

CLAIMS

1. An antibody that binds to IgE, wherein the antibody comprises a variant Fc domain or a FcRn binding fragment thereof that binds to FcRn with increased affinity relative to a wild-type Fc domain, and wherein the variant Fc domain or FcRn binding fragment thereof comprises the amino acids Y, T, E, K, F and Y at EU positions 252, 254, 256, 433, 434 and 436, respectively.
2. The antibody according to claim 1, wherein the variant Fc domain or FcRn binding fragment thereof binds to FcRn with increased affinity relative to a wild-type IgG Fc domain, preferably a wild-type human IgG Fc domain, more preferably a wild-type human IgG1 Fc domain.
3. The antibody according to claim 1 or claim 2, wherein the variant Fc domain or FcRn binding fragment thereof binds to human FcRn with increased affinity at pH 6.0 and pH 7.4.
4. The antibody according to any one of claims 1-3, wherein the binding affinity of the variant Fc domain or FcRn binding fragment thereof for human FcRn at pH 6.0 is stronger than K_D 15 nM, and/or wherein the binding affinity of the variant Fc domain or FcRn binding fragment thereof for human FcRn at pH 7.4 is stronger than K_D 320 nM.
- ~~5. The antibody according to any one of claims 1-4, wherein the variant Fc domain or FcRn binding fragment thereof comprises at least one amino acid selected from the following: 237M; 238A; 239K; 248I; 250A; 250F; 250I; 250M; 250Q; 250S; 250V; 250W; 250Y; 252F; 252W; 252Y; 254T; 255E; 256D; 256E; 256Q; 257A; 257G; 257I; 257L; 257M; 257N; 257S; 257T; 257V; 258H; 265A; 270F; 286A; 286E; 289H; 297A; 298G; 303A; 305A; 307A; 307D; 307F; 307G; 307H; 307I; 307K; 307L; 307M; 307N; 307P; 307Q; 307R; 307S; 307V; 307W; 307Y; 308A; 308F; 308I; 308L; 308M; 308P; 308Q; 308T; 309A; 309D; 309E; 309P; 309R; 311A; 311H; 311I; 312A; 312H; 314K; 314R; 315A; 315H; 317A; 325G; 332V; 334L; 360H; 376A; 378V; 380A; 382A; 384A; 385D; 385H; 386P; 387E; 389A; 389S; 424A; 428A; 428D; 428F; 428G; 428H; 428I; 428K; 428L; 428N; 428P; 428Q; 428S; 428T; 428V; 428W; 428Y; 433K; 434A; 434F; 434H; 434S; 434W; 434Y; 436H; 436I and 436F, wherein the positions are defined in accordance with EU numbering, and/or wherein the variant Fc domain or FcRn binding fragment thereof comprises at least one amino acid substitution selected from: G237M; P238A; S239K; K248I; T250A; T250F; T250I; T250M; T250Q; T250S; T250V; T250W; T250Y; M252F; M252W; M252Y; S254T; R255E; T256D; T256E; T256Q; P257A; P257G; P257I; P257L; P257M; P257N; P257S; P257T; P257V; E258H; D265A; D270F; N286A; N286E; T289H; N297A; S298G; V303A; V305A; T307A; T307D; T307F; T307G; T307H; T307I; T307K; T307L; T307M; T307N; T307P; T307Q; T307R; T307S; T307V; T307W; T307Y; V308A; V308F; V308I; V308L; V308M; V308P; V308Q; V308T; V309A; V309D; V309E; V309P; V309R; Q311A; Q311H; Q311I; D312A; D312H; L314K; L314R; N315A; N315H; K317A; N325G; I332V; K334L; K360H; D376A; A378V; E380A; E382A;~~

N384A; G385D; G385H; Q386P; P387E; N389A; N389S; S424A; M428A; M428D; M428F; M428G; M428H; M428I; M428K; M428L; M428N; M428P; M428Q; M428S; M428T; M428V; M428W; M428Y; H433K; N434A; N434F; N434H; N434S; N434W; N434Y; Y436H; Y436I and Y436F, wherein the positions are defined in accordance with EU numbering.

