Claims

1. Peptide or peptide complex, preferably isolated monoclonal antibody or antigen binding fragment thereof, wherein said peptide or peptide complex, antibody or fragment specifically binds to the I-domain of a human α2-integrin, said antibody or fragment comprising a heavy chain variable region (VH) domain and a light chain variable region (VL) domain, wherein said antibody or fragment cross-reacts with a non-human primate α2-integrin but does not cross-react with a non-primate α2-integrin.

2. Peptide or peptide complex, preferably isolated monoclonal antibody or antigen binding fragment thereof, wherein said peptide or peptide complex, antibody or fragment specifically binds to the I-domain of a human α2-integrin, said antibody comprising a heavy chain variable region (VH) domain and a light chain variable region (VL) domain, wherein said antibody or fragment competes with a reference antibody for binding to the epitope of the reference antibody, said reference antibody comprising a light chain encoded by the plasmid as deposited with the DSMZ under accession No. DSM 23944 and a heavy chain encoded by either (i) the plasmid as deposited with the DSMZ under accession DSM 23946 or (ii) the plasmid as deposited with the DSMZ under accession No. DSM 23945.

3. Peptide or peptide complex preferably isolated monoclonal antibody or antigen binding fragment thereof, comprising one or more of the following components a to f:

a) LCDR1, wherein LDR1 is RASESVESYGNSFIY (SEQ ID NO:6) or a functionally active variant thereof,

b) LCDR2, wherein LDR2 is LASNLAS (SEQ ID NO:7) or a functionally active variant thereof,

c) LCDR3, wherein LDR3 is QQNNEDPYT (SEQ ID NO:8) or a functional active variant thereof,

d) HCDR1, wherein HDR1 is (GYTFTSYWMN, SEQ ID NO:3) or a functionally active variant thereof,

e) HCDR2, wherein HDR2 is RIDPSDSETHYNQKFK (SEQ ID NO:4) or a functionally active variant thereof, and

f) HCDR3, wherein HDR3 is VGRGYFDY (SEQ ID NO:5) or a functional active variant thereof,

and wherein the one or more of the components a) to f) are arranged to allow for binding of the peptide or peptide complex to α2 integrin.

4. Peptide or peptide complex according to one of the claims 1-3,

(i) wherein components a) to c) are comprised in a variable domain of a light chain (VL); and/or

(ii) wherein components d) to f) are comprised in a variable domain of a heavy chain (VH); and/or

(iii) wherein the peptide or peptide complex is an antibody; and/or

(iv) wherein the peptide or peptide complex is a monoclonal antibody, a chimeric antibody, a humanized antibody, a Fab, a Fab', a F(ab')2, a Fv, a disulfide linked Fv, a scFv, a $(scFv)_2$, a single domain antibody, a diabody, a multispecific antibody, a dual specific antibody, a isotype antibody, a dual variable domain antibody and a bispecific antibody; and/or

(v) wherein the peptide or peptide complex comprises a heavy chain immunoglobulin constant domain selected from the group consisting of: a human IgM constant domain, a human IgGl constant domain, a human IgG2 constant domain, a human IgG3 constant domain, domain, a human IgG4 constant domain, a human IgE constant domain, and a human IgA constant domain; and/or

(vi) wherein the functionally active variant is a functionally active fragment consisting of at least 90 % sequence identity to any of the amino acid sequences of SEQ ID NOS: 3 to 8; and/or

(vii) wherein the functionally active variant is a functionally active variant having at least 70 %, preferably at least 80 %, more preferably at least 90 % sequence identity to an amino acid sequence of any of SEQ ID NOS: 3 to 8, particularly wherein the functionally active variant is derived from the amino acid sequences of any of SEQ ID NOS: 3 to 8 one or more conservative amino acid substitution; and/or

(viii) comprising the amino acid sequence of

- SEQ ID NO: 1, or a functionally active variant thereof, and/or
- SEQ ID NO: 2, or a functionally active variant thereof, and/or

- SEQ ID NO: 9, or a functionally active variant thereof, and/or
- SEQ ID NO: 10, or a functionally active variant thereof, and/or
- SEQ ID NO: 11, or a functionally active variant thereof, or

(ix) consisting of the amino acid sequence of

- SEQ ID NO: 1, or a functionally active variant thereof, and
- SEQ ID NO: 2, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30, even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s)

or

(x) consisting of the amino acid sequence of

- SEQ ID NO: 9, or a functionally active variant thereof, and
- SEQ ID NO: 10, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30, even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s)

or

(xi) consisting of the amino acid sequence of

- SEQ ID NO: 9, or a functionally active variant thereof, and
- SEQ ID NO: 11, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30, even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s).

