: 13); and~~
- ~~— a CDR3 according to Abm that is the amino acid sequence ARYWATGSEYEFDY (SEQ ID NO: 14).~~

~~3. Amino acid sequence according to claim 1, that can bind to human serum albumin with an affinity of less than 500 pM, as determined using Surface Plasmon Resonance on ProteOn.~~

42. Amino acid sequence according to ~~any of the preceding claims~~ claim 1, that is a heavy-chain immunoglobulin single variable domain.

53. Amino acid sequence according to any of the preceding claims, that is a VHH, a humanized VHH or a camelized VH₂.

64. Amino acid sequence according to any of the preceding claims, that has:

- a degree of sequence identity with the sequence of SEQ ID NO: 15, in which the CDR's and any C-terminal extension that may be present are not taken into account for determining the degree of sequence identity, of at least 85%, preferably at least 90%, more preferably at least 95%;

and/or that has:

- no more than 7, preferably no more than 5, such as only 3, 2 or 1 "amino acid differences", not taking into account the CDRs and any C-terminal extension that may be present, with the sequence of SEQ ID NO: 15.

75. Amino acid sequence according to any of the preceding claims, that contains, compared to the sequence of SEQ ID NO:15, one or more mutations that reduce the binding by pre-existing antibodies such that after the mutation, at the indicated position, one of the following amino acid residues is present: 11L, 11K, 11V, 14A, 14P, 41A, 41L, 41P, 41S, 41T, 42E, 42G, 87A, 87T, 89A, 89L, 89T, 108L, 110K, 110Q, 112K and/or 112Q, or any suitable combination of said mutations, said positions determined according to Kabat numbering.

86. Amino acid sequence according to any of the preceding claims, that is a VHH and that contains, compared to the sequence of SEQ ID NO:15, one or more humanizing substitutions.

97. Amino acid sequence that is an immunoglobulin single variable domain capable of binding to human serum albumin and that is chosen from SEQ ID NO's: 15 to 77.

108. Protein, polypeptides or other construct, compound, molecule or chemical entity that comprises at least one amino acid sequence according to any of claims 1 to 97.

119. Protein, polypeptide or other construct, compound, molecule or chemical entity according to claim 108, that comprises at least one therapeutic moiety or entity.

1210. Protein, polypeptide or other construct, compound, molecule or chemical entity according to claim 108 or 119 that is a fusion protein.

~~13~~11. Protein, polypeptide or other construct, compound, molecule or chemical entity according to any of claims ~~10-8~~ to ~~12~~10, that is such that:

- when it has an ISVD at its C-terminal end, then the C-terminal ISVD of said protein, polypeptide, compound, construct has a C-terminal extension (X)_n at its C-terminal end; and/or
- when it has an ISVD at its C-terminal end, then at least said the C-terminal ISVD contains one or more mutations that reduce the binding of pre-existing antibodies such that after the mutation, at the indicated position, one of the following amino acid residues is present: 11L, 11K, 11V, 14A, 14P, 41A, 41L, 41P, 41S, 41T, 42E, 42G, 87A, 87T, 89A, 89L, 89T, 108L, 110K, 110Q, 112K and/or 112Q, or any suitable combination of said mutations, said positions determined according to Kabat numbering; and/or
- when it has an ISVD at its N-terminal end, then the N-terminal ISVD of said protein, polypeptide, compound, construct preferably contains a D at position 1; and/or
- in which said ISVDs which protein, polypeptide or other compound may also have ISVD at its N-terminal end, in which case said N-terminal ISVD end preferably has a D or an E1D at position 1; and/or
- preferably, essentially all of the ISVDs present in said protein, polypeptide, compound, construct contain one or more mutations that reduce the binding of pre-existing antibodies

~~14~~12. Nucleic acid that encodes the immunoglobulin single variable domain according to any of claims 1 to ~~9~~7, or the compound or polypeptide according to any of claims ~~10-8~~ to ~~13~~11.

~~15~~13. Non-human hosts or host cells that contain the nucleic acid according to claim ~~14~~12, and/or that express the immunoglobulin single variable domain according to any of claims 1 to ~~9~~7, or the compound or polypeptide according to any of claims ~~10-8~~ to ~~13~~11.

~~16~~14. Method for preparing the immunoglobulin single variable domain according to any of claims 1 to ~~9~~7, or the compound or polypeptide according to any of claims ~~10-8~~ to ~~13~~11, which method comprises cultivating or maintaining a host cell under conditions such that said host cell produces or expresses the immunoglobulin single variable domain according to any of claims 1 to ~~9~~7, or the compound or polypeptide according to any of claims ~~10-8~~ to ~~13~~11, and optionally further comprises isolating the immunoglobulin single

variable domain according to any of claims 1 to ~~9~~7, or the compound or polypeptide according to any of claims ~~10-8~~10-7 to ~~13~~11.

~~17~~15. Pharmaceutical composition comprising a protein, polypeptide or other construct, compound, molecule or chemical entity according to any of claims ~~10-8~~10-7 to ~~13~~11.