CLAIMS

1. A multispecific antibody or antigen-binding fragment thereof capable of stimulating the enzymatic activity of FIXa towards FX comprising a first antigen-binding site capable of binding to FIX (SEQ ID NO:1) and/or the activated form thereof (FIXa), and a second antigen-binding site capable of binding to FX (SEQ ID NO:2) and/or the activated form thereof (FXa) wherein

the first antigen-binding site is capable of binding to an epitope comprising amino acid residues L337, R338, S339, T340 and K341 of FIX(a), and wherein

the second antigen-binding site is capable of binding an epitope comprising amino acid residues

i) E103, Q104, V108, R113, T116, L117, D119, I125, T127, E228, F229, Y230, E266, R287, P291, I292, P304, L419, K420, D423, R424, M426, K427 and T428 of FX(a)

or

ii) E103, Q104, V108, R113, T116, L117, A118, D119, I125, T127, S227, E228, Y230, R287, I292, L303, P304, L419, K420, D423, R424, M426, K427 and T428 of FX(a).

2. The antibody or antigen-binding fragment thereof according to claim 1, wherein the first antigen-binding site comprises

a. a paratope comprising amino acid residues H30, D31, W53, S102, S104, Y106 and N107 in the heavy chain variable domain (SEQ ID NO:51) and amino acid residues Y91 and S92 in the light chain variable domain (SEQ ID NO:55), optionally comprising one or two substitution(s) in the nine recited paratope amino acid residues,

and the second antigen-binding site comprises

b. a paratope comprising amino acid residues K23, G24, S25, G26, Y27, W33, D52, S54, D55, Y57, S77, L99, H100, Y101, Y102, N103 and S104 in the heavy chain variable domain (SEQ ID NO:483) and amino acid residues S30, S31, Y33, Y50, Q52, S54, R55, R57, Y92 and D94 in the light chain variable domain (SEQ ID NO:487), optionally comprising one, two or three substitutions in the 27 recited paratope amino acid residues, or

c. a paratope comprising amino acid residues K23, S25, G26, Y27, F29, W33, D52, S54, D55, F57, S77, H100, Y101, Y102, N103 and S104 in the heavy chain variable domain (SEQ ID NO:467) and amino acid residues V29, S30, S31, Y33, Y50, Q52, S54, R55, R57 and D94 in the light chain variable domain (SEQ ID NO:471), optionally comprising one, two or three substitutions in the 26 recited paratope amino acid residues.

3. The antibody or antigen-binding fragment thereof according to claim 2, wherein said substitutions are conservative substitutions.

4. A multispecific antibody or antigen-binding fragment thereof capable of binding to FIX (SEQ ID NO:1) and/or the activated form thereof (FIXa), and capable of binding to FX (SEQ ID NO:2) and/or the activated form thereof (FXa), wherein said multispecific antibody comprises an anti-FIX(a) antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, and an anti-FX(a) antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein

a. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:36, 37 and 38, respectively, and
   the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:40, 41 and 42, respectively, and
   the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
   the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473 and 474, respectively, or
b. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:36, 37 and 38, respectively, and
   the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:40, 41 and 42, respectively, and
   the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:484, 485 and 486, respectively, and
   the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:488, 489 and 490, respectively, or
c. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:44, 45 and 46, respectively, and
   the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:48, 49 and 50, respectively, and
   the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
   the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473 and 474, respectively, or
d. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:52, 53 and 54, respectively, and

the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:56, 57 and 58, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473 and 474, respectively, or

e. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:52, 53 and 54, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:56, 57 and 58, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:484, 485 and 486, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:488, 489 and 490, respectively, or

f. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:68, 69 and 70, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:72, 73 and 74, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473 and 474, respectively, or

g. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:68, 69 and 70, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:72, 73 and 74, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:484, 485 and 486, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:488, 489 and 490, respectively, or

h. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1203, 1204 and 1205, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1207, 1208 and 1209, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and

the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively, or

i. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1211, 1212 and 1213, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1215, 1216 and 1217, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively, or

j. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1219, 1220 and 1221, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1223, 1224 and 1225, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively, or

k. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1227, 1228 and 1229, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1231, 1232 and 1233, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively, or

l. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1235, 1236 and 1237, respectively, and
the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1239, 1240 and 1241, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively, or

m. the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1243, 1244 and 1245, respectively, and

the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:1247, 1248 and 1249, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and
the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473, and 474, respectively.

