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KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME,
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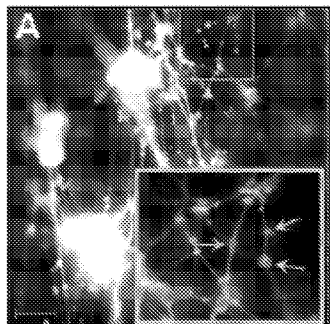


FIG. 1A

(57) Abstract: The disclosure relates to methods for inhibiting the stability of a biofilm comprising contacting the biofilm with an effective amount of an agent that interferes with the binding of a polyamine to DNA in the biofilm. Also provided herein are methods for treating a biofilm in a subject comprising administering to the subject infected with a biofilm an effective amount of an agent that interferes with the binding of a polyamine to the DNA in the biofilm. Further described herein are methods for treating a biofilm in a patient suffering from systemic lupus erythematosus (SLE) and/or cystic fibrosis (CF) comprising administering an effective amount of an agent that interferes with the conversion of B-DNA to Z-DNA in the biofilm or its local environment.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/40008

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 31/16, 31/40, 31/43, 31/65, 31/132, 31/165, 31/404, 31/407, 31/496, 31/505 (2019.01)

CPC - A61K 31/16, 31/40, 31/43, 31/65, 31/132, 31/165, 31/404, 31/407, 31/496, 31/505, 31/546, 31/7036, 35/741, 35/744, 35/747, 39/39, 39/395, 39/02, 39/40; A01N 33/04, 33/06, 37/44; C07K 16/12, 16/1203

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)

See Search History document

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

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 2017/023863 A1 (RESEARCH INSTITUTE AT NATIONWIDE CHILDREN'S HOSPITAL) 9 February 2017; paragraphs [0002], [0176], [0179], [0209], [0240], [0246]-[0248], [0496], [0584]-[0585]	1-8, 9/1, 9/5, 25, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 53/48-49 ----- 16-17, 23, 27-28, 50/48-49, 51/48-49, 52/48-49
X -- Y	(JUNKINS, RD et al.) Autophagy Enhances Bacterial Clearance during P. aeruginosa Lung Infection. PLOS. 28 August 2013, Vol. 8, No. 8; page 1-13; abstract; page 3, 2nd column, 4th paragraph; page 9, 2nd column, 3rd paragraph; DOI: 10.1371/journal.pone.0072263	24-26 ----- 30
X -- Y	US 2017/0197028 A1 (GOLDSMITH, DS) 13 July 2017; paragraphs [0117], [0145], [0518], [0579]	31-32, 33/31-32 ----- 34/31-32, 35/31-32
Y	JP 5670783 B2 (KAO CORP) 18 February 2015; page 2, 5th paragraph; page 3, 4th paragraph	16-17, 51/48-49
Y	US 2017/0215417 A1 (LIVIONEX, INC.) 3 August 2017; abstract; claim 9	23, 52/48-49
Y	(VANHELDEN, PD et al.) A new assay for anti-DNA antibodies in serum which includes the measurement of anti-Z-DNA. Clinical & Experimental Immunology. August 1987, Vol. 69, No. 2; pages 394-402; page 2, 4th paragraph; page 8, 2nd paragraph	27, 30, 34/31-32

 Further documents are listed in the continuation of Box C.
 See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"D" document cited by the applicant in the international application	"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
"E" earlier application or patent but published on or after the international filing date	"&" document member of the same patent family
"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	

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/40008

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	(FENG, J et al.) Identification of new compounds with high activity against stationary phase <i>Borrelia burgdorferi</i> from the NCI compound collection. <i>Emerging Microbes & Infections</i> . 3 June 2015, Vol. 4; pages 1-16; page 2, 2nd column, 3rd paragraph; page 11, 2nd column, 2nd paragraph; DOI: 10.1038/emi.2015.31	28, 35/31-32
Y	WO 2018/050814 A1 (VIRBAC) 22 March 2018; abstract; paragraph [0003]	50/48-49
A	US 2015/0342848 A1 (BHUSHAN, R et al.) 3 December 2015; entire document	1-8, 9/1, 9/5, 16-17, 23-28, 30-32, 33/31-32, 34/31-32, 35/31-32, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 50/48-49, 51/48-49, 52/48-49, 53/48-49
A	(SOYER-GOBILLARD, MO et al.) Location of B- and Z-DNA in the Chromosomes of a Primitive Eukaryote Dinoflagellate. <i>The Journal of Cell Biology</i> . August 1990, Vol. 111, No. 2; pages 293-308; DOI: 10.1083/jcb.111.2.293	1-8, 9/1, 9/5, 16-17, 23-28, 30-32, 33/31-32, 34/31-32, 35/31-32, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 50/48-49, 51/48-49, 52/48-49, 53/48-49
A	WO 2015/048484 A2 (TRELIS BIOSCIENCE, LLC) 2 April 2015; entire document	1-8, 9/1, 9/5, 16-17, 23-28, 30-32, 33/31-32, 34/31-32, 35/31-32, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 50/48-49, 51/48-49, 52/48-49, 53/48-49
P, X	WO 2018/187615 A1 (CURZA GLOBAL, LLC et al.) 11 October 2018; entire document	1-8, 9/1, 9/5, 16-17, 23-28, 30-32, 33/31-32, 34/31-32, 35/31-32, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 50/48-49, 51/48-49, 52/48-49, 53/48-49

