

[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 refers to 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 wherein said variable light chain exhibits at least 97% sequence identity to the amino acid sequence according to SEQ ID NO: 1 or SEQ ID NO: 3, respectively; and (b) a variable heavy chain, wherein the variable heavy 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, and wherein said variable heavy chain exhibits at least 97% sequence identity to the amino acid sequence according to SEQ ID NO: 2 or SEQ ID NO: 4, respectively, and 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, as measured by surface plasmon resonance; (ii) a K_D value for the binding to human serum albumin of less than 50 nM, at pH values of about 5.5 and at about 7.4, 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, 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, as determined by differential scanning fluorimetry, when samples are diluted in citrate-phosphate buffers at pH values ranging from 3.5 to 7.5, and containing 0.15-0.25 M NaCl, and (vi) less than 3% loss of monomeric content at 37°C during 28 days in a stress stability study, when the antibody of the invention is at a starting concentration of 10 mg/ml.

[0014] In a second aspect, the present disclosure refers to a pharmaceutical composition comprising multispecific polypeptide construct as described herein, wherein said second bioactive domain is able to specifically interact with a target of therapeutic relevance, 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

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 wherein said variable light chain exhibits at least 97 % sequence identity to the amino acid sequence according to SEQ ID NO: 1 or 3, respectively;
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, wherein said variable heavy chain exhibits at least 97 % sequence identity to the amino acid sequence according to SEQ ID NO: 2 or 4, respectively,
and
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, as measured by surface plasmon resonance;
 - (ii) a K_D value for the binding to human serum albumin of less than 50 nM, at pH values of about 5.5 and at about 7.4, 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, 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, as determined by differential scanning fluorimetry, when samples are diluted in citrate-phosphate buffers at pH values ranging from 3.5 to 7.5, and containing 0.15-0.25 M NaCl, and (vi) less than 3% loss of monomeric content at 37°C during 28 days in a stress stability study, when the antibody of the invention is at a starting concentration of 10 mg/ml.

2. The antibody or functional fragment thereof according to claim 1, wherein said antibody or functional fragment thereof comprises (i) a variable light chain exhibiting at least 97% sequence identity to the VL sequence according to SEQ ID NO: 1, and a VH chain exhibiting at least 97% sequence identity to the VH sequence according to SEQ ID NO: 2, or (ii) a variable light chain exhibiting at least 97% sequence identity to the VL sequence according to SEQ ID NO: 3, and a VH chain exhibiting at least 97% sequence identity to the VH sequence according to SEQ ID NO: 4.
3. A nucleic acid sequence or a collection of nucleic acid sequences encoding the antibody or functional fragment thereof according to claim 1 or 2.
4. A vector or a collection of vectors comprising the nucleic acid sequence or the collection of nucleic acid sequences of claim 3.
5. A method for producing the antibody or functional fragment thereof of claim 1 or 2, comprising the step of expressing the nucleic acid sequence or the collection of nucleic acid sequences of claim 3, or the vector or collection of vectors of claim 4.
6. 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 claim 1 or 2, into a multispecific construct comprising at least a second bioactive domain, and, optionally, one or more additional bioactive domains.

7. The method of claim 6, wherein said second bioactive domain is a second antibody or functional fragment thereof.
8. A multispecific polypeptide construct comprising (i) an antibody or functional fragment thereof according to claim 1 or 2; and (ii) a second bioactive domain; and, optionally, (iii) one or more additional bioactive domains.
9. The multispecific polypeptide construct of claim 8, wherein said second bioactive domain is a second antibody or functional fragment thereof.
10. A pharmaceutical composition comprising the multispecific polypeptide construct of claim 8 or 9, wherein said second bioactive domain is able to specifically interact with a target of therapeutic relevance, and optionally a pharmaceutically acceptable carrier and/or excipient