WHAT IS CLAIMED:

1. An isolated antibody which competes for binding to human tissue factor with the murine antibody 10H10, wherein the antibody binding domains are adapted to a human framework (FR) region, and having the structure of FR1-CDR1-FR2-CDR2-FR3-CDR3 wherein the FR amino acid sequences are unaltered from the amino acid sequences encoded by human germline gene sequences where the germline is recognized in the IMGT database and the CDR sequences bear not less than 50% sequence identity to the murine 10H10 CDRs represented by SEQ ID NO: 6-11 and 27.

2. The isolated antibody of claim 1, wherein the antibody does not compete with FVIIa for tissue factor binding and does not substantially block the procoagulant, amidolytic activity of the TF-VIIa complex but which does block TF-VIIa mediated signaling as measured by cytokine IL-8 release from MDA-MB-231 cells.

3. The antibody of claim 2, wherein one or more of the CDR sequences are selected from sequences of SEQ ID NO: 6-11 and 27.

4. The antibody of claim 3, wherein the three light chain CDR sequences, L-CDR1, L-CDR2 and L-CDR3 are represented by SEQ ID NO: 9-11, respectively,.

5. The antibody of claim 3, wherein the three heavy chain CDR sequences, H-CDR1, H-CDR2 and H-CDR3 are represented by SEQ ID NO: 6-8, respectively or by SEQ ID NO: 6, 27 and 8, respectively.

6. The antibody of claim 3, wherein L-CDR1, L-CDR2 and L-CDR3 are represented by SEQ ID NO: 9-11, respectively, and the three heavy chain CDR sequences, H-CDR1, H-CDR2 and H-CDR3 are represented by SEQ ID NO: 6-8, respectively or by SEQ ID NO: 6, 27 and 8, respectively.

7. The antibody of claim 1, wherein the human HC variable region frameworks are derived from an IGHV family 1, 3 or 5 member as represented by the IMGT database.

8. The antibody of claim 7, comprising a HC variable region selected from SEQ ID NO: 12-21.

9. The antibody of claim 1, wherein the human LC variable region frameworks are derived from a human IGKV family two or four member.

10. The antibody of claim 9, comprising a LC variable region selected from SEQ ID NO: 22-26.

11. The antibody of claim 1, wherein the human HC variable region frameworks are derived from a human germline gene family selected from IGHV5 and IGKV2.

12. The antibody of claim 1, comprising a HC variable region selected from SEQ ID NO: 12-21 and a human LC variable region selected from SEQ ID NO: 22-26.

13. The antibody of claim 1, comprising a HC variable region having the H-CDR3 of SEQ ID NO: 8, an H-CDR1 having a sequence selected from SEQ ID NO: 6, 62-83; an H-CDR2 having a sequence selected from SEQ ID NO: 7, 27, and 84-107; and a HC FR4 region, optionally, selected from IGVJ4 (SEQ ID NO: 60) or a variant thereof.

14. The antibody of claim 1, comprising a LC variable region having an L-CDR1 having a sequence selected from SEQ ID NO: 9, 108-116; an L-CDR2 having a sequence selected from SEQ ID NO: 10 and 117-120; and an L-CDR3 having a sequence selected from SEQ ID NO: 11 and 121-128; and a LC FR4 region, optionally, selected from IGKJ2 (SEQ ID NO: 61) or a variant thereof.

15. The antibody of claim 1, comprising a HC variable region having the H-CDR3 of SEQ ID NO: 8; an H-CDR1 having a sequence selected from SEQ ID NO: 6, 62-83; an H-CDR2 having a sequence selected from SEQ ID NO: 7, 27, and 84-107; and a HC FR4 region, optionally, selected from IGVJ4 (SEQ ID NO: 60) or a variant thereof, and a LC variable domain having an L-CDR1 having a sequence selected from SEQ ID NO: 9, 108-116; an L-CDR2 having a sequence selected from SEQ ID NO: 10 and 117-120; and an L-CDR3 having a sequence selected from SEQ ID NO: 11 and 121-128; and a LC FR4 region, optionally, selected from IGKJ2 (SEQ ID NO: 61) or a variant thereof.

16. The antibody of claim 1, wherein the HC human framework sequences are derived from IGHV5_a and the HC variable region has the sequence selected from SEQ ID NO: 19, 129-155.

