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(71) Applicant *(for all designated States except US)*: EURONA MEDICAL AB [SE/SE]; Kungsängsvägen 29, P.O. Box 398, S–751 06 Uppsala (SE).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: NORBERG, Leif, Torbjörn [SE/SE]; Backvägen 14 B, S–756 52 Uppsala (SE). ANDERSSON, Maria, Kristina [SE/SE]; Backvägen 14 B, S–756 52 Uppsala (SE). LINDSTRÖM, Per, Harry, Rutger [SE/SE]; Svankkärsvägen 26 A, S–756 53 Uppsala (SE).

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(54) Title: METHODS FOR ASSESSING CARDIOVASCULAR STATUS AND COMPOSITIONS FOR USE THEREOF

(57) Abstract

The present invention provides methods for assessing cardiovascular status in an individual, which comprise determining the sequence at one or more polymorphic positions within the human genes encoding angiotensin converting enzyme (ACE), angiotensinogen (AGT), and/or type 1 angiotensin II receptor (AT1). The invention also provides isolated nucleic acids endoding ACE, AGT, and AT1 polymorphisms, nucleic acid probes that hybridize to polymorphic positions, kits for the prediction of cardiovascular status, and nucleic acid and peptide targets for use in identifying candidate cardiovascular drugs.

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INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/IB 98/00475

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12Q1/68 C07K14/72 C07K14/575 C12N9/48

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 08048 A (INST NAT SANTE RECH MED ;UNIV UTAH RES FOUND (US)) 14 April 1994 see page 5, line 5 - line 23 see page 8, line 12 - page 9, line 4 see page 12, line 1 - line 30	1-5,13, 34
A		6-8, 18-20

X	WO 96 05324 A (INST NAT SANTE RECH MED ;SOUBRIER FLORENT (FR); CAMBIEN FRANCOIS () 22 February 1996 see abstract; claim 6 see page 9, line 18 - line 27	1-7,12, 14,34
A		8,9, 15-17, 21-23

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

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
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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	Ceder, O

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INTERNATIONAL SEARCH REPORT

Int .tional Application No
PCT/IB 98/00475

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 00360 A (INST NAT SANTE RECH MED) 7 January 1993 see abstract; claims 1,2 see page 1, line 15 - line 18 see page 4, line 23 - line 30 see page 7, line 6 - line 12	1-3,10, 12,15,17
A	---	16
X	TIRET L ET AL: "SYNERGISTIC EFFECT OF ANGIOTENSIN-CONVERTING ENZYME AND ANGIOTENSIN-II TYPE 1 RECEPTOR GENE POLYMORPHISMS ON RISK OF MYOCARDIAL INFARCTION" LANCET THE, vol. 344, 1 October 1994, pages 910-913, XP000619739 cited in the application see abstract see page 910, right-hand column see page 912, right-hand column - page 913, left-hand column	1-5
A	-----	6,7

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. ional Application No
PCT/IB 98/00475

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9408048 A	14-04-1994	US 5374525 A	20-12-1994
		AU 670990 B	08-08-1996
		AU 5725094 A	26-04-1994
		CA 2145415 A	14-04-1994
		EP 0665898 A	09-08-1995
		JP 8505043 T	04-06-1996
		NZ 259092 A	28-05-1996
		US 5589584 A	31-12-1996
		US 5763168 A	09-06-1998
WO 9605324 A	22-02-1996	FR 2723590 A	16-02-1996
WO 9300360 A	07-01-1993	FR 2678285 A	31-12-1992
		CA 2111953 A	07-01-1993
		EP 0591332 A	13-04-1994
		JP 6508524 T	29-09-1994
		US 5736323 A	07-04-1998