

exemplary Fab fragment specifically binding to VEGF and IL-6 is disclosed in WO2012/163520.

There is a need for improved therapeutic antibodies that bind to VEGF and IL-1beta.

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SUMMARY

The present disclosure relates to bispecific anti-VEGF/anti-IL-1beta antibodies and methods of using the same.

10 The disclosure provides an antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a variable light chain domain (VL domain) and a variable heavy chain domain (VH domain), wherein the VEGF paratope comprises amino acid residues from CDR-H2, CDR-L1 and CDR-L3 of the antibody, wherein the IL-1beta paratope comprises amino acid residues from the CDR-H1, CDR-H3 and CDR-L2 of the antibody.

15 In one aspect, the present disclosure provides an antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a variable light chain domain (VL domain) and a variable heavy chain domain (VH domain), wherein the VEGF paratope comprises amino acid residues from CDR-H2, CDR-L1 and CDR-L3 of the antibody, wherein the IL-1beta paratope comprises amino acid residues from the CDR-H1, CDR-H3 and CDR-L2 of the antibody, wherein the antibody comprises a VH sequence of SEQ ID NO:11 and a VL sequence of SEQ ID NO:12.

20 In one example the disclosure provides an antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a VL domain and a VH domain, wherein the pair of the variable light chain domain and the variable heavy chain domain simultaneously binds to human VEGF and human IL-1beta.

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In one example the disclosure provides an antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a VL domain and a VH domain, wherein none of the amino acids that are comprised in the VEGF paratope are comprised in the IL-1beta paratope.

In one example the disclosure provides an antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a VL domain and a VH domain, wherein the antibody binds to the same epitope on human VEGF and to the same epitope on human IL-1beta as an antibody with a variable heavy chain domain of SEQ ID NO: 11 and a variable light chain domain of SEQ ID NO: 12.

PATENT CLAIMS

1. An antibody that binds to human VEGF and to human IL-1beta, comprising a VEGF paratope and an IL-1beta paratope within one cognate pair of a variable light chain domain (VL domain) and a variable heavy chain domain (VH domain), wherein the VEGF paratope comprises amino acid residues from CDR-H2, CDR-L1 and CDR-L3 of the antibody, wherein the IL-1beta paratope comprises amino acid residues from the CDR-H1, CDR-H3 and CDR-L2 of the antibody, wherein the antibody comprises a VH sequence of SEQ ID NO:11 and a VL sequence of SEQ ID NO:12.
2. An antibody that specifically binds to human VEGF and to human IL-1beta, comprising a VH sequence of SEQ ID NO:11 and a VL sequence of SEQ ID NO:12.
3. The antibody of claim 1 or 2 comprising a heavy chain amino acid sequence of SEQ ID NO:20 and a light chain amino acid sequence of SEQ ID NO:19.
4. The antibody of any one of the preceding claims, wherein an antibody Fab fragment of the antibody binds (i) to human VEGF121 with a K_D of less than 10 pM as measured by surface plasmon resonance, and (ii) to human IL-1beta with a K_D of less than 30 pM as measured by surface plasmon resonance.
5. The antibody of any one of the preceding claims, wherein an antibody Fab fragment of the antibody exhibits an aggregation onset temperature of more than 70 °C.
6. The antibody of any one of the preceding claims, wherein an antibody Fab fragment of the antibody exhibits a melting temperature of more than 80 °C as measured by dynamic light scattering.
7. The antibody of any one of the preceding claims, wherein the antibody is a bispecific antibody fragment.
8. An isolated nucleic acid encoding the antibody of any of claims 1 to 7.
9. A host cell comprising the nucleic acid of claim 8.

10. An expression vector comprising the nucleic acid of claim 8.

11. A method of producing an antibody that binds to human VEGF and to human IL-1beta comprising culturing the host cell of claim 9 so that the antibody is produced.