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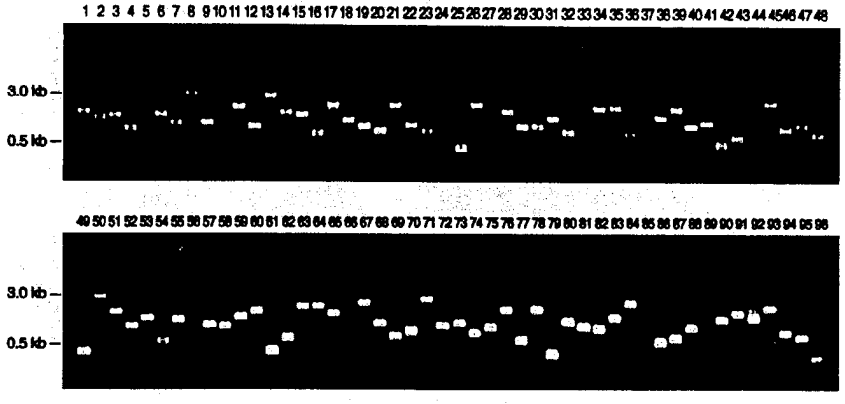
(54) Title: METHODS FOR DETECTION AND USE OF DIFFERENTIALLY EXPRESSED GENES IN DISEASE STATES



(57) Abstract

The present invention relates to methods and compositions for the detection, diagnosis, prevention and treatment of a disease, specifically cardiac, kidney or inflammatory disease, and related disorders. The present invention also relates to compositions and methods useful in the diagnosis, prevention and therapeutic treatment of a disease, specifically cardiac, kidney or inflammatory disease. Specifically, methods and compositions are provided for the diagnostic evaluation and prognosis of conditions involving a disease, specifically cardiac, kidney or inflammatory disease, for the identification of subjects exhibiting a predisposition to such conditions, for modulating the effect of these differentially expressed genes, for monitoring patients undergoing clinical evaluation for the prevention and treatment of a disease, specifically cardiac, kidney or inflammatory disease, and its disorders, and for monitoring the efficacy of compounds used in clinical trials.

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INTERNATIONAL SEARCH REPORT

Inter ›nal Application No
PCT/US 99/29941

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/17 A61K38/18 C07K14/47 C07K14/475 C12N15/12
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)
IPC 7 A61K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE EMBL [Online] ACCESION NUMBER X57352, 26 May 1993 (1993-05-26) LEWIN A.R. ET AL: "Molecular analysis of a human interferon-inducible gene family" XP002136677 abstract & EUR. J. BIOCHEM. 199:417-423, 1991 --- -/--	1-72

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in 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

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"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
8 May 2000	10. 08. 2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fernandez y Branas, F

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MASUDA H ET AL: "Bone loss due to estrogen deficieny is compensated in transgenic mice overexpressing human osteoblast stimulating factor-1" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,US,ACADEMIC PRESS INC. ORLANDO, FL, vol. 238, no. 238, 1997, pages 528-533-533, XP002100860 ISSN: 0006-291X abstract page 533, column 1, paragraph 1 ---	1-5, 7-12,14, 15, 17-24, 65-72
A	IMAI S ET AL: "Osteoblast recruitment and bone formation enhanced by cell matrix-associated heparin-binding growth-associated molecule (HB-GAM)" THE JOURNAL OF CELL BIOLOGY,US,ROCKEFELLER UNIVERSITY PRESS, vol. 143, no. 4, 16 November 1998 (1998-11-16), pages 1113-1128-1128, XP002102012 ISSN: 0021-9525 abstract page 1127, column 1, paragraph 1 figure 9 ---	1-5, 7-12,14, 15, 17-24, 65-72
A	DATABASE EMBL [Online] ACCESION NUMBER T12736, 1996 COLLEY KJ ET AL: "Antisense oligonucleotides of pleiotrophin" XP002136678 abstract -& WO 96 02257 A (GEORGETOWN UNIVERSITY) ---	1-3, 5-13, 25-32, 35-47, 49-72
A	DATABASE EMBL [Online] ACCESION NUMBER Q94159, 1995 MIZUSHIMA S ET AL: "DNA ENCODING A PROTEIN PROMOTING PG12 PRODUCTION" XP002136679 abstract -& WO 94 29448 A (NAWATA H.) ---	1,2,5-9, 12,13, 25-34, 38,39
X	MAEDA K. ET AL: "Analysis of an expression profile of genes in the human adipose tissue" GENE, vol. 190, 1997, pages 227-235, XP002136672 abstract; table 1 --- -/--	38,39

INTERNATIONAL SEARCH REPORT

Inter ›nal Application No
PCT/US 99/29941

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HELLER R.A. ET AL: "Discovery and analysis of inflammatory disease-related genes using cDNA microarrays" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, vol. 94, 1997, pages 2150-2155, XP002136673 the whole document ---	38,39
X	SCHENA M. ET AL: "parallel human genome analysis: Microarray-based expression monitoring of 1000 genes" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, vol. 93, 1996, pages 10614-10619, XP002136674 the whole document ---	38,39
X,P	WO 99 38973 A (CORIXA CORP) 5 August 1999 (1999-08-05) Seq Id 119 claim 33 -----	38,39

INTERNATIONAL SEARCH REPORT

Inte. ational application No.
PCT/US 99/29941

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 1-3, 5, 8-10, 12, 16 (all partially)
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:

see FURTHER INFORMATION sheet PCT/ISA/210

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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

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 an additional fee, this Authority did not invite payment of any additional fee.

