

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
1 August 2002 (01.08.2002)

PCT

(10) International Publication Number
WO 02/059150 A2

(51) International Patent Classification⁷: **C07K 14/705**

(21) International Application Number: PCT/GB02/00005

(22) International Filing Date: 2 January 2002 (02.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0100119.7 3 January 2001 (03.01.2001) GB

(71) Applicant (for all designated States except US): **THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN** [GB/GB]; Regent Walk, Aberdeen, Grampian AB24 3FX (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **WISCHIK, Claude, Michel** [FR/GB]; Department of Mental Health, University of Aberdeen, University Medical Buildings, Foresterhill, Aberdeen, Aberdeenshire AB25 2ZD (GB). **RICKARD, Janet, Elizabeth** [GB/GB]; Department of Mental Health, University of Aberdeen, University Medical Buildings, Foresterhill, Aberdeen, Aberdeenshire AB25 2ZD (GB). **HORSLEY, David** [GB/GB]; Department of Mental Health, University of Aberdeen, University Medical Buildings, Foresterhill, Aberdeen, Aberdeenshire AB25 2ZD (GB). **HARRINGTON, Charles, Robert** [GB/GB]; Department of Mental Health, University of Aberdeen, University Medical Buildings, Foresterhill, Aberdeen, Aberdeenshire AB25 2ZD (GB). **THEURING, Franz** [DE/DE]; University Hospital Charite, Institute of Pharmacology and Toxicology, Dorotheenstr. 94, 10117 Berlin

(DE). **STAMER, Karsten** [DE/DE]; University Hospital Charite, Institute of Pharmacology and Toxicology, Dorotheenstr. 94, 10117 Berlin (DE). **ZABKE, Claudia** [DE/DE]; University Hospital Charite, Institute of Pharmacology and Toxicology, Dorotheenstr. 94, 10117 Berlin (DE).

(74) Agents: **KREMER, Simon, M.** et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, 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, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, 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, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

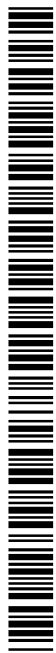
Published:

— 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.

(54) Title: MATERIALS AND METHODS RELATING TO PROTEIN AGGREGATION IN NEURODEGENERATIVE DISEASE

(57) Abstract: Disclosed are methods of inducing or modelling the pathological state of an aggregating disease protein (ADP - e.g. tau protein) which is associated with a disease state in which the ADP aggregates pathologically (e.g. Alzheimer's disease) through an induced conformational polymerisation interaction, the method being characterised by the step of providing a membrane-localisable fusion protein comprising (i) an aggregating portion, which is derived from the ADP, or from a protein which initiates pathological aggregation of the ADP, (ii) a heterologous membrane-localising portion. Membrane-localisation of the ADP-based fusion protein is believed to cause the high-affinity capture site of the ADP protein to become exposed such that aggregation of further ADP, which may be native or heterologous to the system, to be promoted. The method can be carried out in vitro, or in cell- and animal-models, and may be used to screen for modulators of the aggregation process by monitoring aggregation e.g. by monitoring the production of the ADP-related degradation products resulting from the aggregation. Also provided are materials, processes for use in or with the methods.



WO 02/059150 A2