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(54) Title: CANCER SUSCEPTIBILITY LOCI

(57) Abstract: The present invention relates to the identification of genetic loci associated with susceptibility to tumour and cancer development, particularly risk of colorectal cancer and tumour. The invention relates to the analysis of these loci in samples obtained from individuals, and kits for use in such analysis.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68

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)
C12Q

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 practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BRODERICK ET AL.: "Lack of a relationship between the common 18q24 variant rs12953717 and risk of chronic lymphocytic leukemia." 19000101, February 2008 (2008-02), XP008102551 the whole document	1-12, 43, 45-47
P,X	WO 2008/046964 A (JAAKKOLA PANU [FI]; HEIKKINEN PEKKA [FI]) 24 April 2008 (2008-04-24) page 2, paragraphs 2,3 claim 8	1-12, 43, 45-47

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

☒ See patent family annex.

* 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 document 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.
- *Z* document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2008/003454

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BRODERICK PETER ET AL: "A genome-wide association study shows that common alleles of SMAD7 influence colorectal cancer risk" NATURE GENETICS, vol. 39, no. 11, November 2007 (2007-11), pages 1315-1317, XP002516278 ISSN: 1061-4036 the whole document	1-12,43, 45-47
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P,X	WO 2008/106785 A (CANCER CARE ONTARIO [CA]; UNIV MCGILL [CA]; COTTERCHIO MICHELLE [CA];) 12 September 2008 (2008-09-12) examples 212-217 claim 25	1-12,43, 45-47
X	WATANABE YUKIO ET AL: "A catalog of 106 single-nucleotide polymorphisms (SNPs) and 11 other types of variations in genes for transforming growth factor-beta1 (TGF-beta1) and its signaling pathway" JOURNAL OF HUMAN GENETICS, vol. 47, no. 9, 2002, pages 478-483, XP002516284 ISSN: 1434-5161 the whole document	1-11
Y		12
Y	HALDER S K ET AL: "Smad7 induces tumorigenicity by blocking TGF-beta-induced growth inhibition and apoptosis" EXPERIMENTAL CELL RESEARCH, ACADEMIC PRESS, US, vol. 307, no. 1, 1 July 2005 (2005-07-01), pages 231-246, XP004908935 ISSN: 0014-4827 the whole document	1-12,43, 45-47

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2008/003454

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HE WEI ET AL: "Smads mediate signaling of the TGFbeta superfamily in normal keratinocytes but are lost during skin chemical carcinogenesis" ONCOGENE, vol. 20, no. 4, 25 January 2001 (2001-01-25), pages 471-483, XP002516279 ISSN: 0950-9232 the whole document	1-12
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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2008/003454

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 03/070082 A (IDGENE PHARMACEUTICALS LTD [IL]; DARVASI ARIEL [IL]; ZAK NAOMI [IL]) 28 August 2003 (2003-08-28) claim 394	4-11
Y	WO 2005/014782 A (ALNYLAM PHARMACEUTICALS [US]; WOPPMANN CLAUDIA [DE]; VORNLOCHER HANS-P) 17 February 2005 (2005-02-17) page 61, last paragraph	4-11
Y	US 2003/215528 A1 (GRAHAM CHARLES H [CA] ET AL) 20 November 2003 (2003-11-20) paragraph [0058]	4-11
A	MONTELEONE G ET AL: "BLOCKING SMAD7 RESTORES TGF-BETA1 SIGNALING IN CHRONIC INFLAMMATORY BOWEL DISEASE" JOURNAL OF CLINICAL INVESTIGATION, AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, US, vol. 108, no. 4, 1 August 2001 (2001-08-01), pages 601-609, XP001152527 ISSN: 0021-9738 the whole document	
A	LITTLE J ET AL: "Family history, metabolic gene polymorphism, diet and risk of colorectal cancer." EUROPEAN JOURNAL OF CANCER PREVENTION : THE OFFICIAL JOURNAL OF THE EUROPEAN CANCER PREVENTION ORGANISATION (ECP) DEC 1999, vol. 8 Suppl 1, December 1999 (1999-12), pages S61-S72, XP008102586 ISSN: 0959-8278 the whole document	
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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2008/003454

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LANDSTROM M ET AL: "Smad7 mediates apoptosis induced by transforming growth factor beta in prostatic carcinoma cells" CURRENT BIOLOGY, CURRENT SCIENCE, GB, vol. 10, no. 9, 4 May 2000 (2000-05-04), pages 535-538, XP002252297 ISSN: 0960-9822 the whole document	
A	XIE ET AL.: "Loss of Smad Signaling in Human Colorectal Cancer Is associated with Advanced Disease and Poor Prognosis" 19000101, vol. 9, no. 4, 1 July 2003 (2003-07-01), pages 302-312, XP008102550 the whole document	
A	WO 2006/012361 A (UNIV SOUTHERN CALIFORNIA [US]; LENZ HEINZ-JOSEF [US]) 2 February 2006 (2006-02-02) page 1, paragraph 4 - page 2, paragraph 2 claims 23,24	
A	EP 1 314 787 A (KUDOH NORIO [JP]) 28 May 2003 (2003-05-28) claims 1-8	
A	BOULAY JEAN-LOUIS ET AL: "Combined copy status of 18q21 genes in colorectal cancer shows frequent retention of SMAD7" GENES CHROMOSOMES AND CANCER, vol. 31, no. 3, July 2001 (2001-07), pages 240-247, XP002516294 ISSN: 1045-2257 the whole document	
A	KORCHYNSKYI OLEXANDER ET AL: "Expression of Smad proteins in human colorectal cancer" INTERNATIONAL JOURNAL OF CANCER, vol. 82, no. 2, 19 July 1999 (1999-07-19), pages 197-202, XP002516295 ISSN: 0020-7136 the whole document	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2008/003454

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 additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an 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 reportcovers 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 - 12, 43 and 47 (all completely), 45, 46 (all partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-12, 43 and 47 (all completely), 45,46 (all partially)

Methods and kits using/detecting polymorphisms in the SMAD7 gene.

Invention 2: claims 13-20, 44 and 48 (all completely), 45,46 (all partially)

Methods and kits using/detecting polymorphisms in the HMPS/CRAC1 gene.

3. claims: Invention 3: claims 21-42 and 49-54 (all partially)

Methods and kits using/detecting polymorphisms in the region 117650000-117870000 of chromosome 8.

Invention 4: claims 21-42 and 49-54 (all partially)

Methods and kits using/detecting polymorphisms in the region 8730000-8810000 or in the region 76789000-76811000 of chromosome 10.

5. claims: Invention 5: claims 21-42 and 49-54 (all partially)

Methods and kits using/detecting polymorphisms in the region 63108000-63170000 of chromosome 4.

6. claims: Invention 6: claims 21-42 and 49-54 (all partially)

Methods and kits using/detecting polymorphisms in the region 231840000-231868000 of chromosome 1.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2008/003454

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