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- with international search report (Art. 21(3))
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24 September 2020 (24.09.2020)

(54) Title: ANTIBODIES THAT BIND TUMOR TISSUE, AND THEIR DIAGNOSTIC AND THERAPEUTIC USES

(57) Abstract: Provided herein are antibodies that bind to tumor tissue through a binding interaction with an extracellular RNA-protein complex. Such antibodies are used in methods of inducing an immune response and methods of inhibiting tumor cell growth. Additionally provided are methods of producing such antibodies.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2020/018350

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/00 A61P35/00 C07K16/06 C07K16/44
ADD.

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)
A61K A61P C07K

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 practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DEFALCO JEFF ET AL: "Non-progressing cancer patients have persistent B cell responses expressing shared antibody paratopes that target public tumor antigens", CLINICAL IMMUNOLOGY, ACADEMIC PRESS, US, vol. 187, 12 October 2017 (2017-10-12), pages 37-45, XP085352017, ISSN: 1521-6616, DOI: 10.1016/J.CLIM.2017.10.002 the whole document ----- -/--	19-24, 78-90, 93,96, 99-102



Further documents are listed in the continuation of Box C.



See patent family 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 application or patent 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

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06/08/2020

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2020/018350

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BAIA G. ET AL.: "Mining the cancer immuno-responsome: The identification of functional antitumor antibodies from patients receiving checkpoint inhibitors", CANCER RES., vol. 78, no. 13 SUPP, 3966, July 2018 (2018-07), XP002799732, abstract -----	19-24, 78-90, 93,96, 99-102
A	US 2018/100864 A1 (DEFALCO JEFF [US] ET AL) 12 April 2018 (2018-04-12) the whole document -----	19-24, 78-90, 93,96, 99-102

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2020/018350

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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.: 1-18, 25-77, 91, 92, 94, 95, 97, 98, 103-117
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 No. III Observations where unity of invention is lacking (Continuation of item 3 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 fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-18, 25-77, 91, 92, 94, 95, 97, 98, 103-117

The present application provides a family of related antibodies that bind to tumor tissue, derived from an antibody isolated from a patient treated for NSCLC. The prototype of this family is ATRC-101; many variants are also disclosed, which differ slightly from ATRC-101 in only a few point mutations in the CDRs. These antibodies have tumor selective binding. It is indicated that their binding is ribonuclease sensitive, therefore it can be inferred that they bind to some protein-RNA complex. However, the application does not disclose which complex.

Claims 1-18 attempt to cover any antibody that binds a polyadenylated RNA-protein complex. Such claims are a pure shot in the dark, and so lack clarity, support and disclosure in the sense of Art. 5-6 PCT that it is impossible to search them.

Claims 25-26 are hardly any better. Not only they cover mix-and-match permutations of CDRs that are not necessarily disclosed and supported in the description, but they also cover mutants thereof, where so many mutations are allowable that the identity of the respective CDRs can be completely changed. Therefore, these claims do not provide useful features to distinguish them from claims 1-18, and accordingly follow the same fate.

Claims 27, 34, 35, 38, 41, 44, 47, 50 define the CDRs via alleged consensus sequences. However, the SEQ IDs provided for searching these claims (SEQ IDs 1728-1739) are not consensus sequences at all - they reflect specific examples falling within the general formula, and only mention in the annotations that certain amino acids can be changed. Without a sequence in the format suitable for searching the consensus as such, it is not possible to carry out a search. Claim 31 does not refer to a SEQ ID at all, therefore a fortiori it cannot be searched.

Claim 28-30, 75-77 cover a mix-and-match of permutations and combinations of hundreds of sequences, the combination of which may or may not be supported in the description. There are so many alternative that the claim does not comply with the provisions of clarity and conciseness required pursuant to Art 6 PCT.

Claims 32-33 define the scope of protection through in-house names that have no recognized meaning in the art. Such claims so lack clarity that they cannot be searched as such. Claims 91-92, 94 are meaningless, since they provide only for vectors encoding only one chain, respectively only one CDR. They so lack disclosure, support and clarity that a search is not meaningful.

There are 117 claims on file, of which 23 are independent. Of these: claims 1, 19, 25, 34, 116, 117 are in the product category (polypeptide/antibody); claims 91-94 are all independent concerning vectors; claims 96-98 are all independent concerning host cells; claims 78, 81, 103-107 are all independent concerning medical uses. The number of claims is manifestly excessive pursuant to Rule 6.1(a) PCT, and the unnecessary proliferation of independent claims leads to lack of conciseness and clarity. It is moreover manifest that there are many claims, be they independent or

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

dependent, which overlap for no good reason. In the circumstances, only ONE independent claim in each category will be searched, together with its dependent claims and independent claims referring back to it. The present claims can be grouped as follows:

- a) Claims 1-18, partly
75-115 (group of independent claim 1)
- b) Claims 19-24, partly
75-115 (group of independent claim 19)
- c) Claims 25-33, partly
75-115 (group of independent claim 25)
- d) Claims 34-74, partly
75-115 (group of independent claim 34)
- e) Claim
116 (independent claim 116)
- f) Claim
117 (independent claim 117)

Since claims 1-18 cannot be searched, the first searchable set of claims is that of

- Claims 19-24 (antibodies)
- Claims 78-80 (inducing an immune response)
- Claims 81-89 (treating cancer)
- Claim 90 (diagnosis
oa tumor comprising an extracellular RNA complex)
- Claim 93
(expression vector encoding the VH and VL)
- Claim 96, 99-100 (host
cell for the vector)
- Claim 101(method of producing an antibody)
- Claim 102 (a method of identifying an antibody by mutagenizing the
nucleic acid encoding the VH or VL)

All other claims, being redundant and/or not searchable, will be excluded from the scope of the search.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2020/018350

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2018100864 A1	12-04-2018	US 2015011405 A1 US 2018100864 A1	08-01-2015 12-04-2018
