(54) Title: NOVEL CO-STIMULATORY MOLECULES

(A) Plasmid encoding Ag+CD28BP

(B) Plasmid encoding Ag+CTLA-4BP

(57) Abstract: The invention provides polynucleotides and polypeptides encoded therefrom having advantageous properties, including an ability of the polypeptides to preferentially bind a CD28 or CTLA-4 receptor at a level greater or less than the ability of human B7-1 to bind CD28 or CTLA-4, or to induce or inhibit altered level of T cell proliferation response greater compared to that generated by human B7-1. The polypeptides and polynucleotides of the invention are useful in therapeutic and prophylactic treatment methods, gene therapy applications, and vaccines.
Published: — with international search report

Date of publication of the international search report:
21 August 2003

Information about Correction:
Previous Correction:
see PCT Gazette No. 06/2003 of 6 February 2003, Section II

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.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C12Q1/68 C12N15/10 C07K16/28
A61K38/17

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 C12N C12Q A61K

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

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

BIOSIS, EPO-Internal, SEQUENCE SEARCH, MEDLINE, EMBL, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X Further documents are listed in the continuation of box C. X 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 invention 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
I: 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
Y: 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
X: 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
K: document member of the same patent family

Data of the actual completion of the international search: 14 February 2003

Data of mailing of the international search report: 23 MAY 2003

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (31-70) 340-2040, Tx. 31 861 epo nl,
Fax: (31-70) 340-3016

Authorized officer
LE CORNEC N.D.R.
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### Documents Considered to Be Relevant

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- **claims**

INTERNATIONAL SEARCH REPORT

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.: 171-173 and 201-211 partially 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:

see additional sheet

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. [x] 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.:
   1-18,28-79,131,167-168,171-238,240-247,250-258 all partially

Remark on Protest
   [ ] The additional search fees were accompanied by the applicant's protest.
   [x] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:


Polypeptide represented by the amino acid sequence ID no.48 and its corresponding nucleic acid sequence represented by the polynucleotide sequence ID no.1. Antibodies. Pharmaceutical compositions. Therapeutic uses.


Subject-matter essentially the same as in subject 1 but restricted to the respective proteins with sequence ID’s 49-68, 174-221, 283, 285, 290-293 and the corresponding nucleic acid sequences (Table 3).

For the sake of conciseness, the first invention has been described in detail, and the further inventions have been defined by analogy thereto.

Invention 76: claims 19-27 totally and 171-173, 201-211, 213-215, 241, 243-247 partially

Subject-matter is essentially the same as in subject 1 but restricted to the respective proteins with seq.ID.284. Each of the claimed variants of seq.ID.284 (34 positions with two possibilities and 3 further positions with three possibilities) in principle constitutes a separate invention. However, since the number of possible peptides is extremely large, and since they are not supported by the description (Art. 6 PCT), the ISA has not asked for additional search fees in respect of these variants. Should the applicant insist that one or more of these variants constitute patentable inventions, the ISA shall perform (an) additional search(es) for them, provided payment for the respective inventions is accompanied by an exact specification of the protein of the invention concerned.

Inventions 77-136: claims 80-96, 101-128, 130, 132-164, 171-237, 241-247, 250-258 all partially and 249 completely as far as applicable

Subject-matter essentially the same as in subject 1 but
restricted to the respective proteins with sequence ID's 69-92, 222-247, 286-289 and the corresponding nucleic acid sequences (table 4). The same applies for sequence ID no.287 as was stated above in invention 76 concerning sequence ID no.284.

Invention 137: claim 97-100 totally and 114-126, 231-237 partially

Subject-matter essentially the same as in subject 1 but restricted to the Polypeptide comprising a sequence that differs from a human B7-1 sequence (seq ID no.278) in at least two mutations.


Subject-matter essentially the same as in subject 1 but restricted to the respective Polypeptide represented by a sequence ID no.263-272 and the corresponding nucleic acid sequences.

Inventions 148-149: claims 169-230, 253-258 all partially

Subject-matter essentially the same as in subject 1 but restricted to the respective Polypeptides represented by sequence ID no.93 and no.94 and their respective corresponding nucleic acid sequences ID no.46 and no.47.
## INTERNATIONAL SEARCH REPORT

**Information on patent family members**

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