

- at least one amino acid residue from amino acid residues 114 to 142 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over amino acid residues 114 to 142 of hGPVI (SEQ ID NO: 13); and
- at least one amino acid residue from amino acid residues 165 to 187 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over amino acid residues 165 to 187 of hGPVI (SEQ ID NO: 13).

In one aspect of the present disclosure, there is provided an isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or a fragment thereof,

wherein the variable region of the heavy chain comprises the following CDRs:

VH-CDR1: GYTFTSYNMH (SEQ ID NO: 1);

VH-CDR2: GIYPGNNGDTSYNQKFQG (SEQ ID NO: 2); and

VH-CDR3: GTVVGDWYFDV (SEQ ID NO: 3); and

wherein the variable region of the light chain comprises the following CDRs:

VL-CDR1: RSSQSLENSNGNTYLN (SEQ ID NO: 4);

VL-CDR2: RVSNRFS (SEQ ID NO: 5); and

VL-CDR3: LQLTHVPWT (SEQ ID NO: 6).

In one embodiment, the conformational epitope bound by the isolated humanized protein of the present disclosure comprises at least one amino acid residue from amino acid residues 121 to 135 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over amino acid residues 121 to 135 of hGPVI (SEQ ID NO: 13); and at
5 least one amino acid residue from amino acid residues 169 to 183 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over amino acid residues 169 to 183 of hGPVI (SEQ ID NO: 13).

The present disclosure also relates to an isolated humanized protein binding to human Glycoprotein VI (hGPVI), wherein said protein has a K_D for binding to hGPVI less than
10 15 nM, wherein said K_D is measured by surface plasmon resonance using 960 to 1071 RU of soluble human GPVI and using PBS pH 7.4 as running buffer. In one embodiment, the isolated humanized protein of the present disclosure does not induce a GPVI depletion phenotype *in vivo*.

In one embodiment, the protein of the present disclosure is an antibody molecule
15 selected from the group consisting of a whole antibody, a humanized antibody, a single chain antibody, a Fv, a Fab; or an antibody fragment selected from the group consisting of a unibody, a domain antibody, and a nanobody; or a monomeric antibody mimetic selected from the group consisting of an affibody, an affilin, an affitin, an adnectin, an atrimer, an evasin, a DARPin, an anticalin, an avimer, a fynomer, and a versabody.

20 In one embodiment, the antibody of the present disclosure is monovalent.

In one embodiment, the variable region of the heavy chain comprises at least one of the following CDRs:

VH-CDR1: GYTFTSYNMH (SEQ ID NO: 1);

The present disclosure further relates to a composition comprising the protein binding to human GPVI as defined hereinabove.

In another aspect of the present disclosure, there is provided a composition comprising the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or
5 fragment thereof disclosed herein.

The present disclosure further relates to a pharmaceutical composition comprising the protein binding to human GPVI as defined hereinabove and at least one pharmaceutically acceptable excipient.

In a further aspect of the present disclosure, there is provided a pharmaceutical
10 composition comprising the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof disclosed herein and at least one pharmaceutically acceptable excipient.

In one embodiment, the pharmaceutical composition of the present disclosure is for treating, or for use in treating, a GPVI-related condition.

15 In one embodiment, said GPVI-related condition is a cardiovascular disease selected from arterial and venous thrombosis, restenosis, acute coronary syndrome and ischemic cerebrovascular accidents.

In a further aspect of the present disclosure, there is provided use of the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof as
20 defined hereinabove for the manufacture of a medicament for treating a GPVI-related condition.

The present disclosure further relates to the use of the antibody against human GPVI of the present disclosure for detecting GPVI in a biological sample.

Another object of the present disclosure is an expression vector comprising at least one of SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12 or any sequence having a nucleic acid sequence that shares at least 60% of identity with said SEQ ID NO: 10-12.

5 In another aspect of the present disclosure, there is provided an expression vector comprising at least one nucleic acid sequence encoding a heavy chain or a light chain of an antibody disclosed herein, wherein said expression vector comprises at least one of SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12 or any sequence having a nucleic acid sequence that shares at least 95% of identity with said SEQ ID NO: 10-12.

10 DETAILED DESCRIPTION

“**Glycoprotein VI (GPVI)**” is a platelet membrane glycoprotein that is involved in platelet-collagen interactions. GPVI is a transmembrane collagen receptor expressed on the surface of platelets. In one embodiment, the amino acid sequence of human GPVI is SEQ ID NO: 13 (accession number: BAA89353.1) or any amino acid sequence
15 presenting at least about 90% identity with SEQ ID NO: 13, preferably at least about 91, 92, 93, 94, 95, 96, 97, 98, 99% identity or more with SEQ ID NO: 13.