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6. The antibody according to any one of claims 1-5, wherein the variant Fc domain or FcRn binding fragment thereof comprises the amino acids:

(i) Y, T, E, K, F and Y at EU positions 252, 254, 256, 433, 434 and 436, respectively;

(ii) Q and L at EU positions 250 and 428, respectively;

10 (iii) P and A at EU positions 308 and 434, respectively;

(iv) P and Y at EU positions 308 and 434, respectively; or

(v) Y, E and Y at EU positions 252, 286 and 434, respectively, and/or wherein the variant Fc domain or FcRn binding fragment thereof comprises the amino acid substitutions:

(i) M252Y, S254T, T256E, H433K and N434F;

15 (ii) T250Q and M428L;

(iii) V308P and N434A;

(iv) V308P and N434Y; or

(v) M252Y, N286E and N434Y.

20 57. The antibody according to any one of claims 1-46, wherein the variant Fc domain or FcRn binding fragment thereof comprises the amino acid substitutions M252Y, S254T, T256E, H433K and N434F.

25 68. The antibody according to any one of claims 1-57, wherein the variant Fc domain or FcRn binding fragment thereof does not comprise the combination of amino acids Y, P and Y at EU positions 252, 308 and 434, respectively, or does not comprise the combination of amino acid substitutions: M252Y, V308P and N434Y.

30 9. An antibody that binds to IgE, wherein the antibody comprises a variant Fc domain or a FcRn binding fragment thereof, said variant Fc domain or FcRn binding fragment comprising the amino acids Y, T, E, K, F and Y at EU positions 252, 254, 256, 433, 434 and 436, respectively.

35 710. The antibody according to any one of claims 1-69, wherein the variant Fc domain or FcRn binding fragment thereof is a variant human Fc domain or FcRn binding fragment thereof, preferably a variant IgG Fc domain or FcRn binding fragment thereof, more preferably a variant IgG1 Fc domain or FcRn binding fragment thereof.

811. The antibody according to any one of claims 1-710, wherein the variant Fc domain or FcRn binding fragment thereof consists of no more than 20, optionally no more than 10, or optionally no more than 5 amino acid substitutions as compared with the corresponding wild-type Fc domain.

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912. The antibody according to any one of claims 1-811, wherein the variant Fc domain comprises or consists of the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 3, or wherein the variant Fc domain comprises or consists of the amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7.

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103. The antibody according to any one of claims 1-912, wherein the variant Fc domain or FcRn binding fragment thereof is comprised within a variant Fc region, said variant Fc region consisting of two Fc domains or FcRn binding fragments thereof.

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114. The antibody according to claim 103, wherein the two Fc domains or FcRn binding fragments of the variant Fc region are identical, optionally wherein the two Fc domains of the variant Fc region each comprise or consist of the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 3, or optionally wherein the two Fc domains of the variant Fc region each comprise or consist of the amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7.

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125. The antibody according to claim 103 or claim 114, wherein the variant Fc region has increased affinity for CD16a.

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136. The antibody according to claim 103 or claim 114, wherein the Fc domains of the variant Fc region do not comprise an N-linked glycan at EU position 297, or wherein the Fc domains of the variant Fc region comprise an afucosylated N-linked glycan at EU position 297, or wherein the Fc domains of the variant Fc region comprise an N-linked glycan having a bisecting GlcNac at EU position 297 of the Fc domains.

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147. The antibody according to any one of claims 1-136, wherein the antibody binds to the CH3 domain of IgE, and/or wherein the antibody inhibits binding of IgE to FcεRI, and/or wherein the antibody inhibits mast cell or basophil degranulation.

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158. The antibody according to any one of claims 1-147, wherein the antibody is not anaphylactic.

169. The antibody according to any one of claims 1-158, wherein the antibody exhibits lower antigen-binding activity at acidic pH than at neutral pH, optionally wherein the ratio of antigen-binding activity at acidic pH and at neutral pH is at least 2 as measured by KD(at acidic pH)/KD(at neutral pH).

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1720. The antibody according to claim 169, wherein one or more CDRs comprises one or more His substitutions.

1824. The antibody according to any one of claims 1-1720, wherein the antibody is an IgG antibody, preferably an IgG1 antibody.

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1922. The antibody according to any one of claims 1-1824, wherein the antibody is a humanised or germlined variant of a non-human antibody.

