CLAIMS

1. A tetrahedral antibody comprising a first, second, third, and fourth domain, wherein:

a) each of the first and second domains are selected from the group consisting of a Fab domain and an Fc domain,

b) each of the first and second domains comprise:

i) a first polypeptide chain comprising a first N-terminus and a first C-terminus of the domain, and

ii) a second polypeptide chain comprising a second N-terminus and a second C-terminus of the domain,

c) the first domain and the second domain are joined to each other by a non-peptidyl linkage wherein the non-peptidyl linkage is a non-covalent linkage

(1) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the second domain,

(2) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the second domain,

(3) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the second domain, or

(4) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the second domain,

wherein the first and second dimerizing polypeptides are each an ACE2 collectrin-like domain (CLD) dimerizing polypeptide,

d) if the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first N-terminus of the first domain, then the third domain is attached at its C-terminus by a peptide bond or via a peptide linker to

i) the N-terminus of the first dimerizing polypeptide,

ii) the second N-terminus of the first domain, or

iii) the N-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the first domain,

e) if the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first C-terminus of the first domain, then the third domain is attached at its N-terminus by a peptide bond or via a peptide linker to

i) the C-terminus of the first dimerizing polypeptide,

ii) the second C-terminus of the first domain, or

iii) the C-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the first domain,

f) if the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first N-terminus of the second domain, then the fourth domain is attached at its C-terminus by a peptide bond or via a peptide linker to

i) the N-terminus of the second dimerizing polypeptide,

ii) the second N-terminus of the second domain, or

iii) the N-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the second domain,

g) if the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first C-terminus of the second domain, then the fourth domain is attached at its N-terminus by a peptide bond or via a peptide linker to

i) the C-terminus of the second dimerizing polypeptide,

ii) the second C-terminus of the second domain, or

iii) the C-terminus of a fourth dimerizing polypeptide, wherein the fourth dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the second domain.

2. The tetrahedral antibody of claim 1, wherein:

a) the first domain is an Fc domain and the second domain is a Fab domain,

b) the first and second domains are Fc domains,

c) the first and second domains are Fab domains,

d) the third and fourth domains are Fab domains,

e) the third and/or fourth domain are selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein,

f) the third domain is selected from the group of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein, and the fourth domain is a Fab,

g) the third domain is IL-15,

h) the third domain is IL-15 and the fourth domain is an IL-15Rα sushi domain,

i) the third domain is IL-15 and the fourth domain is a Fab,

j) the third and fourth domains are each the ACE2 peptidase domain (PD),

k) the first and second domains are Fc domains, and the third and fourth domains are selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein,

l) the first and second domains are Fc domains, the third domain is selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein, and the fourth domain is Fab,

m) the first and second domains are Fc domains and the third and fourth domains are Fab domains,

n) the first and second domains are Fc domains and the third and fourth domains are each the ACE2 peptidase domain (PD),

o) the first domain is an Fc domain and the second, third and fourth domains are Fab domains,

p) the first domain is an Fc domain, the second domain is a Fab domain, the third domain is IL-15, and the fourth domain is an IL-15Rα sushi domain, or

q) the first domain is an Fc domain, the second domain is a Fab domain, the third domain is IL-15, and the fourth domain is a Fab domain.

3. The tetrahedral antibody of claim 1, wherein:

a) the first dimerizing polypeptide is the same as the second dimerizing polypeptide, and

b) the dimerizing polypeptides form a homodimer.

4. The tetrahedral antibody of claim 3, wherein the first dimerizing polypeptide comprises one or more disulfide bonds with the second dimerizing polypeptide, preferably wherein:

a) the one or more disulfide bonds are at the interface between the first and second dimerizing polypeptides, more preferably wherein:

i) if the first and second dimerizing polypeptides are collectrin-like domain or collectrin, and the one or more disulfide bonds are in the second and fourth helices of the collectrin-like domain or corresponding region in collectrin, or

b) the one or more disulfide bonds are between an immunoglobulin hinge region, or portion thereof comprising at least one cysteine, appended at the N-terminus and/or C-terminus of the first and second dimerizing polypeptides, wherein said hinge regions are appended directly to the first and second dimerizing polypeptides or via peptide linkers, preferably wherein the first and second dimerizing polypeptides are collectrin-like domain or collectrin.