5. Peptide or peptide complex according to one of the claims 1 - 4;

- wherein the functionally active variant of LDR1 comprises the mutation at amino acid position 11, particularly 11Asn→Gln; and/or
- wherein the functionally active variant of HDR2 comprises the mutation at amino acid position 6, particularly 6Asp→Glu; and/or

- wherein the functionally active variant of SEQ ID NO: 1 comprises one or more mutations at amino acid positions 9, 12, 15, 22, 34, 46, 47, 80, 83, 85, 87 and/or 89, particularly selected from the group consisting of 9Ala→Ser, 12Ala→Ser, 15Leu→Val, 15Leu→Pro, 22Ser→Thr, 34Asn→Gln, 46Gln→Lys, 47Ala→Pro, 80Asp→Asn, 83Glu→Gln, 85Asp→Glu, 87Ala→Thr and 89Thr→Asn; and/or
- wherein the functionally active variant of SEQ ID NO: 2 comprises one or more mutations at amino acids positions 5, 7, 11, 12, 17, 20, 38, 40, 43, 55, 61, 65, 66, 67, 76, 81, 82, 87, 91, 93, 112, 113 and/or 116, particularly selected from the group consisting of 5His→Val, 7Pro→Ser, 11Leu→Val, 12Val→Lys, 17Pro→Ser, 20Leu→Val, 38Lys→Arg, 40Arg→Ala, 43Arg→Gln, 55Asp→Glu, 61Asn→Ala, 65Lys→Gln, 66Asp→Gly, 67Lys→Arg, 76Ser→Thr, 81Ile→Met, 82Gln→Glu, 87Thr→Arg, 91Ser→Thr, 93Val→Lys, 112Thr→Leu, 113Leu→Val and 116Ser→Val .

6. The Peptide or peptide complex according to any of the claims 1-5, wherein said antibody or fragment specifically binds to the I-domain of the human α2-integrin with nM binding affinity.

7. The Peptide or peptide complex according to any of the claims 1-6, wherein said peptide or peptide complex inhibits the interaction of the human α2-integrin with collagen *in vitro*, thereby inhibiting the activation of platelets due to adhesion of said platelets to said collagen.

8. The Peptide or peptide complex according to any of the previous claims, said heavy chain variable region domain comprising the heavy chain HCDR3 of SEQ ID NO:5.

9. The Peptide or peptide complex according to any of the previous claims, said heavy chain variable region domain comprising the heavy chain CDRs of SEQ ID NO:3 (HCDR1), SEQ ID NO:4 (HCDR2), and SEQ ID NO:5 (HCDR3), or functionally active variants thereof.

10 .The Peptide or peptide complex according to claim 9, wherein the functionally active variant of HCDR2 comprises the mutation Asp→Glu at amino acid position 6.

11. The Peptide or peptide complex according to any one of the previous claims, said light chain variable region domain comprising the light chain LCDR3 of SEQ ID NO:8.

12. The Peptide or peptide complex according to any one of the previous claims, said light chain variable region domain comprising the light chain CDRs of SEQ ID NO:6 (LCDR1), SEQ ID NO:7 (LCDR2), and SEQ ID NO:8 (LCDR3), or functionally active variants thereof.

13. The Peptide or peptide complex according to claim 12, wherein the functionally active variant of LCDR1 comprises the mutation Asn→Gln at amino acid position 11.

14. The Peptide or peptide complex according to any one of the previous claims, said heavy chain variable region (VH) domain having at least 90%, 95%, 97% or 99% sequence identity to the VH sequence of SEQ ID NO: 2.

15. The Peptide or peptide complex according to claim 14, wherein said heavy chain variable region (VH) domain comprises the sequence of SEQ ID NO:2 or a functionally active variant thereof.

16. The Peptide or peptide complex according to any one of the previous claims, said light chain variable region (VL) domain having at least 90%, 95%, 97% or 99% sequence identity to the VL sequence of SEQ ID NO: 1.