(SEQ ID NO: 13)

MSPSPTALFCLGLCLGRVPA (Signal peptide)

CLAIMS

1. An isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or a fragment thereof,

5 wherein the variable region of the heavy chain comprises the following CDRs:
VH-CDR1: GYTFTSYNMH (SEQ ID NO: 1);
VH-CDR2: GIYPGNGDTSYNQKFQG (SEQ ID NO: 2); and
VH-CDR3: GTVVGDWYFDV (SEQ ID NO: 3); and
 wherein the variable region of the light chain comprises the following CDRs:

10 **VL-CDR1:** RSSQSLENSNGNTYLN (SEQ ID NO: 4);
VL-CDR2: RVSNRFS (SEQ ID NO: 5); and
VL-CDR3: LQLTHVPWT (SEQ ID NO: 6).
2. The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to claim 1, wherein said antibody or fragment thereof

15 binds to an epitope comprising at least one amino acid residue from amino acid residues 114 to 142 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over amino acid residues 114 to 142 of hGPVI (SEQ ID NO: 13); and at least one amino acid residue from amino acid residues 165 to 187 of hGPVI (SEQ ID NO: 13) or from a sequence sharing at least 60% of identity over

20 amino acid residues 165 to 187 of hGPVI (SEQ ID NO: 13).
3. The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to claim 1 or claim 2, wherein said antibody or fragment thereof has a KD for binding to hGPVI less than 15 nM, wherein said KD is measured by surface plasmon resonance using 960 to 1071 RU of soluble

25 human GPVI and using PBS pH 7.4 as running buffer and wherein said isolated humanized antibody does not induce a GPVI depletion phenotype in vivo.
4. The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims 1 to 3, being an antibody molecule selected from the group consisting of a whole antibody, a humanized

antibody, a single chain antibody, a Fv, a Fab; or an antibody fragment selected from the group consisting of a unibody, a domain antibody, and a nanobody.

- 5 **5.** The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **4**, being a monovalent antibody.
- 10 **6.** The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **5**, wherein the amino acid sequence encoding the heavy chain variable region is SEQ ID NO: **7** and the amino acid sequence encoding the light variable region is SEQ ID NO: **8**, or any sequence having an amino acid sequence that shares at least 60% of identity with said SEQ ID NO: **7** or **8**.
- 15 **7.** The isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **5**, wherein the amino acid sequence encoding the heavy chain variable region is SEQ ID NO: **7** and the amino acid sequence encoding the light variable region is SEQ ID NO: **9**, or any sequence having an amino acid sequence that shares at least 60% of identity with said SEQ ID NO: **7** or **9**.
- 20 **8.** A composition comprising the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **7**.
- 9.** A pharmaceutical composition comprising the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **7** and at least one pharmaceutically acceptable excipient.
- 25 **10.** Use of the isolated humanized antibody binding to human Glycoprotein VI (hGPVI) or fragment thereof according to any one of claims **1** to **7** for the manufacture of a medicament for treating a GPVI-related condition.
- 11.** The use according to claim **10**, wherein said GPVI-related condition is a cardiovascular disease selected from arterial and venous thrombosis, restenosis, acute coronary syndrome, ischemic cerebrovascular accidents, cerebral vascular

diseases, venous thromboembolism diseases, thrombotic microangiopathies, and vascular purpura.

- 5 **12.** The use according to claim **10**, wherein said GPVI-related condition is a cardiovascular disease selected from coronary artery diseases and cerebral artery diseases.
- 10 **13.** The use according to claim **10**, wherein said GPVI-related condition is a cardiovascular disease selected from atherothrombosis, ischemic events, acute coronary artery syndrome, myocardial infarction, stroke, percutaneous coronary intervention, stenting thrombosis, ischemic restenosis, acute ischemia, chronic ischemia, diseases of the aorta and its branches, peripheral artery disease, venous thrombosis, acute phlebitis, pulmonary embolism, cancer-associated thrombosis, inflammatory thrombosis and thrombosis associated to infection.
- 15 **14.** An expression vector comprising at least one nucleic acid sequence encoding a heavy chain or a light chain of an antibody according to any one of claims **1** to **7**, wherein said expression vector comprises at least one of SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12 or any sequence having a nucleic acid sequence that shares at least 95% of identity with said SEQ ID NO: 10-12.