

[0011] The solution for this problem that has been provided by the present invention, i.e. novel anti-HSA antibodies and fragments thereof, has so far not been achieved or suggested by the prior art.

SUMMARY

[0012] The present disclosure relates to novel antibodies that are specific for human serum albumin (HSA).

[0013] Thus, in a first aspect, the present disclosure relates to an antibody or functional fragment thereof which is specific for human serum albumin, comprising: a variable light chain, wherein the variable light chain comprises, from N-terminus to C-terminus, the regions LFW1-LCDR1-LFW2-LCDR2-LFW3-LCDR3-LFW4, wherein each LFW designates a light chain framework region, and each LCDR designates a light chain complementarity-determining region, and wherein said LCDRs together exhibit at least 90% sequence identity to the corresponding LCDRs taken from a VL sequence according to SEQ ID NO: 1 or SEQ ID NO: 3;

and

a variable heavy chain, wherein the variable light chain comprises, from N-terminus to C-terminus, the regions HFW1-HCDR1-HFW2-HCDR2-HFW3-HCDR3-HFW4, wherein each HFW designates a heavy chain framework region, and each HCDR designates a heavy chain complementarity-determining region, and wherein said HCDRs together exhibit at least 90% sequence identity to the corresponding HCDRs taken from a VH sequence according to SEQ ID NO: 2 or SEQ ID NO: 4.

[0014] In a second aspect, the present disclosure relates to a pharmaceutical composition comprising the antibody or functional fragment thereof of the present disclosure, and optionally a pharmaceutically acceptable carrier and/or excipient.

[0015] In a third aspect, the present disclosure relates to a nucleic acid sequence or a collection of nucleic acid sequences encoding the antibody or functional fragment thereof of the present disclosure.

[0016] In a fourth aspect, the present disclosure relates to a vector or a collection of vectors comprising the nucleic acid sequence or the collection of nucleic acid sequences of the present disclosure.

[0016a] In a fifth aspect, the present disclosure relates to a method for producing the antibody or functional fragment thereof as described herein, comprising the step of expressing the nucleic acid sequence or the collection of nucleic acid sequences as described herein, or the vector or collection of vectors as described herein.

[0017] In an example, the present disclosure relates to a host cell, particularly an expression host cell, comprising the nucleic acid sequence or the collection of nucleic acid sequences of the present disclosure, or the vector or collection of vectors of the present disclosure.

[0018] In another example, the present disclosure relates to a method for producing the antibody or functional fragment thereof of the present disclosure, comprising the step of expressing the nucleic acid sequence or the collection of nucleic acid sequences of the present disclosure, or the vector or collection of vectors of the present disclosure, or the host cell, particularly the expression host cell, of the present disclosure.

[0019] In a sixth aspect, the present disclosure relates to a method of generating a multispecific construct, comprising the step of cloning, in one or more steps, one or more nucleic acid sequences encoding the antibody or functional fragment thereof according to the present disclosure, into a multispecific construct comprising at least a second bioactive domain, and, optionally, one or more additional bioactive domains.

[0020] In an seventh aspect, the present disclosure relates to a multispecific polypeptide construct comprising (i) an antibody or functional fragment thereof as described herein; and (ii) a second bioactive domain; and, optionally, (iii) one or more additional bioactive domains.

[0021] In a eighth aspect, the present disclosure relates to the antibody or functional fragment thereof of the present disclosure, or to a multispecific polypeptide construct

comprising the antibody or functional fragment thereof of the present disclosure for use as a medicament.

[0021a] In a ninth aspect, the present disclosure relates to the use of the antibody or functional fragment thereof as described herein, or the pharmaceutical composition as described herein, or the multispecific polypeptide construct as described herein in the manufacture of a medicament for treating a disease.

[0022] In an example, the present disclosure relates to the use of the antibody or functional fragment thereof of the present disclosure, or a multispecific polypeptide construct comprising the antibody or functional fragment thereof of the present disclosure in the manufacture of a medicament.

[0023] In an example, the present disclosure relates to a method of treating a subject suffering from a disease, particularly a human disease, comprising administering to said subject an effective amount of the antibody or functional fragment thereof of the present disclosure or a multispecific polypeptide construct comprising the antibody or functional fragment thereof of the present disclosure.

[0024] In an example, the present disclosure relates to use of the antibody or functional fragment thereof of the present disclosure, or to a multispecific polypeptide construct comprising the antibody or functional fragment thereof of the present disclosure in the treatment of a disease, particularly a human disease.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] **Figure 1** shows pharmacodynamic parameters of PRO462 following intravenous administration (3 mg/ml) to cynomolgus monkeys (3 per group, average shown; data see Table 8, Example 7). Blood samples were taken over a period of 21 days. The graph shows the mean group plasma concentrations of PRO462. Later time points are omitted because of the development of anti-drug antibodies.

[0026] **Figure 2** shows the results of the mouse PK study discussed in Example 6 (mean group plasma concentrations of PRO497 in male CD-1 mice intravenously dosed with 5 mg/kg of test article; data see Table 9).

[0027] **Figure 3** shows the structure of the multispecific construct PRO497.

DETAILED DESCRIPTION OF THE INVENTION

[0028] The present disclosure relates to novel antibodies that are specific for human serum albumin (HSA).