203. The antibody according to claim 1922, wherein the non-human antibody is camelid-derived.

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214. The antibody according to any one of claims 1-203, wherein the antibody comprises a variable heavy chain domain (VH) and a variable light chain domain (VL) wherein the VH and VL domains comprise the CDR sequences selected from the group consisting of:

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(i) HCDR3 comprising SEQ ID NO: 11; HCDR2 comprising SEQ ID NO: 10; HCDR1 comprising SEQ ID NO: 9; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 54;

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(ii) HCDR3 comprising SEQ ID NO: 14; HCDR2 comprising SEQ ID NO: 13; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 58; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 57;

(iii) HCDR3 comprising SEQ ID NO: 17; HCDR2 comprising SEQ ID NO: 16; HCDR1 comprising SEQ ID NO: 15; LCDR3 comprising SEQ ID NO: 61; LCDR2 comprising SEQ ID NO: 60; and LCDR1 comprising SEQ ID NO: 59;

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(iv) HCDR3 comprising SEQ ID NO: 19; HCDR2 comprising SEQ ID NO: 18; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 61; LCDR2 comprising SEQ ID NO: 60; and LCDR1 comprising SEQ ID NO: 59;

(v) HCDR3 comprising SEQ ID NO: 27; HCDR2 comprising SEQ ID NO: 26; HCDR1 comprising SEQ ID NO: 25; LCDR3 comprising SEQ ID NO: 66; LCDR2 comprising SEQ ID NO: 67; and LCDR1 comprising SEQ ID NO: 54;

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(vi) HCDR3 comprising SEQ ID NO: 22; HCDR2 comprising SEQ ID NO: 21; HCDR1 comprising SEQ ID NO: 20; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 69; and LCDR1 comprising SEQ ID NO: 68;

- (vii) HCDR3 comprising SEQ ID NO: 30; HCDR2 comprising SEQ ID NO: 29; HCDR1 comprising SEQ ID NO: 28; LCDR3 comprising SEQ ID NO: 72; LCDR2 comprising SEQ ID NO: 71; and LCDR1 comprising SEQ ID NO: 70;
- (viii) HCDR3 comprising SEQ ID NO: 33; HCDR2 comprising SEQ ID NO: 32; HCDR1 comprising SEQ ID NO: 31; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 54;
- (ix) HCDR3 comprising SEQ ID NO: 22; HCDR2 comprising SEQ ID NO: 23; HCDR1 comprising SEQ ID NO: 34; LCDR3 comprising SEQ ID NO: 63; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 62;
- (x) HCDR3 comprising SEQ ID NO: 37; HCDR2 comprising SEQ ID NO: 36; HCDR1 comprising SEQ ID NO: 35; LCDR3 comprising SEQ ID NO: 75; LCDR2 comprising SEQ ID NO: 74; and LCDR1 comprising SEQ ID NO: 73;
- (xi) HCDR3 comprising SEQ ID NO: 38; HCDR2 comprising SEQ ID NO: 21; HCDR1 comprising SEQ ID NO: 20; LCDR3 comprising SEQ ID NO: 63; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 62;
- (xii) HCDR3 comprising SEQ ID NO: 40; HCDR2 comprising SEQ ID NO: 39; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 78; LCDR2 comprising SEQ ID NO: 77; and LCDR1 comprising SEQ ID NO: 76;
- (xiii) HCDR3 comprising SEQ ID NO: 43; HCDR2 comprising SEQ ID NO: 42; HCDR1 comprising SEQ ID NO: 41; LCDR3 comprising SEQ ID NO: 81; LCDR2 comprising SEQ ID NO: 80; and LCDR1 comprising SEQ ID NO: 79;
- (xiv) HCDR3 comprising SEQ ID NO: 14; HCDR2 comprising SEQ ID NO: 13; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 82;
- (xv) HCDR3 comprising SEQ ID NO: 45; HCDR2 comprising SEQ ID NO: 44; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 66; LCDR2 comprising SEQ ID NO: 55; and LCDR1 comprising SEQ ID NO: 54;
- (xvi) HCDR3 comprising SEQ ID NO: 48; HCDR2 comprising SEQ ID NO: 47; HCDR1 comprising SEQ ID NO: 46; LCDR3 comprising SEQ ID NO: 85; LCDR2 comprising SEQ ID NO: 84; and LCDR1 comprising SEQ ID NO: 83;
- (xvii) HCDR3 comprising SEQ ID NO: 50; HCDR2 comprising SEQ ID NO: 49; HCDR1 comprising SEQ ID NO: 12; LCDR3 comprising SEQ ID NO: 88; LCDR2 comprising SEQ ID NO: 87; and LCDR1 comprising SEQ ID NO: 86; and
- (xviii) HCDR3 comprising SEQ ID NO: 53; HCDR2 comprising SEQ ID NO: 52; HCDR1 comprising SEQ ID NO: 51; LCDR3 comprising SEQ ID NO: 91; LCDR2 comprising SEQ ID NO: 90; and LCDR1 comprising SEQ ID NO: 89.