5. The tetrahedral antibody of claim 1, additionally comprising a fifth and/or sixth domain, wherein:

a) the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first N-terminus of the first domain, and wherein

i) the fifth domain is attached at its C-terminus by a peptide bond or via a peptide linker to:

(1) the N-terminus of the first dimerizing polypeptide,

(2) the second N-terminus of the first domain, or

(3) the N-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the first domain,

b) the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first C-terminus of the first domain, and wherein

i) the fifth domain is attached at its N-terminus by a peptide bond or via a peptide linker to:

(1) the C-terminus of the first dimerizing polypeptide,

(2) the second C-terminus of the first domain, or

(3) the C-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the first domain,

c) the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first N-terminus of the second domain, and wherein

i) the sixth domain is attached at its C-terminus by a peptide bond or via a peptide linker to:

(1) the N-terminus of the second dimerizing polypeptide,

(2) the second N-terminus of the second domain, or

(3) the N-terminus of a fourth dimerizing polypeptide, wherein the fourth dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the second domain, or

d) the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first C-terminus of the second domain, and wherein

i) the sixth domain is attached at its N-terminus by a peptide bond or via a peptide linker to:

(1) the C-terminus of the second dimerizing polypeptide,

(2) the second C-terminus of the second domain, or

(3) the C-terminus of a fourth dimerizing polypeptide, wherein the fourth dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the second domain.

6. The tetrahedral antibody of claim 5, wherein:

a) the first and second domains are Fc domains and the fifth domain is a first type of Fab domain,

b) the first and second domains are Fc domains, and the third and fifth domains are independently selected from the group consisting of a first type of Fab domain and a second type of Fab domain,

c) the first and second domains are Fc domains, and the fourth and fifth domains are independently selected from the group consisting of a first type of Fab domain and a second type of Fab domain,

d) the first and second domains are Fc domains, and the third, fourth, and fifth domains are independently selected from the group consisting of a first type of Fab domain, a second type of Fab domain, and a third type of Fab domain,

e) the first domain is an Fc domain, and the second and fifth domains are independently selected from the group consisting of a first type of Fab domain and a second type of Fab domain,

f) the first domain is an Fc domain, and the second, third, and fifth domains are independently selected from the group consisting of a first type of Fab domain, a second type of Fab domain, and a third type of Fab domain,

g) the first domain is an Fc domain, and the second, fourth, and fifth domains are independently selected from the group consisting of a first type of Fab domain, a second type of Fab domain, and a third type of Fab domain,

h) the first domain is an Fc domain, and the second, third, fourth, and fifth domains are independently selected from the group consisting of a first type of Fab domain, a second type of Fab domain, a third type of Fab domain, and a fourth type of Fab domain, or

i) the first and second domains are Fc domains, the third and fourth domains are the ACE2 peptidase domain (PD), and the fifth and sixth domains are Fab domains.

7. The tetrahedral antibody of claim 5, further comprising a seventh and/or eight domain, wherein:

a) the first domain is joined to the second domain via a covalent linkage attached to the first N-terminus of the first domain or via a first dimerizing polypeptide attached to the first N-terminus of the first domain, and wherein

i) the seventh domain is attached at its N-terminus by a peptide bond or via a peptide linker to:

(1) the first C-terminus of the first domain, or

(2) the second C-terminus of the first domain,

b) the first domain is joined to the second domain via a covalent linkage attached to the first C-terminus of the first domain or via a first dimerizing polypeptide attached to the first C-terminus of the first domain, and wherein

i) the seventh domain is attached at its C-terminus by a peptide bond or via a peptide linker to:

(1) the first N-terminus of the first domain, or

(2) the second N-terminus of the first domain,

c) the second domain is joined to the first domain via a covalent linkage attached to the first N-terminus of the second domain or via a second dimerizing polypeptide attached to the first N-terminus of the second domain, and wherein

i) the eighth domain is attached at its N-terminus by a peptide bond or via a peptide linker to:

(1) the first C-terminus of the second domain, or

(2) the second C-terminus of the second domain, or

d) the second domain is joined to the first domain via a covalent linkage attached to the first C-terminus of the second domain or via a second dimerizing polypeptide attached to the first C-terminus of the second domain, and wherein

i) the eighth domain is attached at its C-terminus by a peptide bond or via a peptide linker to:

(1) the first N-terminus of the second domain, or

(2) the second N-terminus of the second domain.