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/40008

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.:
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:

3. Claims Nos.: 10-15, 18-21, 40-43, 47, 54-55
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:

-Please see supplemental page-

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 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.:
1-8, 9/1, 9/5, 16-17, 23-28, 30-32, 33/31-32, 34/31-32, 35/31-32, 38/1, 38/5, 39/38/1, 39/38/5, 44/38/1, 44/38/5, 45/38/1, 45/38/5, 46/38/1, 46/38/5, 48-49, 50/48-49, 51/48-49, 52/48-49, 53/48-49

- 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.

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, Claims 1-9, 16-17, 23-25, 26-28 (each in-part), 30-35, 37-39, 44-46, and 48-53 are directed toward contacting a biofilm with an effective amount of an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent is not an HMGB1 protein.

Group II, Claims 22, 26-28 (each in-part), 29, and 36 are directed toward contacting a biofilm with an effective amount of an agent that interferes with the binding of a polyamine to DNA in the biofilm, wherein the agent comprises an HMGB1 protein.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include an agent that is not an HMGB1 protein, not present in Group II; the special technical features of Group II include an agent that is an HMGB1 protein, not present in Group I.

Groups I and II share the technical features including: a method for inhibiting the stability of a biofilm, comprising contacting the biofilm in vitro with an effective amount of a protein or biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof, wherein the contacting comprises coating a surface with an effective amount of a protein or biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof; a method for treating a biofilm in a patient suffering from systemic lupus erythematosus (SLE) and/or cystic fibrosis (CF), comprising administering an effective amount of a protein or biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof; a method for treating a biofilm producing infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy, the method comprising administering an effective amount of a protein or biologically active fragment thereof and anti-B-DNA antibody or fragment or derivative thereof.

However, these shared technical features are previously disclosed by WO 2015/048484 A2 (TRELLIS BIOSCIENCE, LLC) in view of the publication entitled 'Location of B- and Z-DNA in the Chromosomes of a Primitive Eukaryote Dinoflagellate' by Gobillard, et al. (hereinafter 'Gobillard') and US 2016/0303172 A1 (INSTITUT GUSTAVE ROUSSY) (hereinafter 'Roussy').

Trellis discloses a method for inhibiting the stability of a biofilm (method for dissolving a biofilm (inhibiting the stability of a biofilm); paragraph [0007]), comprising contacting the biofilm in vitro with an effective amount of a protein (paragraphs [0007], [0070]), wherein the contacting comprises coating a surface with an effective amount of a protein (wherein the contacting comprises coating a surface with an effective amount of a protein; paragraphs [0003], [0007]); a method for treating a biofilm in a patient suffering from systemic lupus erythematosus (SLE) and/or cystic fibrosis (CF) (a method for treating a biofilm in a patient suffering from cystic fibrosis (CF); paragraph [0011]), comprising administering an effective amount of a protein (comprising administering an effective amount of a protein; paragraphs [0007], [0011]); a method for treating a biofilm producing infection (paragraph [0037]), the method comprising administering an effective amount of a protein (paragraphs [0007], [0070]). Trellis further discloses wherein a major component of biofilms is DNA (paragraph [0002]).

Trellis does not disclose an anti-B-DNA antibody or fragment or derivative thereof and an infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy.

Gobillard discloses an anti-B-DNA antibody (abstract).

Roussy discloses an infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy (determining the effects of antineoplastic treatment, including platinum-based chemotherapy, on the increase of unfavorable bacteria in the gut (infection) incident to administration of a platinum-based chemotherapy in the patient; paragraphs [0109], [0156]-[0164], [0253]).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the disclosure of Trellis to include an anti-B-DNA antibody, as disclosed by Gobillard, in order to provide a method to inhibit Z-DNA formation thereby preventing biofilm production. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the disclosure of Trellis to include an infection incident to administration of a platinum-based chemotherapy in a patient receiving or having received the chemotherapy, as disclosed by Roussy, in order to provide a method to treat biofilm in a cancer patient receiving platinum-based chemotherapy.

Since none of the special technical features of the Groups I and II inventions are found in more than one of the inventions, and since all of the shared technical features are previously disclosed by a combination of the Trellis, Gobillard, and Roussy references, unity of invention is lacking.