

CLAIMS

1. An antibody or an antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL),
 wherein said VH domain comprises, essentially consists of, or consists of
 - 5 an amino acid sequence according to SEQ ID NO: 10 (QVQLVQSGAE
 VKKPGASVKV SCKASGYSFT TFWMDWVRQA PGQGLEWIGR
 IDPSDSESL DQRFKDRVMT TVDKSTSTVY MELSSLRSED
 TAVYYCARGN DGYYGFAIWG QGTLVTVSS, VH4) or
 an amino acid sequence having at least 80% sequence identity with SEQ ID NO:
 10, wherein said amino acid sequence having at least 80% sequence identity with
 SEQ ID NO: 10 comprises the CDR1H, CDR2H, and CDR3H sequences of SEQ
 ID NO: 20 to 22, respectively, and wherein said amino acid sequence having at
 least 80% sequence identity with SEQ ID NO: 10 comprises a V at amino acid
 position 5, an E at amino acid position 10, a K at amino acid position 12, a K at
 15 amino acid position 13, an A at amino acid position 16, an A at amino acid
 position 40, and/or a T at the amino acid position 76, and
 wherein said VL domain comprises, essentially consists of, or consists of
 - 20 an amino acid sequence according to SEQ ID NO: 16 (DIQMTQSPSS
 LSASVGDRVT ITCKASQSVD YDGDSYMKWY QQKPGKAPKL
 LIYAASNLSQ GVPSTRFSGSG SGTDFLTIS SLQPEDFATY
 YCQQSNEDPY TFGQGTKLEI K, V_K4) or
 an amino acid sequence having at least 80% sequence identity with SEQ ID NO:
 16, wherein said amino acid sequence having at least 80% sequence identity with
 SEQ ID NO: 16 comprises the CDR1L, CDR2L, CDR3L sequences of SEQ ID
 25 NO: 23 to 25, respectively, and wherein said amino acid sequence having at least
 80% sequence identity with SEQ ID NO: 16 comprises an A at amino acid
 position 13, a V at amino acid position 15, a D at amino acid position 17, a V at
 amino acid position 19, a T at amino acid position 22, a K at amino acid position
 46, an A at amino acid position 47, an S at amino acid position 64, a T at amino
 acid position 78, an S at amino acid position 80, an S at amino acid position 81,
 30 an L at amino acid position 82, a Q at amino acid position 83, an F at amino
 acid position 87, and/or a Q at amino acid position 104.

2. An antibody or an antigen-binding fragment thereof comprising a heavy chain variable domain (VH) and a light chain variable domain (VL),
 wherein said VH domain comprises, essentially consists of, or consists of
 an amino acid sequence according to SEQ ID NO: 17 (QVQLVQSGX⁹E
 X¹¹KKPGASVKX²⁰ SCKASGYSFT TFWMDWVX³⁸QA PGQGLEWX⁴⁸GR
 IDPSDSESRL DQX⁶³FKDRX⁶⁸TX⁷⁰ TVDKSTSTVY MX⁸²LSSX⁸⁶X⁸⁷SED
 X⁹¹AVYYCARGN DGYYGFAYWG QGTLVTVSS), wherein X⁹ is A or P, X¹¹
 is L or V, X²⁰ is I or V, X³⁸ is K or R, X⁴⁸ is I or M, X⁶³ is K or R, X⁶⁸ is A or V,
 X⁷⁰ is L or M, X⁸² is E or Q, X⁸⁶ is L or P, X⁸⁷ is R or T, and X⁹¹ is S or T, or
 an amino acid sequence according to SEQ ID NO: 17 having one, two or three
 amino acid substitutions, wherein said amino acid sequence having one, two or
 three amino acid substitutions comprises the CDR1H, CDR2H, CDR3H
 sequences of SEQ ID NO: 20 to 22, respectively, and
 wherein said VL domain comprises, essentially consists of, or consists of
 an amino acid sequence according to SEQ ID NO: 18 (DIX³X⁴TQSPX⁹S
 LX¹²ASVGDRVT ITCKASQSVD YDGDSYMKWY QQKPGKAPKL
 LIYAASNLS GX⁶²PSRFSGSG SGTDFTLTIS SLQX⁸⁴EDFATY
 YCQQSNEDPY TFGQGTKLEI K), wherein X³ is V or Q, X⁴ is L or M, X⁹ is
 A or S, X¹² is A or S, X⁶² is I or V, and X⁸⁴ is E or P, or
 an amino acid sequence according to SEQ ID NO: 18 having one, two, three,
 four, five, six, or seven amino acid substitutions, wherein said amino acid
 sequence having one, two, three, four, five, six, or seven amino acid substitutions
 comprises the CDR1L, CDR2L, CDR3L sequences of SEQ ID NO: 23 to 25,
 respectively.
3. The antibody or the antigen-binding fragment thereof according to claim 1 or 2,
 wherein said VH domain comprises, essentially consists of, or consists of an amino acid
 sequence selected from the group consisting of VH1 to VH5 (SEQ ID NO: 7 to 11);
 and/or
 said VL domain comprises, essentially consists of, or consists of an amino acid sequence
 selected from the group consisting of Vκ1 to Vκ4 (SEQ ID NO: 13 to 16).
4. The antibody or the antigen-binding fragment thereof according to any one of claims 1
 to 3, wherein said antibody or said antigen-binding fragment thereof comprises:

- a) a VH domain comprising, essentially consisting of, or consisting of an amino acid sequence according to SEQ ID NO: 10 (VH4) and a VL domain comprising, essentially consisting of, or consisting of an amino acid sequence according to SEQ ID NO: 16 (Vk4), or
- 5 b) a VH domain comprising, essentially consisting of, or consisting of an amino acid sequence according to SEQ ID NO: 11 (VH5) and a VL domain comprising, essentially consisting of, or consisting of an amino acid sequence according to SEQ ID NO: 15 (Vk3).
- 10 5. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 4, wherein the antibody is a humanized antibody.
6. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 5, further comprising a constant domain, wherein said constant domain comprises,
- 15 essentially consists of, or consists of an amino acid sequence according to SEQ ID NO: 19 (IgG4 WT constant), wherein said amino acid sequence according to SEQ ID NO: 19 optionally comprises one or more of the following amino acid exchanges:
- an amino acid exchange S108P;
 - 20 - the amino acid exchanges T130Q and M308L;
 - the amino acid exchanges M132Y, S134T, and T136E.
7. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 5, wherein the antigen-binding fragment of an antibody is selected from the group
- 25 consisting of Fab fragments, Fab' fragments, F(ab')₂ fragments, Fd fragments, Fv fragments, disulfide-linked Fvs (dsFv), single domain antibodies and single chain Fv (scFv) antibodies.
8. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 7, wherein said antibody or said antigen-binding fragment thereof exhibits one or
- 30 more of the following properties:
- said antibody or said antigen-binding fragment thereof has a binding constant to C5a with a K_d value of 10 nM or less;

- said antibody or said antigen-binding fragment thereof exhibits at least 75% blocking activity for biological effects induced by one molecule C5a;
- said antibody or said antigen-binding fragment thereof does not inhibit CH50 activity in human plasma;
- 5 – said antibody or said antigen-binding fragment thereof has a reduced immunogenicity as compared to IFX-1.

9. A pharmaceutical composition comprising:
the antibody or antigen-binding fragment thereof according to any one of claims 1 to 8;
10 and
further comprising one or more pharmaceutically acceptable carriers, diluents, excipients, fillers, binders, lubricants, glidants, disintegrants, adsorbents, and/or preservatives.

15 10. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 8 for use in medicine.

11. The compound according to any one of claims 1 to 8 for use in the treatment or prevention of a disease or disorder involving pathological C5a activity.

20 12. The compound for use according to claim 11, wherein the disease or disorder is selected from the group consisting of

- autoimmune disorders,
- inflammatory disorders, auto-inflammatory disorders, or related conditions,
- 25 - cardiovascular or cerebrovascular disorders,
- bacterial or viral infections,
- neurodegenerative disorders or related diseases, and
- cancers or precancerous conditions.

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