17. The Peptide or peptide complex according to claim 16, wherein said light chain variable region (VL) domain comprises the sequence of SEQ ID NO:1 or a functionally active thereof.

18. The Peptide or peptide complex according to any one of the previous claims, wherein said heavy chain variable region (VH) domain comprises one or more amino acid substitutions at positions selected from the group consisting of H5, H7, H11, H12, H17, H20, H38, H40, H43, H55, H61, H65, H66, H67, H76, H81, H82, H87, H91, H93, H112, H113 and H116.

19. The Peptide or peptide complex according to claim 18, wherein the one or more amino acid subsitutions are selected from the group consisting 5His→Val, 7Pro→Ser, 11Leu→Val, 12Val→Lys, 17Pro→Ser, 20Leu→Val, 38Lys→Arg, 40Arg→Ala, 43Arg→Gln, 55Asp→Glu, 61Asn→Ala, 65Lys→Gln, 66Asp→Gly, 67Lys→Arg, 76Ser→Thr, 81Ile→Met, 82Gln→Glu, 87Thr→Arg, 91Ser→Thr, 93Val→Lys, 112Thr→Leu, 113Leu→Val and 116Ser→Val .

20. The Peptide or peptide complex according to any one of the previous claims, wherein said light chain variable region (VL) domain comprises one or more amino acid substitutions at positions selected from the group consisting of L9, L12, L15, L22, L34, L46, L47, L80, L83, L85, L87, and L89.

21. The Peptide or peptide complex according to claim 20, wherein the one or more amino acid subsitutions are selected from the group consisting of 9Ala→Ser, 12Ala→Ser, 15Leu→Val, 15Leu→Pro, 22Ser→Thr, 34Asn→Gln, 46Gln→Lys, 47Ala→Pro, 80Asp→Asn, 83Glu→Gln, 85Asp→Glu, 87Ala→Thr and 89Thr→Asn.

22. The Peptide or peptide complex according to any one of the previous claims, said heavy chain variable region (VH) domain having at least 90%, 95%, 97% or 99% sequence identity to a VH sequence selected from the group consisting of SEQ ID NO: 38 (HC1), SEQ ID NO:39 (HC2), SEQ ID NO:40 (HC3), SEQ ID NO:41 (HC4), SEQ ID NO:42 (HC5), SEQ ID NO:43 (HC6), and SEQ ID NO:44 (HC7).

23. The Peptide or peptide complex according to claim 22 said heavy chain variable region (VH) domain comprising a VH sequence selected from the group consisting of SEQ ID NO: 38 (HC1), SEQ ID NO:39 (HC2), SEQ ID NO:40 (HC3), SEQ ID NO:41 (HC4), SEQ ID NO:42 (HC5), SEQ ID NO:43 (HC6), and SEQ ID NO:44 (HC7).

23. The Peptide or peptide complex according to any one of the previous claims, said light chain variable region (VL) domain having at least 90%, 95%, 97% or 99% sequence identity to a VL sequence selected from the group consisting of SEQ ID NO: 33 (LC1), SEQ ID NO:34 (LC2), SEQ ID NO:35 (LC3), SEQ ID NO:36 (LC4), and SEQ ID NO:37 (LC5).

25. The Peptide or peptide complex according to claim 24, said light chain variable region (VL) domain comprising a VL sequence selected from the group consisting of SEQ ID NO: 33 (LC1), SEQ ID NO:34 (LC2), SEQ ID NO:35 (LC3), SEQ ID NO:36 (LC4), and SEQ ID NO:37 (LC5).

26. The Peptide or peptide complex according to any one of the previous claims, wherein said antibody or binding portion is a chimeric antibody or humanized antibody.

27. The Peptide or peptide complex according to any one of the previous claims, wherein the antigen binding portion is selected from the group consisting of a Fab, a Fab', a F(ab')2, a Fv, a disulfide linked Fv, a scFv, and a $(scFv)_2$.

28. The Peptide or peptide complex according to any one of the previous claims, which is selected from the group consisting of a multispecific antibody, a dual specific antibody, a isotype antibody, a dual variable domain antibody and a bispecific antibody.

29. The Peptide or peptide complex according to any one of the previous claims, comprising a heavy chain immunoglobulin constant domain selected from the group consisting of: a human IgM constant domain, a human IgGl constant domain, a human IgG2 constant domain, a human

IgG3 constant domain, domain, a human IgG4 constant domain, a human IgE constant domain, and a human IgA constant domain.

