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(54) Title: GENETIC POLYMORPHISMS ASSOCIATED WITH LIVER FIBROSIS METHODS OF DETECTION AND USES THEREOF

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The present invention is based on the discovery of genetic polymorphisms that are associated with liver fibrosis and related pathologies. In particular, the present invention relates to nucleic acid molecules containing the polymorphisms, variant proteins encoded by such nucleic acid molecules, reagents for detecting the polymorphic nucleic acid molecules and proteins, and methods of using the nucleic acid and proteins as well as methods of using reagents for their detection.
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(57) Abstract: The present invention is based on the discovery of genetic polymorphisms that are associated with liver fibrosis and related pathologies. In particular, the present invention relates to nucleic acid molecules containing the polymorphisms, variant proteins encoded by such nucleic acid molecules, reagents for detecting the polymorphic nucleic acid molecules and proteins, and methods of using the nucleic acid and proteins as well as methods of using reagents for their detection.
What is claimed is:

1. A method for determining whether a human has an increased risk for developing liver fibrosis, comprising:
   a) testing nucleic acid from said human to determine the presence or absence of a polymorphism in gene TLR4 at position 101 of the nucleotide sequence defined by SEQ ID NO:53 or its complement; and
   b) correlating the presence of C at position 101 of SEQ ID NO: 53 or G at position 101 of its complement with said human having said increased risk for developing liver fibrosis.

2. The method of claim 1, wherein said nucleic acid is a nucleic acid extract from a biological sample from said human.

3. The method of claim 2, wherein said biological sample is blood, saliva, or buccal cells.

4. The method of claim 2 or 3, further comprising preparing said nucleic acid extract from said biological sample prior to said testing.

5. The method of any one of claims 1 to 4, wherein said testing comprises nucleic acid amplification.

6. The method of claim 5, wherein said nucleic acid amplification is carried out by polymerase chain reaction.

7. The method of any one of claims 1 to 6, wherein said testing is performed using sequencing, 5' nuclease digestion, molecular beacon assay, oligonucleotide ligation assay, size analysis, single-stranded conformation polymorphism analysis, or denaturing gradient gel electrophoresis (DGGE).
8. The method of any one of claims 1 to 6, wherein said testing is performed using an allele-specific method.

9. The method of claim 8, wherein said allele-specific method is allele-specific probe hybridization, allele-specific primer extension, or allele-specific amplification.

10. The method of claim 8 or 9, wherein said testing is carried out using an allele-specific primer that comprises a sequence selected from the group consisting of SEQ ID NOS: 62, 63, and sequences fully complementary thereto.

11. The method of any one of claims 1 to 10, wherein said human is homozygous for said C or said G.

12. The method of any one of claims 1 to 10, wherein said human is heterozygous for said C or said G.

13. The method of any one of claims 1 to 12, wherein said correlating is performed using computer software.

14. The method of any one of claims 1 to 13, which is an automated method.

15. The method of any one of claims 1 to 14, wherein the human is a hepatitis C virus-infected human.