CLAIMS

1. An antibody or functional fragment thereof which is specific for human serum albumin, comprising:
 - (a) a variable light chain,
wherein the variable light chain comprises, from N-terminus to C-terminus, the regions LFW1-LCDR1-LFW2-LCDR2-LFW3-LCDR3-LFW4, wherein each LFW designates a light chain framework region, and each LCDR designates a light chain complementarity-determining region, and wherein said LCDRs together exhibit at least 90% sequence identity to the corresponding LCDRs taken from a VL sequence according to SEQ ID NO: 1 or SEQ ID NO: 3;
and
 - (b) a variable heavy chain,
wherein the variable light chain comprises, from N-terminus to C-terminus, the regions HFW1-HCDR1-HFW2-HCDR2-HFW3-HCDR3-HFW4, wherein each HFW designates a heavy chain framework region, and each HCDR designates a heavy chain complementarity-determining region, and wherein said HCDRs together exhibit at least 90% sequence identity to the corresponding HCDRs taken from a VH sequence according to SEQ ID NO: 2 or SEQ ID NO: 4.
2. The antibody or functional fragment thereof according to claim 1, wherein said variable light chain is a Vk1 light chain, and/or wherein said variable heavy chain is a VH3 chain.
3. The antibody or functional fragment thereof according to claim 1 or 2, wherein said variable light chain exhibits at least 90% sequence identity to VL sequence according to SEQ ID NO: 1 or SEQ ID NO: 3, and/or wherein said variable heavy chain is a VH3 chain exhibits at least 90% sequence identity to VH sequence according to SEQ ID NO: 2 or SEQ ID NO: 4.
4. The antibody or functional fragment thereof according to any one of claims 1 to 3, wherein said antibody or functional fragment thereof comprises (i) a variable light chain exhibiting at least 90% sequence identity to the VL sequence according to

SEQ ID NO: 1, and a VH chain exhibiting at least 90% sequence identity to the VH sequence according to SEQ ID NO: 2, or (ii) a variable light chain exhibiting at least 90% sequence identity to the VL sequence according to SEQ ID NO: 3, and a VH chain exhibiting at least 90% sequence identity to the VH sequence according to SEQ ID NO: 4.

5. The antibody or functional fragment thereof according to any one of claims 1 to 4, wherein said antibody or functional fragment thereof is characterized by one or more of the following parameters:
 - (i) a K_D value for the binding to human serum albumin of less than 50 nM, particularly less than 3 nM, more particularly less than 1 nM, in particular as measured by surface plasmon resonance;
 - (ii) a K_D value for the binding to human serum albumin of less than 50 nM, particularly less than 3 nM, more particularly less than 1 nM both at pH values of about 5.5 and at about 7.4, in particular as measured by surface plasmon resonance;
 - (iii) a K_D value for the binding to non-human primate and/or rodent serum albumin of less than 250 nM, particularly less than 100 nM, more particularly less than 50 nM, in particular as measured by surface plasmon resonance;
 - (iv) preserved ability of the antibody-bound HSA to bind to FcRn;
 - (v) an average midpoint of thermal unfolding temperature (T_m) exceeding at least 60°C, when expressed in the scDb (single chain diabody format) or scFv (single chain variable fragment format) antibody format, preferably when expressed in the scFv antibody format, as determined by differential scanning fluorimetry, in particular when samples are diluted in citrate-phosphate buffers at pH values ranging from 3.5 to 7.5, particularly at pH 6.4, and containing 0.15-0.25 M NaCl, particularly 0.15 M NaCl, more 0.25 M NaCl; and
 - (vi) less than 3% loss of monomeric content at 37°C during 28 days in a stress stability study, particularly less than 2% loss, in particular when the antibody of the invention is at a starting concentration of 10 mg/ml.
6. A pharmaceutical composition comprising the antibody or functional fragment thereof of any one of claims 1 to 5, and optionally a pharmaceutically acceptable carrier and/or excipient.

7. A nucleic acid sequence or a collection of nucleic acid sequences encoding the antibody or functional fragment thereof according to any one of claims 1 to 5.
8. A vector or a collection of vectors comprising the nucleic acid sequence or the collection of nucleic acid sequences of claim 7.
9. A method for producing the antibody or functional fragment thereof of any one of claims 1 to 5, comprising the step of expressing the nucleic acid sequence or the collection of nucleic acid sequences of claim 6, or the vector or collection of vectors of claim 7.
10. A method of generating a multispecific construct, comprising the step of
 - (a) cloning, in one or more steps, one or more nucleic acid sequences encoding the antibody or functional fragment thereof according to any one of claims 1 to 5, into a multispecific construct comprising at least a second bioactive domain, and, optionally, one or more additional bioactive domains.
11. The method of claim 10, wherein said second bioactive domain is a second antibody or functional fragment thereof.
12. A multispecific polypeptide construct comprising (i) an antibody or functional fragment thereof according to any one of claims 1 to 4; and (ii) a second bioactive domain; and, optionally, (iii) one or more additional bioactive domains.
13. The multispecific polypeptide construct of claim 12, wherein said second bioactive domain is a second antibody or functional fragment thereof.
14. The antibody or functional fragment thereof according to any one of claims 1 to 5, or the pharmaceutical composition according to claim 6, or the multispecific polypeptide construct according to claim 12 or 13 for use as a medicament.
15. Use of the antibody or functional fragment thereof according to any one of claims 1 to 5, or the pharmaceutical composition according to claim 6, or the multispecific

polypeptide construct according to claim 12 or 13 in the manufacture of a medicament for treating a disease.