30. The Peptide or peptide complex according to any one of the previous claims, comprising a human IgG4 constant domain.

31. The Peptide or peptide complex according to according to any of the previous claims, wherein the peptide or peptide complex comprises or consists of an isolated monoclonal anbitody or antigen binding fragment thereof.

32. One or more nucleic acid(s) coding for the peptide or peptide complex according to any of claims 1 to 31.

33. Peptide or peptide complex according to one of the claims 1-31 for use in the treatment, prophylaxis or diagnosis of an α 2- integrin –related disorder or disease.

34. The nucleic(s) of claim 32, wherein the nucleic acid(s) is/are located in a vector.

35. A cell heterologously expressing one of the nucleic acids according to claims 32 or 34.

36. A method for producing a peptide or peptide complex according to any of claims 1 to 31 comprising culturing the cell according to claim 35 under conditions permitting expression of the peptide or peptide complex and optionally recovering the peptide or peptide complex from the host cell.

37. A pharmaceutical composition comprising at least one peptide or peptide complex according to any of claims 1 to 31 and/or at least one nucleic acid according to claim 32 or 34 for use as a medicament.

38. The pharmaceutical composition of claim 37 for use in treating or preventing an α2 integrin-related disease or disorder, preferably selected from the group consisting of thrombosis, a

vascular disease, cancer, including neo-angiogenesis and metastasis, inflammation, inflammatory disease, autoimmune disease and a disease characterized by abnormal or increase angiogenesis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, reactions to transplant, optical neuritis, spinal cord trauma, rheumatoid arthritis, systemic lupus erythematosus (SLE), multiple sclerosis, Reynaud's syndrome, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, scleroderma, cardiovascular disease, psoriasis, and infections that induce an inflammatory response.

39. The pharmaceutical composition of claim 37 for use in treating or preventing a vascular disease and/or thrombosis, particularly in the treatment of acute coronary syndrome, percutaneous coronary intervention, ischemic stroke, carotid artery stenosis or peripheral arterial occlusive disease.

40. A method of diagnosing a disease associated with altered α2 integrin, the method comprising

a) contacting a sample comprising α2 integrin with the peptide or peptide complex of any of claims 1 to 31; and

b) detecting binding of α2 integrin to the peptide or peptide complex; and

c) comparing the binding of step b) with a reference,

wherein a altered α2 integrin binding in the sample relative to the reference is indicative of the disease.

41. Article of manufacture comprising

a) a packaging material,

b) a peptide or peptide complex according to one of the claims 1-31 or 33 or a pharmaceutically acceptable salt thereof or comprising the pharmaceutical composition of one of the claims 36-38

c) a label or a package insert, the insert contained within said packaging material, indicating that said peptide or peptide complex is effective for treatment of a disease or disorder, especially an α 2 integrin-related disease disorder.

42. Diagnostic kit for the diagnosis of an α 2-integrin related disorder or disease comprising a peptide or peptide complex according to one of the claims 1-31 and a suitable packaging, and possibly suitable instructions for using said peptide or peptide complex in the detection of α 2 integrin.

43. Method of treatment or diagnosis of an α 2 integrin-related disorder or disease using one or more peptide or peptide complex according to one of the claims 1-31 and/or one or more nucleic acids according to claim 32 or 34 or one of the pharmaceutical compositions according to one of claims 36-38.

44. A method of diagnosing a disease associated with altered α2 integrin, the method comprising

a) contacting a taken sample of an individual with the peptide or peptide complex of any of claims 1 to 31; and

b) detecting binding of α2 integrin to the peptide or peptide complex; and

c) comparing the binding of step b) with the binding of α2 integrin to the peptide or peptide complex in one or more reference samples,

wherein an altered binding in the taken sample relative to the binding detected in the one or more reference samples is indicative of the disease.

CLAIMS

1. Isolated monoclonal antibody or antigen binding fragment thereof, wherein said antibody or fragment specifically binds to the I-domain of a human α2-integrin, said antibody comprising a heavy chain variable region (VH) domain and a light chain variable region (VL) domain, wherein said antibody or fragment competes with a reference antibody for binding to the epitope of the reference antibody, said reference antibody comprising a light chain being the variable domain and the constant domain according to SEQ ID NO: 9 and a heavy chain being the variable domain and the constant domain according to SEQ ID NO: 10 or being the variable domain and the constant domain according to SEQ ID NO: 11.