17. The antibody of claim 1, wherein the LC human FR sequences are derived from

IGKV2D40_O1 and the LC variable region has the sequence selected from SEQ ID NO: 23, 157-164.

18. The antibody of claim 1, wherein the HC human framework sequences are derived from IGHV5_a and the HC variable region has the sequence selected from SEQ ID NO: 19, 129-155, the LC human FR sequences are derived from IGKV2D40_O1 and the LC variable domain has the sequence selected from SEQ ID NO: 23, 157-164.

19. The antibody of claim 1 having a binding domain derived from IGHV5_a frameworks, defined as non-CDR positions, an H-CDR3 having the sequence SGYYGNSGFAY (SEQ ID NO: 8) and wherein the sequences at the H-CDR-1 and/or H-CDR-2 positions are given by the formulas:

H-CDR1 $GYTFX_1X_2X_3WIE$ **(I)** (SEQ ID NO: 83)

where X1 is selected from A, D, G, I, L, N, P, R, S, T, V, and Y; X2 is selected from A, P, S, and T and X3 is selected from F, H, and Y; or the sequence may be GFTFITYWIA (SEQ ID NO: 81); and

H-CDR2 $DIX_1PGX_2GX_3TX_4$ **(II)** (SEQ ID NO: 107)

where X1 is selected from I and L, X2 is selected from S and T, X3 is selected from A, F, H, and w; and X4 is selected from D, H, I, L, and N; or where H-CDR2 is DILPASSSTN (SEQ ID NO: 105).

20. The antibody of claim 1 having a binding domain wherein the non-CDR positions are derived from IGKV2D40_O1 frameworks and wherein the sequences at the L-CDR-1 and/or LCDR-2 , and L-CDR3 have the sequences given by the formulas:

L-CDR1 $KSSQSLLX_1X_2X_3\ X_4Q\ X_5NYLT$ **(III)** (SEQ ID NO: 116)

where X1 is selected from F, P, S, T, W, and Y; X2 is selected from F, S, T, R, and V; X3 is selected from A, G, P, S, W, Y, AND V; X4 is selected from G, N, and T; and X5 is selected from K, R, and S;

L-CDR2 X_1ASTRX_2S **(IV)** (SEQ ID NO: 120)

where X1 is selected from H and W; X2 is selected from D, E and S;

L-CDR3 $QNDX_1X_2X_3PX_4T$ **(V)** (SEQ ID NO: 128)

where X1 is selected from D, F, and L; X2 is selected from S, T, and Y; where X3 is selected from W, and Y; and X4 is selected from L, and M.

21. A method of treating a human subject suffering from a condition in which TF-expression and local bioactivity resulting from the TF-expression is directly or indirectly related to the condition to be treated which comprises administering to such a subject in need of such treatment an antibody according to claim 1, 3 19 or 20.

22. A method according to claim 21 wherein the condition is cancer.

23. A method according to claim 22 wherein the cancer is selected from primary solid tumors, metastases; carcinomas, adenocarcinomas, melanomas, liquid tumors, lymphomas, leukemias, myelomas, soft tissue cancers, sarcomas, osteosarcoma, thymoma, lymphosarcoma, fibrosarcoma, leiomyosarcoma, lipomas, glioblastoma, astrosarcoma, cancer of the prostate, breast, ovary, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, thyroid, lung, kidney, or bladder.

24. A method according to claim 21 wherein the condition is selected from benign tumors, hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis

25. A pharmaceutical composition useful in treating a subject comprising an antibody of claim 1, 3, 19 or 20 in a pharmaceutically acceptable preparation.

26. A kit comprising an antibody according to claim 1, 3, 19 or 20 in a stable form and instructions for use.

27. An isolated nucleic acid encoding one or more of the antibody binding domains of an antibody according to claim 1, 3 19 or 20.

28. A vector comprising at least one polynucleotide of claim 27.

29. A host cell comprising the vector of claim 28.

30. The isolated antibody or fragment of claim 1, 3, 19 or 20, having an IgG1 or IgG4 isotype.
31. The isolated antibody or fragment of claim 30, wherein the Fc region comprises human IgG1 isotype where the Kabat positions 239 and 332 (which are 242 And 335 of SEQ ID NO: 167) are modified from the wild-type residues S and D, to D and E mutations in the Fc region.