225. The antibody according to ~~any one of claims 1-214~~, wherein the antibody comprises a variable heavy chain domain (VH) and a variable light chain domain (VL) selected from the group consisting of:

- 5 (i) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 92 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 93 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 10 (ii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 94 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 95 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 15 (iii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 96 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 97 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 20 (iv) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 98 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 99 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 25 (v) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 104 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 30 (vi) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;
- 35 (vii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 109 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ 98%, or 99% identity thereto;

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| | (viii) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 110 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 111 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 5 | (ix) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 112 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 10 | (x) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 15 | (xi) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 117 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 20 | (xii) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 118 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 119 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 25 | (xiii) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 120 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 121 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 30 | (xiv) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 122 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 123 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; |
| 35 | (xv) | a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 124 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ <u>98%, or 99%</u> identity thereto, and a VL domain comprising or consisting of the |

amino acid sequence of SEQ ID NO: 125 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto;

(xvi) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 126 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 127 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto;

(xvii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 128 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto; and

(xviii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 130 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto.

236. The antibody according to any one of claims 1-203, wherein the antibody comprises a variable heavy chain domain (VH) and a variable light chain domain (VL) wherein the VH and VL domains comprise the CDR sequences selected from the group consisting of:

(i) HCDR3 comprising SEQ ID NO: 22; HCDR2 comprising SEQ ID NO: 21; HCDR1 comprising SEQ ID NO: 132; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 69; and LCDR1 comprising SEQ ID NO: 68;

(ii) HCDR3 comprising SEQ ID NO: 22; HCDR2 comprising SEQ ID NO: 21; HCDR1 comprising SEQ ID NO: 20; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 69; and LCDR1 comprising SEQ ID NO: 135; and

(iii) HCDR3 comprising SEQ ID NO: 22; HCDR2 comprising SEQ ID NO: 21; HCDR1 comprising SEQ ID NO: 132; LCDR3 comprising SEQ ID NO: 56; LCDR2 comprising SEQ ID NO: 69; and LCDR1 comprising SEQ ID NO: 135.

247. The antibody according to ~~any one of claims 1-236~~ 1-236, wherein the antibody comprises a variable heavy chain domain (VH) and a variable light chain domain (VL) selected from the group consisting of:

(i) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%~~ 98%, or 99% identity thereto, and a VL domain comprising or consisting of the

amino acid sequence of SEQ ID NO: 107 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto;

(ii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto; and

(iii) a VH domain comprising or consisting of the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto, and a VL domain comprising or consisting of the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto.

258. The antibody according to any one of claims 1-~~203~~, wherein the antibody comprises:

a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 22

[GTSYSGSYYYTDPFFGS];

a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 21

[SIYHDGSHTYYADFVKG];

a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 132 [SYVMH];

a variable light chain CDR3 comprising or consisting of SEQ ID NO: 56 [QSADSSGNPV];

a variable light chain CDR2 comprising or consisting of SEQ ID NO: 69 [DDDRRPS]; and

a variable light chain CDR1 comprising or consisting of SEQ ID NO: 135

[QGDRLGSRYYH].

269. The antibody according to claim 258, wherein the antibody comprises a variable heavy chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto, and a variable light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto, or wherein the antibody comprises a variable heavy chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 173 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto, and a variable light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 174 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%, or 99%~~ identity thereto.

2730. The antibody according to any one of claims 1-~~203~~, wherein the antibody comprises:

a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 22

[GTSYSGSYYYTDPFFGS];

a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 21
[SIYHDGSHTYYADFKVG];
a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 20 [SYVMS];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 56 [QSADSSGNPV];
5 a variable light chain CDR2 comprising or consisting of SEQ ID NO: 69 [DDDRRPS]; and
a variable light chain CDR1 comprising or consisting of SEQ ID NO: 135
[QGDRLGSRVYH].