2. The isolated monoclonal antibody or antigen binding fragment thereof of claim 1, wherein said antibody or fragment cross-reacts with a non-human primate α2-integrin but does not cross-react with a non-primate α2-integrin.

3. The isolated monoclonal antibody or antigen binding fragment thereof of claim 1 or 2, comprising one or more of the following components a to f:

a) LCDR1, wherein LCDR1 is RASESVESYGNSFIY (SEQ ID NO:6) or a functionally active variant thereof,

b) LCDR2, wherein LCDR2 is LASNLAS (SEQ ID NO:7) or a functionally active variant thereof,

c) LCDR3, wherein LCDR3 is QQNNEDPYT (SEQ ID NO:8) or a functional active variant thereof,

d) HCDR1, wherein HCDR1 is (GYTFTSYWMN, SEQ ID NO:3) or a functionally active variant thereof,

e) HCDR2, wherein HCDR2 is RIDP SD SETH YNQKFK (SEQ ID NO:4) or a functionally active variant thereof, and

f) HCDR3, wherein HCDR3 is VGRGYFDY (SEQ ID NO:5) or a functional active variant thereof,

and wherein the one or more of the components a) to f) are arranged to allow for binding of the antibody or fragment to α2-integrin, and wherein said variants have at least 10% of the α2-integrin binding activity of the corresponding peptides without sequence alteration.

4. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-3,

(i) wherein components a) to c) are comprised in a variable domain of a light chain (VL); and/or

(ii) wherein components d) to f) are comprised in a variable domain of a heavy chain (VH); and/or

(iii) wherein the antibody or fragment is a chimeric antibody, a humanized antibody, a Fab, a Fab', a F(ab')2, a Fv, a disulfide linked Fv, a scFv, a (scFv)2, a single domain antibody, a diabody, a multispecific antibody, a dual specific antibody, an isotype antibody, a dual variable domain antibody and a bispecific antibody; and/or

(iv) wherein the antibody or fragment comprises a heavy chain immunoglobulin constant domain selected from the group consisting of: a human IgM constant domain, a human IgG1 constant domain, a human IgG2 constant domain, a human IgG3 constant domain, domain, a human IgG4 constant domain, a human IgE constant domain, and a human IgA constant domain; and/or

(v) wherein the functionally active variant is a functionally active fragment consisting of at least 90 % sequence identity to any of the amino acid sequences of SEQ ID NOS: 3 to 8; and/or

(vi) wherein the functionally active variant is a functionally active variant having at least 70 %, preferably at least 80 %, more preferably at least 90 % sequence identity to an amino acid sequence of any of SEQ ID NOS: 3 to 8, particularly wherein the functionally active variant is derived from the amino acid sequences of any of SEQ ID NOS: 3 to 8 with one or more conservative amino acid substitution; and/or

(vii) comprising the amino acid sequence of

- SEQ ID NO: 1, or a functionally active variant thereof, and/or
- SEQ ID NO: 2, or a functionally active variant thereof, and/or
- SEQ ID NO: 9, or a functionally active variant thereof, and/or
- SEQ ID NO: 10, or a functionally active variant thereof, and/or
- SEQ ID NO: 11, or a functionally active variant thereof, or
- (viii) consisting of the amino acid sequence of
- SEQ ID NO: 1, or a functionally active variant thereof, and
- SEQ ID NO: 2, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30,

even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s) or

(ix) consisting of the amino acid sequence of

- SEQ ID NO: 9, or a functionally active variant thereof, and
- SEQ ID NO: 10, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30, even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s) or

(x) consisting of the amino acid sequence of

- SEQ ID NO: 9, or a functionally active variant thereof, and
- SEQ ID NO: 11, or a functionally active variant thereof, and
- optionally 50 additional amino acid residue(s), preferably 1 to 40, more preferably 1 to 30, even more preferably at most 1 to 25, still more preferably at most 1 to 10, most preferably 1, 2, 3, 4 or 5 additional amino acids residue(s);

wherein said variants have at least 10% of the α2-integrin binding activity of the corresponding peptides without sequence alteration.

