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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 May 2003 (22.05.2003)

PCT

(10) International Publication Number
WO 03/042244 A2

(51) International Patent Classification[7]: C07K 14/54

(21) International Application Number: PCT/DK02/00764

(22) International Filing Date:
15 November 2002 (15.11.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2001 01702 16 November 2001 (16.11.2001) DK
60/331,575 16 November 2001 (16.11.2001) US

(71) Applicant *(for all designated States except US)*: **PHARMEXA A/S** [DK/DK]; Kogle Allé 6, DK-2970 Hørsholm (DK).

(71) Applicants and
(72) Inventors: **KLYSNER, Steen** [DK/DK]; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK). **NIELSEN, Finn, Stausholm** [DK/DK]; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK). **BRATT, Tomas** [DK/DK]; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK). **VOLDBORG, Bjørn** [DK/DK]; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK). **MOURITSEN, Søren** [DK/DK]; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK).

(74) Agent: **KOEFOED, Peter**; c/o Pharmexa A/S, Kogle Allé 6, DK-2970 Hørsholm (DK).

(81) Designated States *(national)*: AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK (utility model), SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/042244 A2

(54) Title: NOVEL IMMUNOGENIC MIMETICS OF MULTIMER PROTEINS

(57) Abstract: The present invention relates to novel immunogenic variants of multimeric proteins such as immunogenic variants of interleukin 5 (IL5) and tumour necrosis factor alpha (TNF, TNFα). The variants are, besides from being immunogenic in the autologous host, also highly similar to the native 3D structure of the proteins from which they are derived. Certain variants are monomeric mimics of the multimers, where peptide linkers (inert or T helper epitope containing) ensure a spatial organisation of the monomomer units that facilitate correct folding. A subset of variants are monomer TNFα variants that exhibit a superior capability of assembling into multimers with a high structural similarity to the native protein. Also disclosed are methods of treatment and production of the variants as well as DNA fragments, vectors, and host cells.