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(54) Title **FACTOR IX POLYPEPTIDE MUTANT, ITS USES AND A METHOD FOR ITS PRODUCTION**

(56) References
Cited:

WO-A-99/03496, US-A1- 2008 167 219,
SCHUETTRUMPFF JOERG ET AL: "Factor IX variants improve gene therapy efficacy for hemophilia B", BLOOD, vol. 105, no. 6, 15 March 2005 (2005-03-15), pages 2316-2323, XP002555907, ISSN: 0006-4971

KURACHI S ET AL: "ROLE OF INTRON I IN EXPRESSION OF THE HUMAN FACTOR IX GENE", JOURNAL OF BIOLOGICAL CHEMISTRY,, vol. 270, no. 10, 10 March 1995 (1995-03-10), pages 5276-5281, XP002055415, ISSN: 0021-9258, DOI: 10.1074/JBC.270.16.9289

LU H ET AL: "Gene therapy for hemophilia B mediated by recombinant adeno-associated viral vector with hFIXR338A, a high catalytic activity mutation of human coagulation factor IX", SCIENCE IN CHINA. SERIE C: LIFE SCIENCE, GORDON AND BREACH, AMSTERDAM, NL, vol. 44, no. 6, 1 December 2001 (2001-12-01), pages 585-592, XP009114604, ISSN: 1006-9305, DOI: 10.1007/BF02879352

JONATHAN D. FINN ET AL: "Abstract 694 - FIX-R338L (FIX Padua) as a Successful Alternative for the Treatment of Canine Severe Hemophilia B", BLOOD, AMERICAN SOCIETY OF HEMATOLOGY, US, vol. 114, no. 22, 3 December 2009 (2009-12-03), XP002774527, ISSN: 0006-4971 [retrieved on 2010-10-05]

YAN JING-BIN ET AL: "Transgenic mice can express mutant human coagulation factor IX with higher level of clotting activity.", BIOCHEMICAL GENETICS OCT 2006, vol. 44, no. 7-8, October 2006 (2006-10), pages 349-360, XP019447249, ISSN: 0006-2928

GIANNELLI F ET AL: "HEMOPHILIA B DATABASE OF POINT MUTATIONS AND SHORT ADDITIONS AND DELETIONS", NUCLEIC ACIDS RESEARCH,, vol. 18, no. 14, 1 January 1990 (1990-01-01), pages 4053-4060, XP002774525, ISSN: 0305-1048, DOI: 10.1093/NAR/18.14.4053

ANSON D S ET AL: "THE GENE STRUCTURE OF HUMAN ANTI-HAEMOPHILIC FACTOR IX", EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 3, no. 5, 1 January 1984 (1984-01-01) , pages 1053-1060, XP000872222, ISSN: 0261-4189

DATABASE DATABASE EMBL [Online] 28 January 1986 (1986-01-28), yoshitake s. et al: "Human coagulation factor IX gene, complete cds", XP002774526, retrieved from EBI Database accession no. K02402

SABATINO DENISE E ET AL: "Novel hemophilia B mouse models exhibiting a range of mutations in the Factor IX gene", BLOOD, vol. 104, no. 9, 1 November 2004 (2004-11-01), pages 2767-2774, XP002555908, ISSN: 0006-4971

SIMIONI PAOLO ET AL: "X-linked thrombophilia with a mutant factor IX (factor IX Padua).", THE NEW ENGLAND JOURNAL OF MEDICINE 22 OCT 2009, vol. 361, no. 17, 22 October 2009 (2009-10-22), pages 1671-1675, XP002555909, ISSN: 1533-4406

CHANG JINLI ET AL: "Changing residue 338 in human factor IX from arginine to alanine causes an increase in catalytic activity", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BIRMINGHAM, US, vol. 273, no. 20, 15 May 1998 (1998-05-15) , pages 12089-12094, XP002199691, ISSN: 0021-9258

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav

1. Nukleinsyre for bruk i en genterapibehandling av hemofili B, hvori nevnte nukleinsyre koder for et modifisert FIX-polypeptid, som har minst følgende sekvens:

```
YNSGKLEEFV QGNLERECME EKCSFEEARE VFENTERTE FWKQYVDGDQ
CESNPCLNGG SCKDDINSYE CWCDFGFEGK NCELDVTCNI KNGRCEQFCK
NSADNKVVCS CTEGYRLAEN QKSCEPAVPF PCGRVSVSQT SKLTRAEXVF
PDVDYVNSTE AETILDNITQ STQSFNDFTR VVGGEDAKPG QFPWQVVLNG
KVDAFCGCSI VNEKWIIVTAA HCVETGVKIT VVAGEHNIEE TEHTEQKRN
IRIIPHHNYN AAINKYNHDI ALLELDEPLV LNSYVTPICI ADKEYTNIFL
KFGSGYVSGW GRVFHKGRSA LVLQYLRVPL VDRATCLLST KFTIYNNMFC
AGFHEGGRDS CQGDSSGGPHV TEVEGTSFLT GIISWGEECA MKGKYGIYTK
VSRVYNWIKL KTKLT,
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hvor X representerer A.

2. Nukleinsyre for bruk i en genterapibehandling av hemofili B ifølge krav 1, hvori nevnte nukleinsyre koder for et modifisert FIX-polypeptid som har følgende sekvens:

```
MQRVNMIMAE SPGLITICLL GYLLSAECTV FLDHENANKI LNRPKRYNSG
KLEEFVQGNL ERECMEEKCS FEEAREVFEN TERTTEFWKQ YVDGDQCESN
PCLNGGSCKD DINSYECWCP FGFEGKNCEL DVTCNINKGR CEQFCKNSAD
NKVVCSCTEG YRLAENQKSC EPAVPFPCGR VSVSQTSLT RAEXVFPD
YVNSTEAEI LDNITQSTQS FNDFTRVVGG EDAKPGQFPW QVVLNGKVDA
FCGGSIVNEK WIVTAAHCVE TGVKITVVAG EHNIEETEHT EQKRNIRII
PHHYNAAIN KYNHDIALLE LDEPLVLNSY VTPICIADKE YTNIFLKFGS
GYVSGWGRVF HKGRSALVLQ YLRVPLVDRA TCLLSTKFTI YNNMFCAGFH
EGGRDSCQGD SGGPHVTEVE GTSFLTGIIS WGEECAMKGK YGIYTKVSRV
VNWIKLTKL T,
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hvor X representerer A.

3. Nukleinsyre for bruk ifølge hvilket som helst av kravene 1-2, hvori nukleinsyren er omfattet av en viral vektor.

4. Nukleinsyre for bruk ifølge krav 3, hvori den virale vektoren er adeno-assosiert virus.