8. The tetrahedral antibody of claim 5, wherein:

a) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains and the fifth and sixth domains are anti-CD19 Fab domains;

b) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains and the fifth and sixth domains are anti-CD20 Fab domains;

c) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains, the fifth and sixth domains are anti-CD19 Fab domains, and each dimerizing polypeptide is an ACE2 CLD;

d) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains and the fifth and sixth domains are anti-CD20 Fab domains, and each dimerizing polypeptide is an ACE2 CLD;

e) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains, the fifth and sixth domains are anti-CD19 Fab domains, each dimerizing polypeptide is an ACE2 CLD, and the first and second domains are each connected to their respective dimerizing polypeptides via a peptide linker;

f) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains and the fifth and sixth domains are anti-CD20 Fab domains, each dimerizing polypeptide is an ACE2 CLD, and the first and second domains are each connected to their respective dimerizing polypeptides via a peptide linker.

9. The tetrahedral antibody of claim 8, wherein:

a) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains and the fifth and sixth domains are anti-CD19 Fab domains, and the seventh and eighth domains are single chain 4-1BB ligands;

b) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains, the fifth and sixth domains are anti-CD20 Fab domains, and the seventh and eighth domains are single chain 4-1BB ligands;

c) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains, the fifth and sixth domains are anti-CD19 Fab domains, the seventh and eighth domains are single chain 4-1BB ligands, and each dimerizing polypeptide is an ACE2 CLD;

d) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains and the fifth and sixth domains are anti-CD20 Fab

domains, the seventh and eighth domains are single chain 4-1BB ligands, and each dimerizing polypeptide is an ACE2 CLD;

e) the first and second domains are Fc domains, the third and fourth domains are anti-CD20 Fab domains, the fifth and sixth domains are anti-CD19 Fab domains, the seventh and eighth domains are single chain 4-1BB ligands, each dimerizing polypeptide is an ACE2 CLD, and the first and second domains are each connected to their respective dimerizing polypeptides via a peptide linker; or

f) the first and second domains are Fc domains, the third and fourth domains are anti-CD19 Fab domains and the fifth and sixth domains are anti-CD20 Fab domains, the seventh and eighth domains are single chain 4-1BB ligands, each dimerizing polypeptide is an ACE2 CLD, and the first and second domains are each connected to their respective dimerizing polypeptides via a peptide linker.

10. The tetrahedral antibody of claim 8, wherein:

a) the anti-CD19 Fab domain comprises

i) the CDRs of each of the heavy and lights chains of FMC63, preferably wherein the anti-CD19 Fab is the Fab domain of FMC63;

ii) the CDRs of each of the heavy and lights chains of FMC60, preferably wherein the anti-CD19 Fab is the Fab domain of FMC60; or

iii) the CDRs of each of the heavy and lights chains of FMC59, preferably wherein the anti-CD19 Fab is the Fab domain of FMC59; and/or

b) the anti-CD20 Fab domain comprises the CDR of rituximab, preferably wherein the anti-CD20 Fab is the Fab domain of rituximab.

11. The tetrahedral antibody of claim 8, wherein the Fc domains are characterized by one or more or all of the following features:

a) are heterodimers,

b) are IgG1 Fc domains,

c) comprise a silencing mutation such that the Fc domain lacks Fc gamma receptor binding activity, preferably wherein such mutation is one of the following combinations of mutations:

i) P329G/L234A/L235A (PGLALA),

ii) L234A/L235A (LALA),

iii) P331S/ L234A/L235A,

iv) L234F/L235E/P331S, and

v) L234F/L235E/P329G,

d) comprise a mutation that enhances FcRn activity, preferably wherein such mutation extends the half-life of the tetrahedral antibody, preferably wherein the mutation is a combination the following mutations: L309D/Q311H/N434S (DHS), and

e) comprise a mutation that ablates their Protein A binding site, preferably wherein such mutation is H435R/Y436F (HY/RF).

12. The tetrahedral antibody of claim 8, wherein the peptide linkers each have a length of 23 amino acids and are derived from the stalk region of a TNF receptor, preferably wherein the TNF receptor is TNF receptor 1B, still more preferably wherein the peptide linker consists of the amino acid sequence set forth in SEQ ID NO: 4468.