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. [X] 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.:

1-72 (all partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-24, 32-34, 65-72 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claim(s) 35-37 (partially when the methods are carried out in vivo) are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 1-3, 5, 8-10, 12, 16 (all partially)

Present claims 1-3, 5, 8-10, 12 and 16 relate to a compound defined by reference to a desirable characteristic or property, namely the capability to modulate the genes mentioned in claim 1 or their expression products

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds specificaly defined in claims 4, 6, 11, 13, 14, 15, 17, 32 and 65.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence 1-8U or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human 1-8U; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the 1-8U gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human protein 1-8U; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving 1-8U and one or more of prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II; claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is 1-8U.

2. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence prostacyclin stimulating factor or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human prostacyclin stimulating factor; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the prostacyclin stimulating factor gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human protein prostacyclin stimulating factor; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving one or more of 1-8U, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in as far not covered by subject 1;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is prostacyclin stimulating factor.

3. Claims: 1-72 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence osf-2 or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human osf-2; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the osf-2 gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human osf-2; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving osf-2 and one or more of 1-8U, prostacyclin stimulating factor, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-2;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is osf-2.

4. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence tissue specific mRNA protein or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human tissue specific mRNA protein; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the tissue specific mRNA protein gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human tissue specific mRNA protein; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving tissue specific mRNA protein and one or more of 1-8U, prostacyclin stimulating factor, osf-2, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-3; claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is tissue specific mRNA protein.

5. Claims: 1-72 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence IGFBP-6 or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human IGFBP-6; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the IGFBP-6 gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human IGFBP-6;
the methods, antisenses, kits and array of claims 1-62 and 65-72 involving IGFBP-6 and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-4;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is IGFBP-6.

6. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence OSF-1 or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human OSF-1; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the OSF-1 gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human OSF-1; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving OSF-1 and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-5;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is OSF-1.

7. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

diseases by administering modulators of a gene encoding a human protein consisting of native sequence gas-1 or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human gas-1; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the gas-1 gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human gas-1; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving gas-1 and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-6;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is gas-1.

8. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence YMP or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human YMP; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the YMP gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human YMP; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving YMP and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, BTG2, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-7;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is YMP.

9. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence BTG2 or its expression products; claims 25-31, concerning antisense

oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human BTG2; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the BTG2 gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human BTG2; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving BTG2 and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, SDF1a, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-8; claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is BTG2.

10. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence SDF1a or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human SDF1a; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the SDF1a gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human SDF1a; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving SDF1a and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, peripheral benzodiazepine receptor and cellular ligand of annexin II in so far not covered by subjects 1-9; claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is SDF1a.

11. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence peripheral benzodiazepine receptor or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human peripheral benzodiazepine

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receptor; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the peripheral benzodiazepine receptor gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human peripheral benzodiazepine receptor; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving peripheral benzodiazepine receptor and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a and cellular ligand of annexin II, in so far not covered by subjects 1-10;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is peripheral benzodiazepine receptor.

12. Claims: 1-72 (all partially)

Claims 1-24, 32-34 and 65-72 concerning methods of treatment and/or prevention of cardiac, kidney or inflammatory diseases by administering modulators of a gene encoding a human protein consisting of native sequence cellular ligand of annexin II or its expression products; claims 25-31, concerning antisense oligonucleotides capable of hybridizing and inhibiting the translation of the mRNA encoded by a gene encoding human cellular ligand of annexin II; claims 35-37 and 40-62 diagnostic methods and kits for detecting cardiac, kidney or inflammatory disease in a human patient in so far the methods are concerned with the measurement of the expression of the cellular ligand of annexin II gene; claims 38-39 concerning an array of one or more oligonucleotides complementary to reference DNA or RNA sequnces encoding the human cellular ligand of annexin II; the methods, antisenses, kits and array of claims 1-62 and 65-72 involving cellular ligand of annexin II and one or more of 1-8U, prostacyclin stimulating factor, osf-2, tissue specific mRNA protein, IGFBP-6, OSF-1, gas-1, YMP, BTG2, SDF1a, peripheral benzodiazepine receptor, in so far not covered by subjects 1-11;
claims 63-64 concerning the methods of identification of modulators of a differentially expressed cardiac, kidney or inflammatory disease gene in so far the gene is cellular ligand of annexin II.

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Inter ...nal Application No
PCT/US 99/29941

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9602257 A	01-02-1996	AU 3126595 A	16-02-1996
		CA 2195450 A	01-02-1996
		JP 10506003 T	16-06-1998
WO 9429448 A	22-12-1994	JP 7132095 A	23-05-1995
WO 9938973 A	05-08-1999	AU 2344399 A	16-08-1999