10 ~~2831~~. The antibody according to claim ~~2730~~, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 106 or an amino acid
sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto, and a variable
light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 138 or an amino
acid sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto, or
15 wherein the antibody comprises a variable heavy chain domain (VH) comprising the amino acid
sequence of SEQ ID NO: 215 or an amino acid sequence having at least 80%, 90%, 95%, ~~98%~~
~~99% 98%, or 99%~~ identity thereto, and a variable light chain domain (VL) comprising the amino
acid sequence of SEQ ID NO: 174 or an amino acid sequence having at least 80%, 90%, 95%,
~~98% 99% 98%, or 99%~~ identity thereto.

20 ~~2932~~. The antibody according to any one of claims 1-~~1922~~, wherein the antibody comprises:
a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 145
[GSHYFGHWHFAV];
a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 144
[SITYDGSTNYPNPSVKG];
25 a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 143 [SGYSWN];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 149 [QQSHEDPYT];
a variable light chain CDR2 comprising or consisting of SEQ ID NO: 148 [AASYLES]; and
a variable light chain CDR1 comprising or consisting of SEQ ID NO: 147
[RASQSVDYDGDSYMN].

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~~303~~. The antibody according to claim ~~2932~~, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 146 or an amino acid
sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto, and a variable
light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 150 or an amino
35 acid sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto.

~~314~~. The antibody according to any one of claims 1-~~1922~~, wherein the antibody comprises:

a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 197
[ATHYFGHWHFAV];
a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 198
[SIHYDHSTNYNPSVKG];
5 a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 195 [SGHRWE];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 201 [QQNAEDPYT];
a variable light chain CDR2 comprising or consisting of SEQ ID NO: 200 [WGSYLRS];
and
a variable light chain CDR1 comprising or consisting of SEQ ID NO: 203
10 [RASQSVDYDGDHYMN].

325. The antibody according to claim 314, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 206 or an amino acid
sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto, and a variable
15 light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 211 or an amino
acid sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto.

336. The antibody according to any one of claims 1-1922, wherein the antibody comprises:
a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 199
20 [ATHYFGHHHFAV];
a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 196
[SIHYDGSTNYNPSVKG];
a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 195 [SGHRWE];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 201 [QQNAEDPYT];
25 a variable light chain CDR2 comprising or consisting of SEQ ID NO: 200 [WGSYLRS];
and
a variable light chain CDR1 comprising or consisting of SEQ ID NO: 147
[RASQSVDYDGD SYMN].

347. The antibody according to claim 336, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 207 or an amino acid
sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto, and a variable
light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 209 or an amino
acid sequence having at least 80%, 90%, 95%, ~~98% 99% 98%, or 99%~~ identity thereto.

358. The antibody according to any one of claims 1-1922, wherein the antibody comprises:
a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 153
[FSHFSGSNYDYFDY];

a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 152
[EIDPGTFTTNYNEKFKA];
a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 151 [WYWLE];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 157
5 [QQSWSWPTT];
a variable light chain CDR2 comprising or consisting of SEQ ID NO: 156 [YASESIS]; and
a variable light chain CDR1 comprising or consisting of SEQ ID NO: 155
[RASQSIGTNIH].

10 ~~369~~. The antibody according to claim ~~358~~, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 154 or an amino acid
sequence having at least 80%, 90%, 95%, ~~98%-99%-98%~~, or 99% identity thereto, and a variable
light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 158 or an amino
acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%~~, or 99% identity thereto.

15 ~~3740~~. The antibody according to any one of claims 1-~~1922~~, wherein the antibody comprises:
a variable heavy chain CDR3 comprising or consisting of SEQ ID NO: 180
[FSHFSGSNHDYFDY];
a variable heavy chain CDR2 comprising or consisting of SEQ ID NO: 152
20 [EIDPGTFTTNYNEKFKA];
a variable heavy chain CDR1 comprising or consisting of SEQ ID NO: 179 [WYHLE];
a variable light chain CDR3 comprising or consisting of SEQ ID NO: 157
[QQSWSWPTT];
a variable light chain CDR2 comprising or consisting of SEQ ID NO: 156 [YASESIS]; and
25 a variable light chain CDR1 comprising or consisting of SEQ ID NO: 155
[RASQSIGTNIH].