WHAT IS CLAIMED:

1. An isolated antibody which competes for binding to human tissue factor with the murine antibody 10H10, wherein the antibody binding domains are adapted to a human framework (FR) region, and having the structure of FR1-CDR1-FR2-CDR2-FR3-CDR3 wherein the FR amino acid sequences are unaltered from the amino acid sequences encoded by human germline gene sequences where the germline is recognized in the IMGT database and the CDR sequences bear not less than 50% sequence identity to the murine 10H10 CDRs represented by SEQ ID NO: 6-11 and 27.

2. The isolated antibody of claim 1, wherein the antibody does not compete with FVIIa for tissue factor binding and does not substantially block the procoagulant, amidolytic activity of the TF-VIIa complex but which does block TF-VIIa mediated signaling as measured by cytokine IL-8 release from MDA-MB-231 cells.

3. The antibody of claim 2, wherein one or more of the CDR sequences are selected from sequences of SEQ ID NO: 6-11 and 27.

4. The antibody of claim 3, wherein the three light chain CDR sequences, L-CDR1, L-CDR2 and L-CDR3 are represented by SEQ ID NO: 9-11, respectively,.

5. The antibody of claim 3, wherein the three heavy chain CDR sequences, H-CDR1, H-CDR2 and H-CDR3 are represented by SEQ ID NO: 6-8, respectively or by SEQ ID NO: 6, 27 and 8, respectively.

6. The antibody of claim 3, wherein L-CDR1, L-CDR2 and L-CDR3 are represented by SEQ ID NO: 9-11, respectively, and the three heavy chain CDR sequences, H-CDR1, H-CDR2 and H-CDR3 are represented by SEQ ID NO: 6-8, respectively or by SEQ ID NO: 6, 27 and 8, respectively.

7. The antibody of claim 1, wherein the human HC variable region frameworks are derived from an IGHV family 1, 3 or 5 member as represented by the IMGT database.

8. The antibody of claim 7, comprising a HC variable region selected from SEQ ID NO: 12-21.

9. The antibody of claim 1, wherein the human LC variable region frameworks are derived from a human IGKV family two or four member.

10. The antibody of claim 9, comprising a LC variable region selected from SEQ ID NO: 22-26.

11. The antibody of claim 1, wherein the human HC variable region frameworks are derived from a human germline gene family selected from IGHV5 and IGKV2.

12. The antibody of claim 1, comprising a HC variable region selected from SEQ ID NO: 12-21 and a human LC variable region selected from SEQ ID NO: 22-26.

13. The antibody of claim 1, comprising a HC variable region having the H-CDR3 of SEQ ID NO: 8; an H-CDR1 having a sequence selected from SEQ ID NO: 6, 62-83; an H-CDR2 having a sequence selected from SEQ ID NO: 7, 27, and 84-107; and a HC FR4 region, optionally, selected from IGVJ4 (SEQ ID NO: 60) or a variant thereof.

14. The antibody of claim 1, comprising a LC variable region having an L-CDR1 having a sequence selected from SEQ ID NO: 9, 108-116; an L-CDR2 having a sequence selected from SEQ ID NO: 10 and 117-120; and an L-CDR3 having a sequence selected from SEQ ID NO: 11 and 121-128; and a LC FR4 region, optionally, selected from IGKJ2 (SEQ ID NO: 61) or a variant thereof.

15. The antibody of claim 1, comprising a HC variable region having the H-CDR3 of SEQ ID NO: 8; an H-CDR1 having a sequence selected from SEQ ID NO: 6, 62-83; an H-CDR2 having a sequence selected from SEQ ID NO: 7, 27, and 84-107; and a HC FR4 region, optionally, selected from IGVJ4 (SEQ ID NO: 60) or a variant thereof, and a LC variable domain having an L-CDR1 having a sequence selected from SEQ ID NO: 9, 108-116; an L-CDR2 having a sequence selected from SEQ ID NO: 10 and 117-120; and an L-CDR3 having a sequence selected from SEQ ID NO: 11 and 121-128; and a LC FR4 region, optionally, selected from IGKJ2 (SEQ ID NO: 61) or a variant thereof.

16. The antibody of claim 1, wherein the HC human framework sequences are derived from IGHV5_a and the HC variable region has the sequence selected from SEQ ID

NO: 19, 129-155.

