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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.

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(54) Title: POLYMORPHISMS OF PD-1

(57) Abstract: The present invention is based at least in part on the identification of the genomic structure of the human PD-1 gene and on the identification of polymorphic region within the gene. Accordingly, the invention provides nucleic acids having a nucleotide sequence encoding variants of the PD-1 gene and also provides nucleic acids having a PD-1 promoter, intron, exon and 3' UTR sequences, and expression products. The invention also provides methods for identifying specific alleles of polymorphic regions of a PD-1 gene, methods for determining whether a subject has or at risk of developing any disease that is associated with a specific allele of a polymorphic region of a PD-1 gene, and kits for performing such methods.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/10011

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 C07K14/47

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 C07K C12Q

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)
EPO-Internal, BIOSIS, SEQUENCE SEARCH, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FINGER L R ET AL: "The human PD-1 gene: complete cDNA, genomic organization, and developmentally regulated expression in B cell progenitors" GENE: AN INTERNATIONAL JOURNAL ON GENES AND GENOMES, ELSEVIER SCIENCE PUBLISHERS, BARKING, GB, vol. 197, no. 1-2, 15 September 1997 (1997-09-15), pages 177-187, XP004126417 ISSN: 0378-1119 see the whole document --- -/--	1-8, 19-24, 28,29

[X] 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	Date of mailing of the international search report
5 June 2003	24/06/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Grosskopf, R

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/EP 02/10011

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	SHINOHARA T ET AL: "SHORT COMMUNICATION STRUCTURE AND CHROMOSOMAL LOCALIZATION OF THE HUMAN PD-1 GENE (PDCD1)" GENOMICS, ACADEMIC PRESS, SAN DIEGO, US, vol. 23, no. 3, 1 October 1994 (1994-10-01), pages 704-706, XP000647607 ISSN: 0888-7543 see the whole document	1-7
X	DATABASE SWALLPROT 'Online! 1 November 1997 (1997-11-01) retrieved from EBI Database accession no. q15116 XP002243478 abstract The sequence has 9.3 % identity with SEQ ID NO: 35 and 100% identity with SEQ ID NO: 36	19-24, 28,29
T	PROKUNINA LUDMILA ET AL: "A regulatory polymorphism in PDCD1 is associated with susceptibility to systemic lupus erythematosus in humans." NATURE GENETICS, vol. 32, no. 4, 20 December 2002 (2002-12-20), pages 666-669, XP002243477 ISSN: 1061-4036	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/10011

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 6-8
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.1

Although claims 9-15 and 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Although claims 17 and 18 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 6-8

Present claims 4-8 and 19 to 21 relate to an extremely large number of possible products. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the products, said products, however, being not even specifically claimed . In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to SEQ ID NOs: 1, 2 and the proteins of SEQ ID NO: 34 to 37.

In fact, when taking into account that the complete structure both of the genomic and the cDNA are known in the art, a reference to unspecified fragments of any of these two sequences is totally unreasonable and would give rise to an objection for lack of unity. Since, however, it is absolutely impossible to determine the number of alleged inventions, an explicit objection has not been raised.
It goes without saying, that the claims which relate to said products equally have not been searched, respectively would have been searched insofar as they relate to a reasonably defined product.
On the other hand, the only "potentially meaningful" specific fragments i.e. those which comprise a polymorphism, are only claimed as one of uncountable alterantives in the claims.
This does, however, not mean that once said claims were restricted to said specific fragments, a unitary concept would be acknowledged, especially when taking into account that the existence of polymorphisms in human genes is trivial and these fragments form unrelated parts of a known sequence. This Authority is, however, aware of the fact that a lack of unity objection with regard to the various specific subfragments accompanied by a request for further search fees would be unreasonable since such a search would not reveal further documents.

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.