~~3841~~. The antibody according to claim ~~3740~~, wherein the antibody comprises a variable heavy
chain domain (VH) comprising the amino acid sequence of SEQ ID NO: 186 or an amino acid
30 sequence having at least 80%, 90%, 95%, ~~98%-99%-98%~~, or 99% identity thereto, and a variable
light chain domain (VL) comprising the amino acid sequence of SEQ ID NO: 158 or an amino
acid sequence having at least 80%, 90%, 95%, ~~98%-99%-98%~~, or 99% identity thereto.

~~3942~~. An isolated polynucleotide or polynucleotides, which encode the antibody of any one of
35 claims 1-~~3841~~.

~~403~~. An expression vector comprising the polynucleotide or polynucleotides of claim ~~3942~~
operably linked to regulatory sequences which permit expression of the antibody.

414. A host cell or cell-free expression system containing the expression vector of claim 403.
- 5 425. A method of producing a recombinant antibody or antigen binding fragment thereof which comprises culturing the host cell or cell free expression system of claim 414 under conditions which permit expression of the antibody or antigen binding fragment and recovering the expressed antibody or antigen binding fragment.
- 10 436. A pharmaceutical composition comprising an antibody according to any one of claims 1-3841 and at least one pharmaceutically acceptable carrier or excipient.
- ~~47. An antibody according to any one of claims 1-41 or a pharmaceutical composition according to claim 46 for use as a medicament.~~
- 15 48. Use of an antibody according to any one of claims 1-41 or a pharmaceutical composition according to claim 46 in the manufacture of a medicament for treating an antibody-mediated disorder in a subject.
- 20 ~~49. The use according to claim 48, wherein the antibody-mediated disorder is an IgE-mediated disorder.~~
- ~~50. The use according to claim 48 or claim 49, wherein the antibody-mediated disorder is an autoimmune disease.~~
- 25 ~~51. The use according to claim 50, wherein the autoimmune disease is selected from the group consisting of allogenic islet graft rejection, alopecia areata, amyloidosis, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, Alzheimer's disease, antineutrophil cytoplasmic autoantibodies (ANCA), autoimmunocytopenia, autoimmune diseases of the adrenal gland, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune myocarditis, autoimmune neutropenia, autoimmune oophoritis and orchitis, autoimmune thrombocytopenia, autoimmune urticaria, Behcet's disease, bullous pemphigoid, cardiomyopathy, Castleman's syndrome, celiac spruce dermatitis, chronic fatigue immune~~
- 30 ~~disfunction syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic inducible urticaria, chronic spontaneous urticaria, Churg-Strauss syndrome, cicatrical pemphigoid, CREST syndrome, cold agglutinin disease, Crohn's disease, dermatomyositis, discoid lupus, essential mixed cryoglobulinemia, factor VIII deficiency, fibromyalgia-fibromyositis, glomerulonephritis, Grave's disease, Guillain-Barre Syndrome, Goodpasture's syndrome, graft versus host disease (GVHD), Hashimoto's thyroiditis, hemophilia A, idiopathic~~
- 35

pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA neuropathy, IgM
polyneuropathies, immune mediated thrombocytopenia, juvenile arthritis, Kawasaki's disease,
lichen planus, systemic lupus erythematosus, lupus nephritis, Meniere's disease, mixed
connective tissue disease, mycosis fungoides, multiple sclerosis, type 1 diabetes mellitus,
5 Multifocal motor neuropathy (MMN), myasthenia gravis, bullous pemphigoid, pemphigus
vulgaris, pemphigus foliaceus, pernicious anemia, polyarteritis nodosa, polychondritis,
polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis,
polyneuritis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic
arthritis, Reynauld's phenomenon, Reiter's syndrome, rheumatoid arthritis, sarcoidosis,
10 scleroderma, Sharp syndrome, Sjorgen's syndrome, solid organ transplant rejection, stiff man
syndrome, systemic lupus erythematosus, takayasu arteritis, toxic epidermal necrolysis (TEN),
Stevens Johnson syndrome (SJS), temporal arteritis/giant cell arteritis, thrombotic
thrombocytopenia purpura, thrombocytopenia purpura, ulcerative colitis, uveitis, dermatitis
herpetiformis vasculitis, anti-neutrophil cytoplasmic antibody associated vasculitides, vitiligo,
15 and Wegener's granulomatosis.

52. The use according to claim 51, wherein the autoimmune disease is chronic spontaneous
urticaria or bullous pemphigoid.