5. The antibody or antigen-binding fragment thereof according to claim 4, wherein the anti-FIX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:52, 53 and 54, respectively, and the anti-FIX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:56, 57 and 58, respectively, and
the anti-FX(a) antibody heavy chain CDR1-3 sequences are identified by SEQ ID NOs:468, 469 and 470, respectively, and the anti-FX(a) antibody light chain CDR1-3 sequences are identified by SEQ ID NOs:472, 473 and 474, respectively.

6. The antibody or antigen-binding fragment thereof according to claim 4, wherein the anti-FIX(a) antibody or antigen-binding fragment thereof comprises

a. a heavy chain variable domain identified by SEQ ID NO:35 and a light chain variable domain identified by SEQ ID NO:39, or
b. a heavy chain variable domain identified by SEQ ID NO:43 and a light chain variable domain identified by SEQ ID NO:47, or
c. a heavy chain variable domain identified by SEQ ID NO:51 and a light chain variable domain identified by SEQ ID NO:55, or
d. a heavy chain variable domain identified by SEQ ID NO:67 and a light chain variable domain identified by SEQ ID NO:71, or
e. a heavy chain variable domain identified by SEQ ID NO:1202 and a light chain variable domain identified by SEQ ID NO:1206, or
f. a heavy chain variable domain identified by SEQ ID NO:1210 and a light chain variable domain identified by SEQ ID NO:1214, or
g. a heavy chain variable domain identified by SEQ ID NO:1218 and a light chain variable domain identified by SEQ ID NO:1222, or
h. a heavy chain variable domain identified by SEQ ID NO:1226 and a light chain variable domain identified by SEQ ID NO:1230, or
i. a heavy chain variable domain identified by SEQ ID NO:1234 and a light chain variable domain identified by SEQ ID NO:1238, or

j. a heavy chain variable domain identified by SEQ ID NO:1242 and a light chain variable domain identified by SEQ ID NO:1246,

and wherein the anti-FX(a) antibody or antigen-binding fragment thereof comprises

k. a heavy chain variable domain identified by SEQ ID NO:467 and a light chain variable domain identified by SEQ ID NO:471, or

l. a heavy chain variable domain identified by SEQ ID NO:483 and a light chain variable domain identified by SEQ ID NO:487;

or

wherein both said heavy chain variable domain and light chain variable domain in said anti-FIX(a) antibody or antigen-binding fragment thereof and said anti-FX(a) antibody or antigen-binding fragment thereof are at least 96, 97, 98, 99, 99.1 or 99.2 % identical to the recited SEQ ID NOs.

7. The antibody or antigen-binding fragment thereof according to any of claims 4-6, wherein the anti-FIX(a) antibody or antigen-binding fragment thereof comprises a heavy chain variable domain identified by SEQ ID NO:51 and a light chain variable domain identified by SEQ ID NO:55, and wherein the anti-FX(a) antibody or antigen-binding fragment thereof comprises a heavy chain variable domain identified by SEQ ID NO:467 and a light chain variable domain identified by SEQ ID NO:471.

8. A bispecific antibody or antigen-binding fragment thereof capable of binding to FIX (SEQ ID NO:1) and/or the activated form thereof (FIXa), and capable of binding to FX (SEQ ID NO:2) and/or the activated form thereof (FXa), wherein said multispecific antibody comprises an anti-FIX(a) antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, and an anti-FX(a) antibody or antigen-binding fragment thereof comprising a heavy chain and a light chain, wherein the anti-FIX(a) antibody or antigen-binding fragment thereof comprises a heavy chain variable domain identified by SEQ ID NO:51 and a light chain variable domain identified by SEQ ID NO:55, and wherein the anti-FX(a) antibody or antigen-binding fragment thereof comprises a heavy chain variable domain identified by SEQ ID NO:467 and a light chain variable domain identified by SEQ ID NO:471.

9. The antibody or antigen-binding fragment thereof according to any of the previous claims wherein said antibody or antigen-binding fragment thereof is a bispecific antibody.

