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25 February 2010

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(54) Title: CELL LINE, SYSTEM AND METHOD FOR OPTICAL CONTROL OF SECONDARY MESSENGERS

(57) Abstract: A variety of methods, devices and compositions are implemented for light- activated molecules. One such method is implemented for generating secondary messengers in a cell. A nucleotide sequence for expressing a chimeric light responsive membrane protein (e.g., rhodopsin) is modified with one or more heterologous receptor subunits {e.g., an adrenergic receptor (alpha1, Beta2)}. The light responsive membrane protein is expressed in a cell for producing a secondary messenger in response to light.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/45611

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12P 21/06; C12P 21/04 (2009.01)
USPC - 435/69.1; 435/69.7
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(8) - C12P 21/06; C12P 21/04 (2009.01)
USPC - 435/69.1; 435/69.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 530/345, 530/395, 530/402, 530/405

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PWEST(PGPB,USPT,USOC,EPAB,JPAB); Google Scholar: G protein-coupled receptor, GPCR, rhodopsin, adrenergic receptor, adrenoceptor, noradrenaline, norepinephrine, adrenaline, epinephrine, receptor, stimulat$, stimulus, express, expression, expressed, expressing, activate, activation, activated

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2007/0261127 A1 (BOYDEN et al.) 08 November 2007 (08.11.2007) para [0010]-[0011]; [0022]-[0023]; [0026]; [0072]-[0078]; [0117]; [0148]; [0159]; [0183]	1, 3-9 --------- 2, 10
Y	US 2003/0026784 A1 (KOCH et al.) 06 February 2003 (06.02.2003) para [0004]; [0061]-[0065]	2, 10

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
18 November 2009 (18.11.2009)	25 NOV 2009
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)

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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:

Group I: claims 1-10, drawn to a method comprising expressing a chimeric light responsive chimeric rhodopsin-based fusion protein further comprising one or more heterologous receptor subunits.

Group II-III, claim 11, drawn to a nucleotide sequence according to Seq. Id. No.1 or Seq. Id. No.3 and point mutations thereof.

Group IV-V, claim 12, drawn to a cell expressing the amino acid according to Seq. Id. No.2 or Seq. Id No.4 and point mutations thereof.

********** continued on first blank sheet attached **********

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.:
1-10

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/US 09/45611

********** Supplemental Box **********

Continuation of Box No III: Observations where unity of invention is lacking:

The inventions listed as Groups I-V 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 inventions of Group I do not include the inventive concept of a specific nucleotide or amino acid sequence, as required by Groups II-V.

The inventions of Group II-III do not include the inventive concept of a specific amino acid sequence, as required by Groups IV-V.
The inventions of Group IV-V do not include the inventive concept of a specific nucleotide sequence, as required by Groups II-III.

The special technical feature of the inventions listed as Group II-III is the specific nucleotide sequence recited therein. Although both sequences encode for a rodopsin/GPCR chimera, said chimera is obvious over prior art. Specifically, an article titled "The Amino Terminus of the Fourth Cytoplasmic Loop of Rhodopsin Modulates Rhodopsin-Transducin Interaction" by Marin, et al. (THE JOURNAL OF BIOLOGICAL CHEMISTRY 2000, 275(3):1930?1936) discloses "[a] series of rhodopsin mutants was prepared in which portions of the fourth loop were replaced with analogous sequences from the beta2-adrenergic receptor or the m1 muscarinic receptor" (abstract). As the claimed chimeric light responsive chimeric rhodopsin-based fusion protein is obvious over Matin et al, said was known in the art at the time of the invention, structural similarities among the claimed nucleotide sequences do not constitute a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

Similarly, the special technical feature of the inventions listed as Group IV-V is the specific amino acid sequence recited therein. Although both amino acid sequences correspond to a rodopsin/GPCR chimera, said chimera is obvious over Marin, et al., as above. Thus, structural similarities among the claimed amino acid sequences do not constitute a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

Groups I-V therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.