

CLAIMS

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

- 5 - a CDR1 (according to Abm) that is the amino acid sequence GGTFSTYVMG (SEQ ID NO: 12) or an amino acid sequence that has 2 or 1 amino acid difference(s) (as defined herein) with the amino acid sequence of SEQ ID NO: 12; and
- a CDR2 (according to Abm) that is the amino acid sequence AISQNSIHTY (SEQ ID NO: 13) or an amino acid sequence that has 3, 2 or 1 amino acid difference(s) (as defined
10 herein) with the amino acid sequence of SEQ ID NO: 13; and
- a CDR3 (according to Abm) that is the amino acid sequence SRFTSWYTADYEYDY (SEQ ID NO: 14) or an amino acid sequence that has 3, 2 or 1 amino acid difference(s) (as defined herein) with the amino acid sequence of SEQ ID NO: 14,
- wherein the immunoglobulin single variable domain capable of binding to (human) serum
15 albumin cross-blocks the binding of the amino acid sequence of SEQ ID NO:18 to human serum albumin.

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

- 20 - a CDR1 (according to Abm) that is the amino acid sequence GGTFSTYVMG (SEQ ID NO: 12); and
- a CDR2 (according to Abm) that is the amino acid sequence AISQNSIHTY (SEQ ID NO: 13); and
- a CDR3 (according to Abm) that is the amino acid sequence SRFTSWYTADYEYDY (SEQ ID NO: 14).

3. Amino acid sequence according to claim 1, that can bind to human serum albumin with an affinity better than 100nM, preferably better than 50nM, as determined using ProteOn.

30 4. Amino acid sequence according to any of the preceding claims, that is a heavy-chain immunoglobulin single variable domain.

5. Amino acid sequence according to any of the preceding claims, that is a VHH, a humanized VHH or a camelized VH (and in particular, a camelized human VH).

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

- a degree of sequence identity with the sequence of SEQ ID NO: 18 and/or 19 (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%,
5 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" (as defined herein, and not taking into account the CDRs and any C-terminal extension that may be present) with the sequence of SEQ ID NO: 18 and/or 19.

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

- a degree of sequence identity with the sequence of SEQ ID NO: 18 (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%,
15 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" (as defined herein, and not taking into account the CDRs and any C-terminal extension that may be present) with the sequence of SEQ ID NO: 18.

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8. Amino acid sequence according to any of claims 1 to 6, that has:

- a degree of sequence identity with the sequence of SEQ ID NO: 19 (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%,
25 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" (as defined herein, and not taking into account the CDRs and any C-terminal extension that may be present) with the sequence of SEQ ID NO: 19.

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9. Amino acid sequence according to any of the preceding claims, that contains, compared to the sequence of SEQ ID NO:18, one or more mutations that reduce the binding by pre-existing antibodies, such that after the mutation one of the following amino acid residues according to Kabat numbering 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 such substitutions, such as: 11V in combination with 89L or 89T; 11V in combination with 110K or 110Q; or 11V in combination with 89L and 110K or 110Q.

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10. 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:18, one or more humanizing substitutions, that is Q108L or A14P or a suitable combination thereof.

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11. 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: 18 to 44.

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12. 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 11.

13. Protein, polypeptide or other construct, compound, molecule or chemical entity according to claim 12, that comprises at least one therapeutic moiety or entity.

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14. Protein, polypeptide or other construct, compound, molecule or chemical entity according to claim 12 or 13 that is a fusion protein.

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15. Protein, polypeptide or other construct, compound, molecule or chemical entity according to any of claims 12 to 14, that is such that:

- when it has the ISVD at its C-terminal end, then (the C-terminal ISVD of) said protein, polypeptide, compound, construct has a C-terminal extension (X)_n, in which n is 1 to 10; and each X is an amino acid residue that is independently chosen from naturally occurring amino acid residues, at its C-terminal end; and/or
- when it has the 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 as defined in claim 9; and/or
- when it has the 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

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- 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
 - all of the ISVDs present in said protein, polypeptide, compound, construct contain one or more mutations that reduce the binding of pre-existing antibodies as defined in claim 9.
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16. Pharmaceutical composition comprising a protein, polypeptide or other construct, compound, molecule or chemical entity according to any of claims 12 to 15.