13. The tetrahedral antibody of claim 8, wherein the dimerizing polypeptides are each an ACE2 CLD, and wherein each ACE2 CLD comprises or consists of amino acids 616-740 of the ACE2 protein.

14. The tetrahedral antibody of claim 8, wherein such domains and peptide linkers are formed by four different types of polypeptide chains, preferably wherein the four different types of polypeptide chains are denoted L1, H1, L2, and H2, and wherein:

a) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 733, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 707, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 734, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 708, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

b) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 709, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 736, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 710, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

c) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 709, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 737, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 711, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

d) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 738, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 712, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 739, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 713, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

e) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 714, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 741, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 715, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences; or

f) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 714, the L2

chain comprises the amino acid sequence set forth in SEQ ID NO: 742, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 716, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

g) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4801, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4721, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4802, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4722, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

h) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4804, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4724, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

i) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4805, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4725, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

j) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4806, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4726, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4807, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4727, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

k) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4808, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4728, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4809, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO:

4729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

l) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4808, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4728, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

m) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4813, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4772, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

n) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4814, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4773, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

o) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4815, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4774, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4813, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4772, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

p) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4815, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4774, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4814, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4773, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

q) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4816, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4775, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4809, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

r) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4816, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4775, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

s) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4817, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4776, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4809, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

t) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4817, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4776, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

u) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4813, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4793, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

v) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4803, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4723,

the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4814, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4794, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

w) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4815, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4774, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4813, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4793, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

x) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4815, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4774, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4814, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4794, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

y) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4819, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4775, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4809, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences

z) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4819, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4775, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

aa) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4820, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4776, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4809, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO:

4729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences; or

bb) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4820, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4776, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences.

15. The tetrahedral antibody of claim 14, wherein the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4819, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 4775, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4810, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 4730, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences.

16. The tetrahedral antibody of claim 9, wherein such domains and peptide linkers are formed by four different types of polypeptide chains, preferably wherein the four different types of polypeptide chains are denoted L1, H1, L2, and H2, and wherein:

a) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 733, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 707, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 734, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 717, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

b) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 709, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 736, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 718, or

wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

c) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 709, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 737, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 719, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

d) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 738, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 712, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 739, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 720, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

e) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 714, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 741, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 721, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

f) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 714, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 742, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 722, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

g) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 733, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 723, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 734, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 724, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

h) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 725, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 736, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 726, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

i) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 735, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 725, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 737, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 727, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

j) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 738, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 728, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 739, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 729, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences;

k) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 730, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 741, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 731, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences; or

l) the L1 chain comprises the amino acid sequence set forth in SEQ ID NO: 740, the H1 chain comprises the amino acid sequence set forth in SEQ ID NO: 730, the L2 chain comprises the amino acid sequence set forth in SEQ ID NO: 742, and the H2 chain comprises the amino acid sequence set forth in SEQ ID NO: 732, or wherein the L1, H1, L2, and H2 chains are variants with at least 90%, preferably at least 95%, more preferably at least 98% identity to said sequences.

17. A polynucleotide which encodes a polypeptide comprising any one of the polypeptide chains of claim 14.

18. A vector comprising polynucleotides which encode polypeptides comprising the four different types of polypeptide chains of claim 14, wherein each polynucleotide is operably linked to a promoter which directs expression of the polynucleotide in a host cell.

19. A vector comprising one or more polynucleotides of claim 16, wherein each polynucleotide is operably linked to a promoter which directs expression of the polynucleotide in a host cell.

20. A host cell comprising the vector of claim 17 or 18.

21. The host cell of claim 19 for use in a method of producing a tetrahedral antibody.

22. A method of producing a tetrahedral antibody, the method comprising recombinantly expressing the four different types of polypeptide chains of claim 14 in a host cell.

23. A method of producing a tetrahedral antibody, the method comprising recombinantly expressing the vector of claim 17 or 18 in a host cell.

24. A method of producing a tetrahedral antibody comprising four different types of polypeptide chains, the method comprising expressing the four different types of polypeptide chains in the host cell of claim 19.

25. A pharmaceutical composition comprising any one of the tetrahedral antibodies of claims 8 to 15 and one or more pharmaceutically acceptable excipients.

26. A method of treating cancer or inflammatory disease in a subject, the method comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 24, preferably wherein the cancer is B cell cancer.

