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[Continued on next page]

(54) Title: TREATMENTS FOR RETINAL DISORDERS

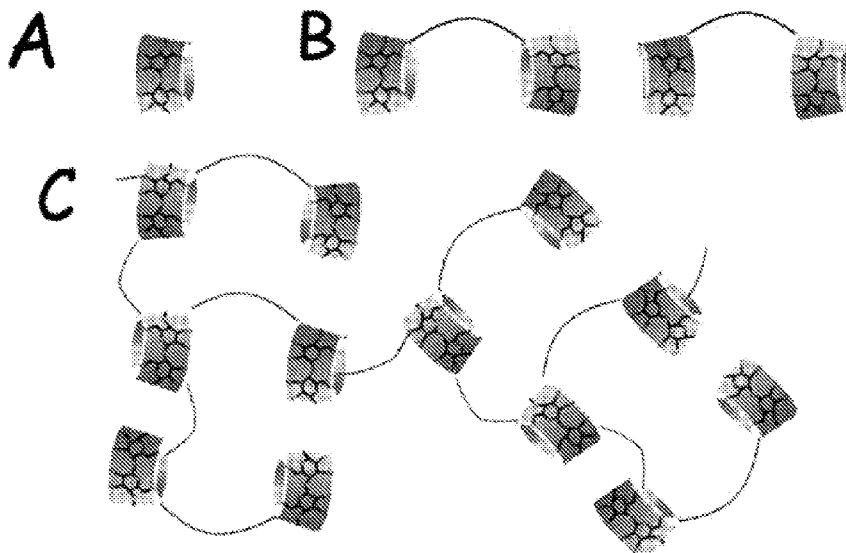


FIG. 2

(57) Abstract: The present invention relates to the use of cyclic oligosaccharides as chemical complexants of lipofuscin bisretinoids (A2E) to prevent and treat eye (i.e., retinal or macular) disease. Monomeric, dimeric, multimeric, or polymeric oligosaccharide rings act as pharmacologic agents to prevent and treat ophthalmologic disorders triggered by the accumulation of lipofuscin in the retinal pigment epithelium (RPE), which occurs as a consequence of either genetic disorders, such as Stargardt Disease (SD) and Best Disease (BD), or aging, such as Age-Related Macular Degeneration (AMD), or other diseases, such as retinitis pigmentosa, and cone-rod dystrophy.





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- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US2012/021997

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC(8) - A61K 31/724 (2014.01)  
 USPC - 514/58  
 According to International Patent Classification (IPC) or to both national classification and IPC

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**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC(8) - A61K 31/70, 31/715, 31/724 (2014.01)  
 USPC - 514/23, 54, 58, 777, 912

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
 CPC - A61K 31/715, 31/724 (2014.02)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Orbit.com, Google Patents, Public AppFT and PatFT, Google Scholar

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | US 2010/0113539 A1 (SCOTT et al) 06 May 2010 (06.05.2010) entire document          | 1-10, 12, 13          |
| Y         |  | 11, 14-19             |
| Y         | US 2001/0021703 A1 (KOSAK) 13 September 2001 (13.09.2001) entire document          | 11, 14                |
| Y         | US 2010/0069471 A1 (MANOHARAN et al) 18 March 2010 (18.03.2010) entire document    | 15-17                 |
| Y         | US 2007/0088014 A1 (EDELMAN et al) 19 April 2007 (19.04.2007) entire document      | 18, 19                |
| A         | US 2007/0275048 A1 (LIU et al) 29 November 2007 (29.11.2007) entire document       | 1-19                  |

Further documents are listed in the continuation of Box C.

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|---|---|
| <p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> | <p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p> |
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| Date of the actual completion of the international search<br>04 April 2014 | Date of mailing of the international search report<br><b>05 MAY 2014</b> |
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| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents<br>P.O. Box 1450, Alexandria, Virginia 22313-1450<br>Facsimile No. 571-273-3201 | Authorized officer:<br>Blaine R. Copenheaver<br><br>PCT Helpdesk: 571-272-4300<br>PCT OSP: 571-272-7774 |
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INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2012/021997

**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.:  
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:

See Extra 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 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.:  
1-19

**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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/021997

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 need to be paid.

Group I: claims 1-19 are drawn to a method for treating a subject suffering from or at risk of lipofuscin-associated retinal damage.

Group II: claims 20-26 are drawn to a method for identifying a compound that binds to a lipofuscin bisretinoid lipid.

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 the Group I, a method for treating a subject suffering from or at risk of lipofuscin-associated retinal damage, the method comprising administering to said subject a cyclic oligosaccharide that targets retinal pigment epithelium cells and has an available binding cavity that complexes a lipofuscin bisretinoid lipid in said retinal pigment epithelium cells, are not present in Group II; and the special technical features of the Group II, a method for identifying a compound that binds to a lipofuscin bisretinoid lipid, are not present in Group I.

Groups I and II share the technical features of a binding cavity that complexes a lipofuscin bisretinoid lipid in retinal pigment epithelium cells. However, these technical features do not represent a contribution over the prior art. Specifically, US 2010/0113539 A1 to Scott et al. teach a cyclic oligosaccharide ("the compositions described herein further comprise cyclodextrins. Cyclodextrins are cyclic oligosaccharides", Para. [1065]) that targets retinal pigment epithelium cells (administering the composition "resulting in a reduction of lipofuscin pigment accumulated in an eye of the subject", where A2E is a lipofuscin pigment, Para. [0270], "in retinal pigment epithelium (RPE) cells", Para. [0933]) and has an available binding cavity ("Cyclodextrins have a hydrophilic exterior, which enhances water-soluble, and a hydrophobic interior which forms a cavity. In an aqueous environment, hydrophobic portions of other molecules often enter the hydrophobic cavity of cyclodextrin to form inclusion compounds.", Para. [1065]) that complexes a lipofuscin bisretinoid lipid in said retinal pigment epithelium cells (the composition comprises compounds "that bind specifically to or interact with A2E A2E-related and/or derived molecules", Para. [0935], where A2E is a lipofuscin pigment, Paras. [1015]-[1016], "A2E has a pyridinium bisretinoid structure" and is a lipofuscin pigment "in retinal pigment epithelium (RPE) cells", Para. [0933], where the hydrophobic/lipophilic cavity may complex the A2E lipid, Paras. [0935];[1065]).

Further, US 2007/0275048 A1 to Liu et al. teach a cyclic oligosaccharide that complexes a lipid (Liu et al., treatment of "age-related macular degeneration (AMD)" of the eye, Paras. [0002];[0055], with a composition comprising "a cyclic oligosaccharide with lipophilic inner cavity and hydrophilic outer surface capable of forming non-covalent inclusion complexes", Para. [0033]).

The inventions listed in Groups I and II therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.