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- (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.
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(54) Title: SCREENING METHOD FOR THE SELECTION OF PEPTIDES OR PROTEINS COMPRISING DISCRETE DIMENSION ASSAYS, GENE MUTATION AND APPLICATION ASSAYS

(57) Abstract: The present invention relates to a screening method for identifying actives (peptides or proteins) with improved performance comprising: (1) screening a library of actives encoded by nucleotide sequences in at least two different discrete dimension assays employing selected parameters and selecting the actives exhibiting improved properties in the discrete dimension assays, (2) collecting nucleotide sequences encoding the selected actives, (3) mutating collected nucleotide sequences, (4) screening actives encoded by the mutated nucleotide sequences in an application assay and selecting actives, which exhibit improved performance.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 02/00160

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/09

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, EP0-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NESS JON E ET AL: "DNA shuffling of subgenomic sequences of subtilisin" NATURE BIOTECHNOLOGY, NATURE PUB. CO, NEW YORK, NY, US, vol. 17, no. 9, September 1999 (1999-09), pages 893-896, XP002191112 ISSN: 1087-0156 the whole document --- -/--	1-13

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 September 2002

Date of mailing of the international search report

19. 09. 2002

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 02/00160

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GIVER L ET AL: "Directed evolution of a thermostable esterase" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 22, 27 October 1998 (1998-10-27), pages 12809-12813, XP002209305 ISSN: 0027-8424 the whole document ---	1-13
A	WO 98 41622 A (NOVONORDISK AS) 24 September 1998 (1998-09-24) claims ---	1-13
A	WO 00 09682 A (MAXYGEN INC (US)) 24 February 2000 (2000-02-24) claims 1,2 -----	1-13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 02/00160

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1, 13
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 13

The wording of claim 1, "actives" and "discrete dimension assays", are undefined and too broadly formulated to perform a meaningful search of the whole of claim 1.

Consequently, a search has been carried out for the general aspects of the invention and for the subject matter as disclosed in the examples of the description.

Claim 13 relates to an extremely large number of "actives". Support in accordance with Article 6 PCT and Disclosure in accordance with Article 5 PCT can, however, only be found for a very limited number of actives. In the present case, the claim lacks support, and the application lacks disclosure to such an extent, that a meaningful search of the whole of the claimed scope would be impossible.

Consequently, the search has been limited to actives provided by the screening method of claim 1. Claim 13 relates to a "product-by-process". However, there may be previously known actives that have not been obtained by the method of claim 13, but that are identical to actives according to claim 13.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK 02/00160

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9841622	A	24-09-1998	AU 6611498 A	12-10-1998
			WO 9841622 A1	24-09-1998
			EP 0996718 A1	03-05-2000
			JP 2001516215 T	25-09-2001
			US 6159688 A	12-12-2000
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WO 0009682	A	24-02-2000	AU 5347999 A	06-03-2000
			EP 1104459 A1	06-06-2001
			JP 2002522072 T	23-07-2002
			WO 0009682 A1	24-02-2000
