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(54) Title: A METHOD FOR NONINVASIVELY AND QUANTITATIVELY MONITORING THERAPEUTIC AND DIAGNOSTIC TRANSGENE EXPRESSION INDUCED BY EX VIVO AND IN VIVO GENE TARGETING IN ORGANS, TISSUES AND CELLS

(57) Abstract: An composition in a method for noninvasively monitoring the expression of therapeutic transgene delivered ex vivo and in vivo for the treatment of diseases includes the step of quantitatively imaging a reporter gene expression which is coupled to a therapeutic gene on a plasmid vector to infer levels, location, or duration of the therapeutic gene expression in the targeted tissues or organs. The reporter gene is imaged using a radiopharmaceutical for scintigraphic imaging of the gene expression interactions with the reporter gene, namely positron emission tomography, gamma camera or single-photon emission computed tomography. The genes are delivered with a liposome encapsulated reporter-therapeutic linked transgene vector with balanced reporter/therapeutic transgene expression. A transgene composition includes the reporter gene linked to the therapeutic gene or genes incorporated in and delivered by a liposome encapsulated reporter-therapeutic linked transgene vector.



WO 2007/109335 A3

INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/68(2006.01);A61K 49/00(2006.01);G21H 5/02(2006.01)

USPC: 435/6;424/9. 1;250/303

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)

U.S. : 435/6;424/9. 1;250/303

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)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X v --- Y /	SEN. L. Noninvasive imaging of ex vivo intracoronarily delivered nonviral therapeutic transgene expression in heart. Molecular Therapy July 2005, Vol. 12. No. 1, pages 49-57.	1-3, 6, 8-1 1, 13, 15-20, 23-27, 29,31-37 ----- 1-3, 6, 8-1 1, 13, 15-20, 23-27,29, 31-37
Y '	RAY.P.Imaging tri-fusion multimodality reporter gene expression in living subjects. Cancer Res. February, 2004, Vol. 64. No. 4, 1323-30	4,7, 12,21,22,28,30
Y	ANTON. M. Co expression of herpesviral thymidine kinase reporter gene and VEGF gene for noninvasive monitoring of therapeutic gene transfer: an in vitro evaluation. J Nucl Med. October 2004, Vol. 45. No. 10, 1743-1746.	4,7,12,21,22,28,30
Y	KIM. D.W. Use of the human elongation factor 1 alpha promoter as a versatile and efficient expression system. Gene. July 1990, Vol. 91. No. 2, 217-223.	12,14,30



Further documents are listed in the continuation of Box C.

D

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
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"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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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WANG. Y. Noninvasive monitoring of target gene expression by imaging reporter gene expression in living animals using improved bicistronic vectors. J Nucl Med. April 2005, Vol. 46. No. 4,667-4674.	1-37
A	BENGEL. F.M. Noninvasive imaging of transgene expression by use of positron emission tomography in a pig model of myocardial gene transfer. Circulation October 2003, Vol. 108. No. 17, pages 2127-2133.	1-37