27. A tetrahedral molecule comprising a first, second, third, and fourth domain, wherein:

a) the first and second domains each independently comprise:

i) a first polypeptide chain comprising a first N-terminus and a first C-terminus of the domain, and

ii) optionally a second polypeptide chain comprising a second N-terminus and a second C-terminus of the domain,

b) the first domain and the second domain are joined to each other by a non-covalent linkage

(1) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the second domain,

(2) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the second domain,

(3) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the first domain, and a second dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the second domain, or

(4) between a first dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first C-terminus of the first domain, and a second

dimerizing polypeptide attached by a peptide bond or via a peptide linker to the first N-terminus of the second domain,

wherein the first and second dimerizing polypeptides are each an ACE2 collectrin-like domain (CLD) ,

c) if the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first N-terminus of the first domain, then the third domain is attached at its C-terminus by a peptide bond or via a peptide linker to

i) the N-terminus of the first dimerizing polypeptide,

ii) the second N-terminus of the first domain if present, or

iii) the N-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the first domain if present,

d) if the first domain is joined to the second domain via a first dimerizing polypeptide attached to the first C-terminus of the first domain, then the third domain is attached at its N-terminus by a peptide bond or via a peptide linker to

i) the C-terminus of the first dimerizing polypeptide,

ii) the second C-terminus of the first domain if present, or

iii) the C-terminus of a third dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the first domain if present,

e) if the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first N-terminus of the second domain, then the fourth domain is attached at its C-terminus by a peptide bond or via a peptide linker to

i) the N-terminus of the second dimerizing polypeptide,

ii) the second N-terminus of the second domain if present, or

iii) the N-terminus of a fourth dimerizing polypeptide, wherein the third dimerizing polypeptide is attached at its C-terminus by a peptide bond or via a peptide linker to the second N-terminus of the second domain if present, and

f) if the second domain is joined to the first domain via a second dimerizing polypeptide attached to the first C-terminus of the second domain, then the fourth domain is attached at its N-terminus by a peptide bond or via a peptide linker to

i) the C-terminus of the second dimerizing polypeptide,

ii) the second C-terminus of the second domain if present, or

iii) the C-terminus of a fourth dimerizing polypeptide, wherein the fourth dimerizing polypeptide is attached at its N-terminus by a peptide bond or via a peptide linker to the second C-terminus of the second domain if present.

28. The tetrahedral molecule of claim 26, wherein

a) the first domain is an Fc domain or Fab domain,

b) the first domain is an Fc domain or Fab domain and the second domain is not an Fc domain or Fab domain,

c) the first domain is an Fc domain and the second domain is a Fab domain,

d) the first and second domains are Fc domains,

e) the first and second domains are Fab domain,

f) the second, third and/or fourth domain are selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein,

g) the third domain is selected from the group of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein, and the fourth domain is a Fab,

h) the third domain is IL-15,

i) the third domain is IL-15 and the fourth domain is an IL-15Rα sushi domain,

j) the third domain is IL-15 and the fourth domain is a Fab,

k) the third and fourth domains are each the ACE2 peptidase domain (PD),

l) the first and second domains are Fc domains, and the third and fourth domains are selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein,

m) the first and second domains are Fc domains, the third domain is selected from the group consisting of (i) a secreted protein, and (ii) the extracellular domain of a transmembrane protein, and the fourth domain is Fab,

n) the first and second domains are Fc domains and the third and fourth domains are Fab domains,

o) the first and second domains are Fc domains and the third and fourth domains are each the ACE2 peptidase domain (PD),

p) the first domain is an Fc domain and the second, third and fourth domains are Fab domains,

q) the first domain is an Fc domain, the second domain is a Fab domain, the third domain is IL-15, and the fourth domain is an IL-15Rα sushi domain, or

r) the first domain is an Fc domain, the second domain is a Fab domain, the third domain is IL-15, and the fourth domain is a Fab.

