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(54) Title: IDENTIFICATION OF A DNA VARIANT ASSOCIATED WITH ADULT TYPE HYPOLACTASIA

(57) Abstract: The present invention relates to a nucleic acid molecule comprising a 5' portion of an intestinal lactase-phlorizine hydrolase (LPH) gene contributing to or indicative of the adult-type hypolactasia wherein said nucleic acid molecule is selected from the group consisting of (a) a nucleic acid molecule having or comprising the nucleic acid sequence of SEQ ID NO: 1, the sequence of SEQ ID NO:1 is also depicted in the Fig. 4 and comprised in the sequence as depicted in the Fig. 8; (b) a nucleic acid molecule having or comprising the nucleic acid sequence of SEQ ID NO: 2, the sequence of SEQ ID NO:2 is also depicted in Fig.5 and comprised in the sequence as depicted in the Fig. 9; (c) a nucleic acid molecule of at least 20 nucleotides the complementary strand of which hybridizes under stringent conditions to the nucleic acid molecule of (a) or (b), wherein said polynucleotide/nucleic acid molecule has at a position corresponding to position -13910 5' from the LPH gene a cytosine residue; and (d) a nucleic acid molecule of at least 20 nucleotides the complementary strand of which hybridizes under stringent conditions to the nucleic acid molecule of (a) or (b), wherein said polynucleotide/nucleic acid molecule has at a position corresponding to position -22018 5' from the LPH gene a guanine residue. The present invention further relates to methods for testing for the presence of or predisposition to adult-type hypolactasia that are based on the analysis of an SNP contained in the above recited nucleic acid molecule. Additionally, the present invention relates to diagnostic composition and kit useful in the detection of the presence of or predisposition to adult-type hypolactasia.

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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N

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)
BIOSIS, SEQUENCE SEARCH, CHEM ABS Data, EMBASE, EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! 18 October 1999 (1999-10-18) SULSTON J.E. ET AL.: "Homo sapiens BAC clone RP11-34L23 from 2, complete sequence." Database accession no. AC011893 XP002244247 100% identity with SEQ ID NOs1 and 2;99,9% identity with SEQ ID NOs 3 and 4. the whole document --- -/--	1

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

[ ] Patent family members are listed in annex.

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'A' document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
13 June 2003	02/07/2003

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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.
X	DATABASE EMBL 'Online! 5 May 1999 (1999-05-05) MAHAIRAS G.G. ET AL.: "HS_5237_A1_G08_SP6E RPCI-11 Human Male BAC Library Homo sapiens genomic clone" Database accession no. AQ515834 XP002244248 80% identity with SEQ ID NO: 1 in 116 nt overlap (nt 24-139) the whole document ---	1
X	DATABASE EMBL 'Online! 26 April 2001 (2001-04-26) HARRINGTON J.J. ET AL.: "RST8055 Athersys RAGE Library Homo sapiens cDNA, mRNA sequence." Database accession no. BG189020 XP002244249 86% identity with SEQ ID NO: 2 in 93 nt overlap (89-180) the whole document ---	1
X	DATABASE EMBL 'Online! 11 November 1999 (1999-11-11) MAHAIRAS G.G. ET AL. : "HS_3081_B2_E03_T7C CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone" Database accession no. AQ892176 XP002244250 75% identity with SEQ ID NO: 3 in 56 nt overlap (302-357) the whole document ---	2
X	DATABASE EMBL 'Online! 3 August 1999 (1999-08-03) MAHAIRAS G.G. ET AL.: "HS_3106_A2_D07_T7C CIT Approved Human Genomic Sperm Library D Homo sapiens genomic clone" Database accession no. AQ781670 XP002244251 81% identity with SEQ ID NO: 4 in 69 nt overlap (83-150) the whole document ---	2
Y	JARVELA IRMA ET AL: "Assignment of the locus for congenital lactase deficiency to 2q21, in the vicinity of but separate from the lactase-phlorizin hydrolase gene." AMERICAN JOURNAL OF HUMAN GENETICS, vol. 63, no. 4, October 1998 (1998-10), pages 1078-1085, XP002244245 ISSN: 0002-9297 the whole document --- -/--	1-40

INTERNATIONAL SEARCH REPORT

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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.
Y	BOLL W ET AL: "STRUCTURE OF THE CHROMOSOMAL GENE AND COMPLEMENTARY DNAS CODING FOR LACTASE PHLORIZIN HYDROLASE IN HUMANS WITH ADULT-TYPE HYPOLACTASIA OR PERSISTENCE OF LACTASE" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 48, no. 5, 1991, pages 889-902, XP009012268 ISSN: 0002-9297 abstract Discussion ---	1-40
Y	WANG YANGXI ET AL: "The lactase persistence/non-persistence polymorphisms is controlled by a cis-acting element." HUMAN MOLECULAR GENETICS, vol. 4, no. 4, 1995, pages 657-662, XP009012156 ISSN: 0964-6906 the whole document ---	1-40
P,X	ENATTAH NABIL SABRI ET AL: "Identification of a variant associated with adult-type hypolactasia." NATURE GENETICS, vol. 30, no. 2, February 2002 (2002-02), pages 233-237, XP002244246 February, 2002 ISSN: 1061-4036 the whole document -----	1-40