10. The antibody or antigen-binding fragment thereof according to any of the previous claims wherein the isotype of said antibody or antigen-binding fragment thereof is IgG1 or IgG4.

11. The antibody or antigen-binding fragment thereof according to any of the previous claims wherein said antibody or antigen-binding fragment thereof is a procoagulant antibody or antigen-binding fragment thereof.

12. The antibody or antigen-binding fragment thereof according to any of claims 4-11 wherein said antibody or antigen-binding fragment thereof is capable of stimulating the enzymatic activity of FIXa.

13. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof according to any of claims 1-12 and one or more pharmaceutically acceptable carrier(s).

14. A kit comprising (i) the antibody or antigen-binding fragment thereof or composition according to any of the previous claims, optionally comprised by an injection device, and (ii) instructions for use.

15. The antibody or antigen-binding fragment thereof, composition or kit according to any of the previous claims for use in the treatment of haemophilia.

16. The antibody or antigen-binding fragment thereof, composition or kit according to claim 15 for use in the treatment of haemophilia A with or without inhibitors.

17. An antibody or antigen-binding fragment thereof capable of binding to FIX (SEQ ID NO:1) and/or the activated form thereof (FIXa) comprising a heavy chain and a light chain wherein

a. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:36, 37 and 38, respectively, and
   the light chain CDR1-3 sequences are identified by SEQ ID NOs:40, 41 and 42, respectively, or
b. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:44, 45 and 46, respectively, and
   the light chain CDR1-3 sequences are identified by SEQ ID NOs:48, 49 and 50, respectively, or

c. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:52, 53 and 54, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:56, 57 and 58, respectively, or

d. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:68, 69 and 70, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:72, 73 and 74, respectively, or

e. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1203, 1204 and 1205, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1207, 1208 and 1209, respectively, or

f. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1211, 1212 and 1213, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1215, 1216 and 1217, respectively, or

g. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1219, 1220 and 1221, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1223, 1224 and 1225, respectively, or

h. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1227, 1228 and 1229, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1231, 1232 and 1233, respectively, or

i. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1235, 1236 and 1237, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1239, 1240 and 1241, respectively, or

j. the heavy chain CDR1-3 sequences are identified by SEQ ID NOs:1243, 1244 and 1245, respectively, and
the light chain CDR1-3 sequences are identified by SEQ ID NOs:1247, 1248 and 1249, respectively;

wherein said antibody or antigen-binding fragment thereof is an intermediate for use in the manufacture of a bispecific antibody which is capable of binding to FIX and/or

the activated form thereof (FIXa), and capable of binding to FX (SEQ ID NO:2) and/or the activated form thereof (FXa).

18. The antibody or antigen-binding fragment thereof according to claim 17, wherein the antibody or antigen-binding fragment thereof comprises

a. a heavy chain variable domain identified by SEQ ID NO:35 and a light chain variable domain identified by SEQ ID NO:39, or
b. a heavy chain variable domain identified by SEQ ID NO:43 and a light chain variable domain identified by SEQ ID NO:47, or
c. a heavy chain variable domain identified by SEQ ID NO:51 and a light chain variable domain identified by SEQ ID NO:55, or
d. a heavy chain variable domain identified by SEQ ID NO:67 and a light chain variable domain identified by SEQ ID NO:71, or
e. a heavy chain variable domain identified by SEQ ID NO:1202 and a light chain variable domain identified by SEQ ID NO:1206, or
f. a heavy chain variable domain identified by SEQ ID NO:1210 and a light chain variable domain identified by SEQ ID NO:1214, or
g. a heavy chain variable domain identified by SEQ ID NO:1218 and a light chain variable domain identified by SEQ ID NO:1222, or
h. a heavy chain variable domain identified by SEQ ID NO:1226 and a light chain variable domain identified by SEQ ID NO:1230, or
i. a heavy chain variable domain identified by SEQ ID NO:1234 and a light chain variable domain identified by SEQ ID NO:1238, or
j. a heavy chain variable domain identified by SEQ ID NO:1242 and a light chain variable domain identified by SEQ ID NO:1246.

19. The antibody or antigen-binding fragment thereof according to claim 18, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable domain identified by SEQ ID NO:51 and a light chain variable domain identified by SEQ ID NO:55.