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SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 08 74 3279

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	DATTA R ET AL: "REACTIVE OXYGEN INTERMEDIATES TARGET CC(A/T)6GG SEQUENCES TO MEDIATE ACTIVATION OF THE EARLY GRWTH RESPONSE 1 TRANSCRIPTION FACTOR GENE BY IONIZING RADIATION", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, NEW YORK, NY, US, vol. 90, no. 6, 15 March 1993 (1993-03-15) , pages 2419-2423, XP000561892, * page 2419 * * abstract * * page 2420 * * page 2422 *	1	INV. C07H21/04 C12N15/00 A61K48/00
X	SCHAEFER GEORGIA ET AL: "Oxidative stress regulates vascular endothelial growth factor-A gene transcription through Sp1- and Sp3-dependent activation of two proximal GC-rich promoter elements.", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 10, 7 March 2003 (2003-03-07), pages 8190-8198, XP002677626, ISSN: 0021-9258 * page 8190 * * abstract *	1,2,6,7, 11-13, 15-28,30	TECHNICAL FIELDS SEARCHED (IPC) A61K

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The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
The Hague	13 June 2012	Sitch, David

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C04)

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Application Number
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DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	SHIMA DAVID T ET AL: "The mouse gene for vascular endothelial growth factor: Genomic structure, definition of the transcriptional unit, and characterization of transcriptional and post-transcriptional regulatory sequences", JOURNAL OF BIOLOGICAL CHEMISTRY, THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, INC, US, vol. 271, no. 7, 1 January 1996 (1996-01-01), pages 3877-3883, XP002176168, ISSN: 0021-9258, DOI: 10.1074/JBC.271.44.27424 * page 3882, right-hand column, paragraph 2 *	1,2,6,7, 11-13, 15-28,30	
X	Loureiro et al: "EGF REGULATION OF VEGF: ROLE IN PROGRESSION OF ERBB2 OVEREXPRESSING MAMMARY TUMORS", , July 2004 (2004-07), XP002677627, Retrieved from the Internet: URL:HTTP://WWW.DTIC.MIL/CGI-BIN/GETTRDOC?AD=ADA427846 [retrieved on 2012-06-13] * paragraph bridging pages 18 and 19 *	1,2,6,7, 11-13, 15-28,30	TECHNICAL FIELDS SEARCHED (IPC)

The supplementary search report has been based on the last set of claims valid and available at the start of the search.

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☒ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

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LACK OF UNITY OF INVENTION
SHEET B

Application Number
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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 13(completely); 1, 2, 6, 7, 11, 12, 15-28, 30(partially)

   At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the VE element consisting of -80 to -50 of the VEGF promoter; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such;

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2. claims: 1, 2, 6, 7, 11, 12, 15-28, 30(all partially)

   At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the E6 element of a region proximal to the promoter of the EGR-1 gene; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such

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3. claims: 1, 2, 6, 7, 11, 12, 15-28, 30(all partially)

   At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the MMP1 element consisting of -2000 to -1546 of the MMP-1 promoter; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such

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4. claims: 3-5, 8-10, 14, 29, 31-33(completely); 1, 2, 6, 7, 11, 12, 15-28, 30(partially)

   At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is a chimaeric promoter containing an E6 element spaced from a VE element by a spacing sequence; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such

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The present application lacks unity of invention in the sense of Art. 82 EPC for the following reasons:
Independent claims are drafted in essence to the following matter:
1) At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells;

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

6) A vector comprising at least a fragment of a reactive oxygen species inducible promoter of a gene highly expressed in cancer cells;
19) A pharmaceutical composition comprising a vector of claim 6;
22) A treatment using the composition of claim 19;
28) A diagnostic method using the promoter of claim 1.
30) A method for expressing a therapeutic gene via use of a vector having a promoter selected from
a) the VE element consisting of -80 to -50 of the VEGF promoter;
b) the E6 element of a region proximal to the promoter of the EGR-1 gene;
c) the MMP1 element consisting of -2000 to -1546 of the MMP-1 promoter.
The most narrowly definable problem which at the same is, a priori, solved by the subject matter of each of these claims is the provision of promoters suitable for expression of a gene in tumours, for therapeutic or diagnostic purposes.
In careful consideration of the claimed solutions to this problem, a priori, the sole single general inventive concept able to be identified by means for which unity of invention can be recognised, is the use of a promoter from a gene highly expressed in cancer cells and which promoter is responsive to reactive oxygen species. Such general inventive concept is enshrined by the generically defined subject matter of claim 1.
D1 pertains to a study of so-called CArG elements from the Egr1 gene (which, according to the present applicant, is a preferred example of a gene highly expressed in cancer cells - see for example present claim 2). In D1, upstream CC(A/T) 6 GG (CArG) elements of the Egr1 gene were cloned into a vector encoding the reporter gene CAR (pTK35CAT). See page 2420, 'reporter assays'. Exposure not only to ionizing radiation, but also the reactive oxygen species H2 O2 was found to lead to activation of the CArG element, with concomittant downstream gene expression (see page 2422, figure 5).
In view of D1, the general inventive concept referred to above is not novel, and as such cannot be seen as the general inventive concept by which unity of invention between the plurality of inventions of the application can be acknowledged. No other general inventive concept serving such purpose has been able to be identified, and the following groups of inventions, not linked by a single general inventive concept, have now been identified:
1. At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the VE element consisting of -80 to -50 of the VEGF promoter; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such;
2. At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the E6 element of a region proximal to the promoter of the EGR-1 gene; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such;
3. At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is the MMP1 element consisting of -2000 to

LACK OF UNITY OF INVENTION
SHEET B

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

-1546 of the MMP-1 promoter; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such;
4. At least a fragment of a reactive oxygen species inducible promoter 'corresponding to', ie from, a gene highly expressed in cancer cells, wherein the promoter fragment is a chimaeric promoter containing an E6 element spaced from a VE element by a spacing sequence; corresponding vector; corresponding method for expressing a therapeutic gene; pharmaceutical composition based on such; diagnostic method based on such.