17. The antibody of claim 1, wherein the LC human FR sequences are derived from IGKV2D40_O1 and the LC variable region has the sequence selected from SEQ ID NO: 23, 157-164.

18. The antibody of claim 1, wherein the HC human framework sequences are derived from IGHV5_a and the HC variable region has the sequence selected from SEQ ID NO: 19, 129-155, the LC human FR sequences are derived from IGKV2D40_O1 and the LC variable domain has the sequence selected from SEQ ID NO: 23, 157-164.

19. The antibody of claim 1 having a binding domain derived from IGHV5_a frameworks, defined as non-CDR positions, an H-CDR3 having the sequence SGYYGNSGFAY (SEQ ID NO: 8) and wherein the sequences at the H-CDR-1 and/or H-CDR-2 positions are given by the formulas:

H-CDR1 $GYTFX_1X_2X_3WIE$ **(I)** (SEQ ID NO: 83)

where X1 is selected from A, D, G, I, L, N, P, R, S, T, V, and Y; X2 is selected from A, P, S, and T and X3 is selected from F, H, and Y; or the sequence may be GFTFITYWIA (SEQ ID NO: 81); and

H-CDR2 $DIX_1PGX_2GX_3TX_4$ **(II)** (SEQ ID NO: 107)

where X1 is selected from I and L, X2 is selected from S and T, X3 is selected from A, F, H, and w; and X4 is selected from D, H, I, L, and N; or where H-CDR2 is DILPASSSTN (SEQ ID NO: 105).

20. The antibody of claim 1 having a binding domain wherein the non-CDR positions are derived from IGKV2D40_O1 frameworks and wherein the sequences at the L-CDR-1 and/or LCDR-2 , and L-CDR3 have the sequences given by the formulas:

L-CDR1 $KSSQSLLX_1X_2X_3\ X_4Q\ X_5NYLT$ **(III)** (SEQ ID NO: 116)

where X1 is selected from F, P, S, T, W, and Y; X2 is selected from F, S, T, R, and V; X3 is selected from A, G, P, S, W, Y, AND V; X4 is selected from G, N, and T; and X5 is selected from K, R, and S;

L-CDR2 X_1ASTRX_2S **(IV)** (SEQ ID NO: 120)

where X1 is selected from H and W; X2 is selected from D, E and S;

L-CDR3 $QNDX_1X_2X_3PX_4T$ (V) (SEQ ID NO: 128)

where X1 is selected from D, F, and L; X2 is selected from S, T, and Y; where X3 is selected from W, and Y; and X4 is selected from L, and M.

21. Use of an antibody according to claim 1, 3 19 or 20 in the manufacture of a medicament for treating a human subject suffering from a condition in which TF-expression and local bioactivity resulting from the TF-expression is directly or indirectly related to the condition to be treated.

22. The use according to claim 21 wherein the condition is cancer.

23. The use according to claim 22 wherein the cancer is selected from primary solid tumors, metastases; carcinomas, adenocarcinomas, melanomas, liquid tumors, lymphomas, leukemias, myelomas, soft tissue cancers, sarcomas, osteosarcoma, thymoma, lymphosarcoma, fibrosarcoma, leiomyosarcoma, lipomas, glioblastoma, astrosarcoma, cancer of the prostate, breast, ovary, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, thyroid, lung, kidney, or bladder.

24. The use according to claim 21 wherein the condition is selected from benign tumors, hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis

25. A pharmaceutical composition useful in treating a subject comprising an antibody of claim 1, 3, 19 or 20 in a pharmaceutically acceptable preparation.

26. A kit comprising an antibody according to claim 1, 3, 19 or 20 in a stable form and instructions for use.

27. An isolated nucleic acid encoding one or more of the antibody binding domains of an antibody according to claim 1, 3 19 or 20.

28. A vector comprising at least one polynucleotide of claim 27.

29. A host cell comprising the vector of claim 28.

30. The isolated antibody or fragment of claim 1, 3, 19 or 20, having an IgG1 or IgG4 isotype.

31. The isolated antibody or fragment of claim 30, wherein the Fc region comprises human IgG1 isotype where the Kabat positions 239 and 332 (which are 242 And 335 of SEQ ID NO: 167) are modified from the wild-type residues S and D, to D and E mutations in the Fc region.