5. The isolated monoclonal antibody or antigen binding fragment thereof according claim 3 or 4;

- wherein the functionally active variant of LCDR1 comprises the mutation at amino acid position 11, particularly HAsn->Gln; and/or
- wherein the functionally active variant of HCDR2 comprises the mutation at amino acid position 6, particularly 6Asp->Glu; and/or
- wherein the functionally active variant of SEQ ID NO: 1 comprises one or more mutations at amino acid positions 9, 12, 15, 22, 34, 46, 47, 80, 83, 85, 87 and/or 89, particularly selected from the group consisting of 9Ala->Ser, 12Ala->Ser, 15Leu->Val, 15Leu->Pro, 22Ser->Thr, 34Asn->Gln, 46Gln->Lys, 47Ala->Pro, 80Asp->Asn, 83Glu->Gln, 85Asp->Glu, 87Ala->Thr and 89Thr->Asn; and/or
- wherein the functionally active variant of SEQ ID NO: 2 comprises one or more mutations at amino acids positions 5, 7, 11, 12, 17, 20, 38, 40, 43, 55, 61, 65, 66, 67, 76, 81, 82, 87, 91, 93, 112, 113 and/or 116, particularly selected from the group consisting of 5His->Val, 7Pro->Ser, HLeu->Val, 12Val->Lys, 17Pro->Ser, 20Leu->Val, 38Lys->Arg, 40Arg->Ala, 43Arg->Gln, 55Asp->Glu, 61Asn->Ala, 65Lys->Gln, 66Asp->Gly, 67Lys->Arg, 76Ser->Thr, 81Ile->Met, 82Gln->Glu, 87Thr->Arg, 91 Ser->Thr, 93Val->Lys, 112Thr->Leu, 113Leu->Val

and 116Ser->Val;
wherein said variants have at least 10% of the α2-integrin binding activity of the corresponding peptides without sequence alteration.

6. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-5, wherein said antibody or fragment inhibits the interaction of the human α2-integrin with collagen in vitro, thereby inhibiting the activation of platelets due to adhesion of said platelets to said collagen.

7. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of the previous claims, (i) said heavy chain variable region domain comprising the heavy chain HCDR3 of SEQ ID NO:5, and preferably comprising the heavy chain CDRs of SEQ ID NO:3 (HCDR1), SEQ ID NO:4 (HCDR2), and SEQ ID NO:5 (HCDR3), or functionally active variants thereof, wherein said variants have at least 10% of the α2-integrin binding activity of the corresponding peptides without sequence alteration, and wherein the functionally active variant of HCDR2 preferably comprises the mutation Asp->Glu at amino acid position 6; and/or (ii) said light chain variable region domain comprising the light chain LCDR3 of SEQ ID NO:8, and preferably comprising the light chain CDRs of SEQ ID NO:6 (LCDR1), SEQ ID NO:7 (LCDR2), and SEQ ID NO:8 (LCDR3), or functionally active variants thereof, wherein said variants have at least 10% of the α2-integrin binding activity of the corresponding peptides without sequence alteration, and wherein the functionally active variant of LCDR1 preferably comprises the mutation Asn->Gln at amino acid position 11.

8. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of the previous claims, wherein said heavy chain variable region (VH) domain comprises one or more amino acid substitutions at positions selected from the group consisting of H5, H7, Hll, H12, H17, H20, H38, H40, H43, H55, H61, H65, H66, H67, H76, H81, H82, H87, H91, H93, H112, Hl13 and Hl16 and/or said light chain variable region (VL) domain comprises one or more amino acid substitutions at positions selected from the group consisting of L9, L12, L15, L22, L34, L46, L47, L80, L83, L85, L87, and L89.

9. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of the previous claims, said heavy chain variable region (VH) domain having at least

90%, 95%, 97% or 99% sequence identity to a VH sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 38 (HC1), SEQ ID NO:39 (HC2), SEQ ID NO:40 (HC3), SEQ ID NO:41 (HC4), SEQ ID NO:42 (HC5), SEQ ID NO:43 (HC6), and SEQ ID NO:44 (HC7) and/or said light chain variable region (VL) domain having at least 90%, 95%, 97% or 99% sequence identity to a VL sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 33 (LCI), SEQ ID NO:34 (LC2), SEQ ID NO:35 (LC3), SEQ ID NO:36 (LC4), and SEQ ID NO:37 (LC5).

