

[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:

(a1) 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 exhibit sequence identity to the corresponding LCDRs taken from the VL sequence according to SEQ ID NO: 1; and wherein said variable light chain exhibits at least 97% sequence identity to the amino acid sequence according to SEQ ID NO: 1; and (b1) 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 exhibit sequence identity to the corresponding HCDRs taken from the VH sequence according to SEQ ID NO: 2, and wherein said variable heavy chain exhibit at least 97% sequence identity to the amino acid sequence according to SEQ ID NO: 2, or (a2) 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 exhibit sequence identity to the corresponding LCDRs taken from the VL sequence according to 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: 3; and (b2) 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 exhibit sequence identity to the corresponding HCDRs taken from the VH sequence according to 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: 4, and wherein said antibody or functional fragment thereof is characterized by one or more of the following parameters: (i) a KD value for the binding to human serum albumin of less than 50 nM, as measured by surface plasmon resonance; (ii) a KD 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 KD 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 (Tm) 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.

CLAIMS

1. An antibody or functional fragment thereof which is specific for human serum albumin, comprising:
 - (a1) 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 exhibit sequence identity to the corresponding LCDRs taken from the VL sequence according to SEQ ID NO: 1; and wherein said variable light chain exhibits at least 97 % sequence identity to the amino acid sequence according to SEQ ID NO: 1;
and
 - (b1) 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 exhibit sequence identity to the corresponding HCDRs taken from the VH sequence according to SEQ ID NO: 2, wherein said variable heavy chain exhibits at least 97 % sequence identity to the amino acid sequence according to SEQ ID NO: 2,
or
 - (a2) 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 exhibit sequence identity to the corresponding LCDRs taken from the VL sequence according to 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: 3;
and
 - (b2) 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 exhibit sequence identity to the corresponding HCDRs taken from the VH sequence according to 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: 4,

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 98% sequence identity to the VL sequence according to SEQ ID NO: 1, and a VH chain exhibiting at least 98% sequence identity to the VH sequence according to SEQ ID NO: 2, or (ii) a variable light chain exhibiting at least 98% sequence identity to the VL sequence according to SEQ ID NO: 3, and a VH chain exhibiting at least 98% 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.