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(54) Title: POLYMORPHISMS IN THE HUMAN MDR-1 GENE AND THEIR USE IN DIAGNOSTIC AND THERAPEUTIC APPLICATIONS

(57) Abstract: Described are general means and methods of diagnosing and treating the phenotypic spectrum as well as the overlapping clinical characteristics with several forms of inherited abnormal expression and/or function of the Multi Drug Resistance-1 (MDR-1) gene. In particular, polynucleotides of molecular variant MDR-1 genes which, for example, are associated with unsufficient and/or altered uptake of drugs by a target cell, and vectors comprising such polynucleotides are provided. Furthermore, host cells comprising such polynucleotides or vectors and their use for the production of variant MDR-1 proteins are described. In addition, variant MDR-1 proteins and antibodies specifically recognizing such proteins as well as concerns transgenic non-human animals comprising the above-described polynucleotide or vectors are provided. Described are also methods for identifying and obtaining inhibitors for therapy of disorders related to the malfunction of the MDR-1 gene as well as methods of diagnosing the status of such disorders. Pharmaceutical and diagnostic compositions comprising the above-described polynucleotides, vectors, proteins, antibodies and inhibitors by the above-described method are provided. Said compositions are particularly useful for diagnosing and treating various diseases with drugs that are substrates, inhibitors or modulators of the MDR-1 gene product.