

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
06 January 2022 (06.01.2022)



(10) International Publication Number
WO 2022/002880 A1

(51) International Patent Classification:

C07K 16/36 (2006.01) A61P 7/02 (2006.01)
C07K 16/38 (2006.01) A61K 39/395 (2006.01)

(21) International Application Number:

PCT/EP2021/067746

(22) International Filing Date:

28 June 2021 (28.06.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

20305723.7 29 June 2020 (29.06.2020) EP

(71) Applicants: **INSERM (INSTITUT NATIONAL DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE)** [FR/FR]; 101, rue de Tolbiac, 75013 Paris (FR). **ASSISTANCE PUBLIQUE-HÔPITAUX DE PARIS (APHP)** [FR/FR]; 3, avenue Victoria, 75004 Paris (FR). **UNIVERSITÉ PARIS-SACLAY** [FR/FR]; BATIMENT BREGUET 3 RUE JOLIOT CURIE, 91190 GIF-SUR-YVETTE (FR).

(72) Inventors: **SALLER, François**; U1176 - CHU DE BICETRE 80 RUE DU GENERAL LECLERC - BATIMENT INSERM GREGORY PINCUS, 94276 LE KREMLIN BICETRE Cedex France (FR). **DENIS, Cécile**; U1176 - CHU DE BICETRE 80 RUE DU GENERAL LECLERC - BATIMENT INSERM GREGORY PINCUS, 94276 LE KREMLIN BICETRE (FR). **BORGEL, Delphine**; CHU DE BICETRE 80 RUE DU GENERAL LECLERC - BATIMENT INSERM GREGORY PINCUS, 94276 LE KREMLIN BICETRE DECEX (FR). **ADAM, Frédéric**; U1176 - CHU DE BICETRE 80 RUE DU GENERAL LECLERC - BATIMENT INSERM GREGORY PINCUS, 94276 LE KREMLIN BICETRE Cedex France (FR). **CHRISTOPHE, Olivier**; INSERM U 1176 - Paris-Sud 80 rue du Général Leclerc, 94276 LE KREMLIN-BICETRE (FR). **LENTING, Peter**; INSERM U1176 - Paris-Sud 80, rue du Général Leclerc, 94276 KREMLIN-BICETRE (FR).

(74) Agent: **INSERM TRANSFERT**; 7 rue Watt, 75013 Paris (FR).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,

CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

(54) Title: ANTI-PROTEIN S SINGLE-DOMAIN ANTIBODIES AND POLYPEPTIDES COMPRISING THEREOF

(57) Abstract: Vitamin K-dependent Protein S (PS) is a natural anticoagulant acting as a non-enzymatic cofactor for both activated protein C (APC) and tissue factor pathway inhibitor (TFPI). The inventors identify an anti-PS nanobody that very surprisingly enhances the APC- cofactor activity of PS through unknown mechanisms. Very interestingly, this nanobody exerts an antithrombotic effect in injured mesenteric microvessels of mice. As a consequence, it10 constitutes a novel class of antithrombotic agents that could be used for the treatment of acute microthrombosis in pathological states such as sepsis, COVID-19, distal microvascular thrombosis induced by stroke, or sickle-cell disease. Thus, the present invention relates to isolated single-domain antibodies (sdAb) directed against protein S (PS) and polypeptides comprising thereof.



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