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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12Q 1/68, C12N 15/10 — A1

(11) International Publication Number: **WO 00/05406**

(43) International Publication Date: 3 February 2000 (03.02.00)

(21) International Application Number: PCT/DK99/00408

(22) International Filing Date: 16 July 1999 (16.07.99)

(30) Priority Data:

PA 1998 00956	20 July 1998 (20.07.98)	DK
60/094,868	29 July 1998 (29.07.98)	US

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(81) Designated States: AE, AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: NOVEL METHODS FOR THE IDENTIFICATION OF LIGAND AND TARGET BIOMOLECULES

(57) Abstract

The invention provides for methods for identification of biologically active biomolecules. In one aspect, a biologically active biomolecule such as RNA or a peptide is identified by incorporating random nucleotide sequences in a scaffold constituted by an enzyme activity modulator, transforming substantially identical host cells with the construct obtained thereby and screening the transformed cells to identify those where a preselected phenotypic trait has been altered. The randomized DNA is subsequently isolated from the phenotypically altered cells and the peptide and/or RNA encoded by the random sequence is determined. In turn, interaction partners which are putative drug targets are identified and isolated by use of the peptide and/or RNA as part of affinity reagents. A preferred scaffold is derived from the potato inhibitor I family of protease inhibitors and exemplified is the barley chymotrypsin inhibitor 2A (CI–2A). Another aspect relates to the identification of novel enzyme inhibitors by using substantially the same approach, but screening specifically for changes in target enzyme activity. Also disclosed are methods of producing the relevant transformation and expression vectors as well as methods for identifying lead compounds and drug targets for use in drug development. Finally, the invention also includes within its scope a method for the preparation of a medicinal product.