29. A non-naturally occurring fusion protein dimer comprising a dimer of a first dimerizing polypeptide and a second dimerizing polypeptide, wherein:

a) the first dimerizing polypeptide is attached by a peptide bond or via a peptide linker at its N-terminus or C-terminus to a first domain, the second dimerizing polypeptide is optionally attached by a peptide bond or via a peptide linker at its N-terminus or C-terminus to a second domain,

b) the first and second dimerizing polypeptides are selected from the group consisting of:

i) a collectrin-like domain (CLD), and

ii) a collectrin domain (CD),

c) the first dimerizing polypeptide is optionally attached by a peptide bond or via a peptide linker at its remaining free N-terminus or C-terminus to a third domain,

d) the second dimerizing polypeptide is optionally attached by a peptide bond or via a peptide linker at its remaining free N-terminus or C-terminus to a fourth domain, and

e) the non-naturally occurring fusion protein dimer:

i) does not comprise an ACE2 PD at the N-terminal side of either dimerizing polypeptide; and/or

ii) does not comprise an ACE2 transmembrane domain at the C-terminal side of either dimerizing polypeptide.

30. A composition comprising at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the tetrahedral antibody of any of claims 1 to 15 as a proportion (w/w) of peptide-containing molecules in the composition.

31. A pharmaceutical composition comprising the composition of claim 29 and one or more pharmaceutically acceptable excipients.

32. The tetrahedral antibody of any one of claims 1 to 3, wherein the first domain is an Fc domain, and the second, third, and fourth domains are Fab domain, wherein:

a) the third and fourth domains comprise a first type of Fab and the second domain comprise a second type of Fab,

i) the first type of Fab is formed by a VH-CH on a H1 or H2 chain, and a VL-CL on a L1 chain, and the second type of Fab is formed by a VL-CH on a H1 chain, and a VH-CL domain on a L2 chain;

ii) the first type of Fab is formed by a VL-CH on a H1 or H2 chain, and a VH-CL on a L1 chain, and the second type of Fab is formed by a VH-CH on a H2 chain, and a VL-CL domain on a L2 chain, or

iii) the first type of Fab is formed by a VH-CH on a H1 or H2 chain, and VL-CL on a L1 chain, and the second type of Fab is formed by a VH-CH on a H2 chain, and a VL-CL domain on a L2 chain,

wherein VL is a kappa and/or lambda light chain V region, and/or

b) the third and fourth domains comprise a first type of Fab and the second domain comprise a second type of Fab, and

i) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations V133E and Q39K in its light chain portion;

ii) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations V133E and Q39E in its light chain portion;

iii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations V133E and Q39K in its light chain portion;

iv) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38K and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations S176E and Q39E in its light chain portion;

v) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations S176E and Q39K in its light chain portion;

vi) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations S176E and Q39E in its light chain portion;

vii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations S176E and Q39K in its light chain portion; or

viii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38K and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations S176E and Q39E in its light chain portion.

33. The tetrahedral antibody of claim 5, wherein the third, fourth, fifth, and sixth domains are Fab domains, wherein

a) the third and fourth domain comprise a first type of Fab, and the fifth and/or sixth domain comprise a second type of Fab, and

i) the first type of Fab is formed by a VH-CH on a H1 chain, and a VL-CL domain on a L1 chain, and the second type of Fab is formed by a VL-CH on a H2 chain, and a VH-CL on a L2 chain;

ii) the first type of Fab is formed by a VL-CH on a H1 chain, and a VH-CL domain on a L1 chain, and the second type of Fab is formed by a VH-CH on a H2 chain, and a VL-CL on a L2 chain; or

iii) the first type of Fab is formed by a VH-CH on a H1 chain, and a VL-CL domain on a L1 chain, and the second type of Fab is formed by a VH-CH on a H2 chain, and a VL-CL on a L2 chain,

wherein VL is a kappa and/or lambda light chain V region, and/or

b) the third and fourth domain comprise a first type of Fab, and the fifth and/or sixth domain comprise a second type of Fab, and

i) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations V133E and Q39K in its light chain portion;

ii) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations V133E and Q39E in its light chain portion;

iii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38E and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations V133E and Q39K in its light chain portion;

iv) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38K and V133K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations S176E and Q39E in its light chain portion;

v) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations S176E and Q39K in its light chain portion;

vi) one type of Fab comprises the mutations Q39K and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its

heavy chain portion, and the mutations S176E and Q39E in its light chain portion;

vii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38E and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38E in its heavy chain portion, and the mutations S176E and Q39K in its light chain portion; or

viii) one type of Fab comprises the mutations Q39E and S183E in its heavy chain portion, and the mutations Q38K and S176K in its light chain portion, and the other type of Fab comprises the mutations S183K and Q38K in its heavy chain portion, and the mutations S176E and Q39E in its light chain portion.