identity to the amino acid sequence of SEQ ID NO: 06, or (c) a VH sequence as in (a) and a VL sequence as in (b).

In one preferred embodiment the humanized antibody comprises a VH sequence of SEQ ID NO: 04 and a VL sequence of SEQ ID NO: 06.

One aspect as reported herein is a humanized antibody that specifically binds to human and cynomolgus IL-1beta, wherein the humanized antibody comprises (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 25, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 27, (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28, (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 29, (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 30, and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 31,

wherein in the heavy chain variable domain at position 48 is an isoleucine amino acid residue, at position 52a is a serine amino acid residue, at position 67 is an alanine amino acid residue, at position 69 is a phenylalanine amino acid residue, at position 71 is a valine amino acid residue and at position 93 is a valine amino acid residue, and

wherein in the light chain variable domain at position 36 is a serine the amino acid residue, wherein all numbering are according to the Kabat numbering system,

and wherein the antibody comprises a VH amino acid sequence having at least 95 % amino acid sequence identity to the amino acid sequence of SEQ ID NO: 04; and a VL amino acid sequence having at least 95 % sequence identity to the amino acid sequence of SEQ ID NO: 06.

In one embodiment the humanized antibody is of the human subclass IgG1 or the human subclass IgG4.

In one embodiment the humanized antibody is of the human subclass IgG1 with a kappa light chain.

In one embodiment the humanized antibody is a monoclonal antibody.

As reported herein is an antibody comprising a VH sequence of SEQ ID NO: 04 and a VL sequence of SEQ ID NO: 06.

In one embodiment the antibody is a bispecific antibody.

In one embodiment the humanized antibody specifically binds to human IL-1beta but does not bind to human IL-1alpha.

In one embodiment the humanized antibody blocks the biological activity of human IL-1beta by inhibiting the binding of human IL-1beta to human IL-1 receptors.

In one embodiment the humanized antibody as reported herein specifically binds to two determinant sites on or close to the receptor binding site of IL-1beta.

In one preferred embodiment the humanized antibody as reported herein blocks the interaction of IL-1R1 and IL-1RAcP with IL-1beta.

In one preferred embodiment the humanized antibody as reported herein blocks the formation of the IL-1 beta signaling complex at the first step of its assembly (i.e. it blocks the association of IL-1 beta and the IL-1R1).

As reported herein is an (isolated) nucleic acid encoding the antibody as reported herein.

As reported herein is a host cell comprising the nucleic acid as reported herein.

As reported herein is a method of producing an antibody as reported herein comprising culturing the host cell as reported herein to produce the antibody and recovering the antibody from the host cell or the cultivation medium.

One aspect as reported herein is a pharmaceutical formulation comprising an antibody as reported herein and optionally a pharmaceutically acceptable carrier.

In one embodiment the pharmaceutical formulation further comprises an additional therapeutic agent. In one embodiment the additional therapeutic agent is an anti-ANG2 antibody or an anti-VEGF antibody.

As reported herein is the antibody as reported herein for use as a medicament. One aspect as reported herein is the humanized antibody as reported herein for use as a medicament.

As reported herein is the antibody as reported herein for use in treating on ocular vascular disease, preferably for use in treating macular degeneration.

The antibody as reported herein for use in inhibiting the interaction between IL-1beta and the IL-1 receptors I and II.

As reported herein is the use of the antibody as reported herein in the manufacture of a medicament. One aspect as reported herein is the use of the humanized antibody as reported herein in the manufacture of a medicament. One aspect as reported herein is the use of the humanized antibody as reported herein in the manufacture of a medicament for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

In one embodiment the medicament is for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.

In one embodiment the medicament is for inhibiting the interaction between IL-1beta and the IL-1 receptors I and II.

As reported herein is a method of treating an individual having on ocular vascular disease, preferably macular degeneration, comprising administering to the individual an effective amount of the antibody as reported herein.

As reported herein is a method of inhibiting the interaction between IL-1beta and the IL-1 receptors I and II in an individual comprising administering to the individual an effective amount of the antibody as reported herein to inhibiting the interaction between IL-1beta and the IL-1 receptors I and II.

Patent Claims

1. A humanized antibody that specifically binds to human and cynomolgus IL-1beta, wherein the humanized antibody comprises (a) a HVR-H1 comprising the amino acid sequence of SEQ ID NO: 25, (b) a HVR-H2 comprising the amino acid sequence of SEQ ID NO: 27, (c) a HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28, (d) a HVR-L1 comprising the amino acid sequence of SEQ ID NO: 29, (e) a HVR-L2 comprising the amino acid sequence of SEQ ID NO: 30, and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 31,

wherein in the heavy chain variable domain at position 48 is an isoleucine amino acid residue, at position 52a is a serine amino acid residue, at position 67 is an alanine amino acid residue, at position 69 is a phenylalanine amino acid residue, at position 71 is a valine amino acid residue and at position 93 is a valine amino acid residue, and

wherein in the light chain variable domain at position 36 is a serine the amino acid residue, wherein all numbering are according to the Kabat numbering system,

and wherein the antibody comprises a VH amino acid sequence having at least 95 % amino acid sequence identity to the amino acid sequence of SEQ ID NO: 04; and a VL amino acid sequence having at least 95 % sequence identity to the amino acid sequence of SEQ ID NO: 06.

2. The humanized antibody according to claim 1 comprising a VH amino acid sequence of SEQ ID NO: 04 and a VL amino acid sequence of SEQ ID NO: 06.

3. The humanized antibody according to claim 1 or 2 wherein the humanized antibody is of the human subclass IgG1 or the human subclass IgG4.

4. The humanized antibody according to any one of claims 1 to 3, wherein the antibody is a bispecific antibody.

5. The antibody according to claim 4, wherein the bispecific antibody comprises

a) a first light chain and a first heavy chain of an antibody specifically binding to a first antigen, and

b) a second light chain and a second heavy chain of an antibody specifically binding to a second antigen, wherein the constant domains CL and CH1 of the second light chain and the second heavy chain are replaced by each other,

wherein either the first antigen or the second antigen is human IL-1beta.

6. The antibody according to claim 5, wherein the antibody is a bivalent antibody.

7. The antibody according to claim 5 or 6 comprising CH3 domains that are altered to increase the heterodimerization of both heavy chains containing these two CH3 domains, wherein one CH3 domain comprises a T366W mutation and the other CH3 domain comprises T366S, L368A, Y407V mutations, wherein all numberings are according to the EU index.

8. The antibody according to claim 5 or 6 comprising CH3 domains that are altered to increase the heterodimerization of both heavy chains containing these two CH3 domains, wherein one CH3 domain comprises Y349C and T366W mutations and the other CH3 domain comprises E356C, T366S, L368A and Y407V mutations, wherein all numberings are according to the EU index

9. The humanized antibody according to any one of claims 1 to 8, wherein the humanized antibody blocks the biological activity of human IL-1beta by inhibiting the binding of human IL-1beta to the human IL-1 receptors.

10. A pharmaceutical formulation comprising an antibody according to any one of claims 1 to 9 and optionally a pharmaceutically acceptable carrier.

11. The pharmaceutical formulation according to claim 10, further comprising an additional therapeutic agent selected from an anti-ANG2 antibody and an anti-VEGF antibody.

12. The humanized antibody according to any one of claims 1 to 9 for use as a medicament.

13. Use of the humanized antibody according to any one of claims 1 to 9 in the manufacture of a medicament.

14. Use of the humanized antibody according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of an ocular vascular disease, preferably for the treatment of macular degeneration.