10. One or more nucleic acid(s) coding for the isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1 to 9, wherein said nucleic acid(s) is/are preferably located in a vector.

11. A cell heterologously expressing one of the nucleic acids according to claim 9.

12. A method for producing an isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1 to 9 comprising culturing the cell according to claim 11 under conditions permitting expression of the isolated monoclonal antibody or antigen binding fragment thereof and optionally recovering the isolated monoclonal antibody or antigen binding fragment thereof from the host cell.

13. A pharmaceutical composition comprising at least one isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1 to 9 and/or at least one nucleic acid according to claim 10 for use as a medicament.

14. The isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-9 or the pharmaceutical composition of claim 13 for use in treating or preventing an α2-integrin-related disease or disorder selected from the group consisting of thrombosis, a vascular disease, cancer, including neo-angiogenesis and metastasis, inflammation, inflammatory disease, autoimmune disease and a disease characterized by abnormal or increase angiogenesis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, reactions to transplant, optical neuritis, spinal cord trauma, rheumatoid arthritis, systemic lupus erythematosus (SLE), multiple sclerosis, Reynaud's syndrome, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, scleroderma, cardiovascular disease, psoriasis, and infections that induce an inflammatory response, preferably for use in treating

or preventing a vascular disease and/or thrombosis, particularly in the treatment of acute coronary syndrome, percutaneous coronary Intervention, ischemic stroke, carotid artery stenosis or peripheral arterial occlusive disease.

15. Article of manufacture comprising

a) a packaging material,

b) an isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-9 or 16 or a pharmaceutically acceptable salt thereof or comprising the pharmaceutical composition of claim 13 or 14,

c) a label or a package insert, the insert contained within said packaging material, indicating that said isolated monoclonal antibody or antigen binding fragment thereof is effective for treatment of a disease or disorder, especially an α2-integrin-related disease disorder selected from the group consisting of thrombosis, a vascular disease, cancer, including neo-angiogenesis and metastasis, inflammation, inflammatory disease, autoimmune disease and a disease characterized by abnormal or increase angiogenesis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, reactions to transplant, optical neuritis, spinal cord trauma, rheumatoid arthritis, systemic lupus erythematosus (SLE), multiple sclerosis, Reynaud's syndrome, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, scleroderma, cardiovascular disease, psoriasis, and infections that induce an inflammatory response..

16. Diagnostic kit for the diagnosis of an α2-integrin related disorder or disease comprising an isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-9 and a suitable packaging, and possibly suitable instructions for using said antibody or fragment in the detection of α2-integrin, wherein said disorder or disease is selected from the group consisting of thrombosis, a vascular disease, cancer, including neo-angiogenesis and metastasis, inflammation, inflammatory disease, autoimmune disease and a disease characterized by abnormal or increase angiogenesis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, reactions to transplant, optical neuritis, spinal cord trauma, rheumatoid arthritis, systemic lupus erythematosus (SLE), multiple sclerosis, Reynaud's syndrome, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, scleroderma, cardiovascular disease, psoriasis, and infections that induce an inflammatory response.

17. Method of diagnosis of an α2-integrin-related disorder or disease using one or more isolated monoclonal antibody or antigen binding fragment thereof according to any one of claims 1-9, wherein said disorder or disease is selected from the group consisting of thrombosis, a vascular disease, cancer, including neo-angiogenesis and metastasis, inflammation, inflammatory disease, autoimmune disease and a disease characterized by abnormal or increased angiogenesis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, reactions to transplant, optical neuritis, spinal cord trauma, rheumatoid arthritis, systemic lupus erythematosus (SLE), multiple sclerosis, Reynaud's syndrome, experimental autoimmune encephalomyelitis, Sjorgen's syndrome, scleroderma, cardiovascular disease, psoriasis, and infections that induce an inflammatory response, and wherein said method comprises

a) contacting a taken sample of an individual with the isolated monoclonal antibody or antigen binding fragment thereof of any one of claims 1 to 9; and

b) detecting binding of α2-integrin to the isolated monoclonal antibody or antigen binding fragment thereof; and

c) comparing the binding of step b) with the binding of α2-integrin to the isolated monoclonal antibody or antigen binding fragment thereof in one or more reference samples, wherein an altered binding in the taken sample relative to the binding detected in the one or more reference samples is indicative of the disease.