GEPHE SUMMARY

Gephebase Gene

MDR1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^MDR1^#gephebase-summary-title)

GepheID

GP00001858

Entry Status

Published

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Xenobiotic resistance (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance^#gephebase-summary-title)

Trait State in Taxon A

sensitive

Trait State in Taxon B

resistant

Ancestral State

Taxon A

Taxonomic Status

Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

Taxon A

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

ABCB1

Synonyms

MDR1; CLCS; P-GP; PGY1; ABC20; CD243; GP170

String

9606.ENSP00000478255 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000478255)

Sequence Similarities

Belongs to the ABC transporter superfamily. ABCB family. Multidrug resistance exporter (TC 3.A.1.201) subfamily.

GO - Molecular Function

GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)
GO:0042626 : ATPase activity, coupled to transmembrane movement of substances (https://www.ebi.ac.uk/QuickGO/term/GO:0042626)

UniProtKB Homo sapiens

P08183 (http://www.uniprot.org/uniprot/P08183)

GenebankID or UniProtKB

()

GO:0090554 : phosphatidylcholine-translocating ATPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0090554)
GO:0005215 : transporter activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005215)
GO:0099038 : ceramide-translocating ATPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0099038)
GO:0090555 : phosphatidylethanolamine-translocating ATPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0090555)

GO - Biological Process

GO:0045332 : phospholipid translocation (https://www.ebi.ac.uk/QuickGO/term/GO:0045332)
GO:0055085 : transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:0055085)
GO:0042493 : response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:0042493)
GO:0000086 : G2/M transition of mitotic cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0000086)
GO:0099040 : ceramide translocation (https://www.ebi.ac.uk/QuickGO/term/GO:0099040)
GO:1901529 : positive regulation of anion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:1901529)
GO:2001225 : regulation of chloride transport (https://www.ebi.ac.uk/QuickGO/term/GO:2001225)
GO:0047484 : regulation of response to osmotic stress (https://www.ebi.ac.uk/QuickGO/term/GO:0047484)
GO:0072089 : stem cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0072089)

GO - Cellular Component

GO:0016021 : integral component of membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0016324 : apical plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016324)
GO:0016020 : membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016020)
GO:0070062 : extracellular exosome (https://www.ebi.ac.uk/QuickGO/term/GO:0070062)
GO:0009986 : cell surface (https://www.ebi.ac.uk/QuickGO/term/GO:0009986)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title)

SNP Coding Change

Synonymous

Molecular Details of the Mutation

C3435T - synonymous mutation Ile - The SNP at position 26/3435 that changes the codon from ATC to ATT (Ile) reduces the codon usage from 47% to 35% (RSCU values change from 20.9 to 15.8). Leads to similar mRNA and protein levels but altered conformation of the protein.

Experimental Evidence

Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Association Mapping^#gephebase-summary-title)

	Taxon A	Taxon B	Position
Codon	ATC	ATT	-
Amino-acid	Ile	Ile	-

Main Reference

A "silent" polymorphism in the MDR1 gene changes substrate specificity. (2007) (https://pubmed.ncbi.nlm.nih.gov/17185560)

Authors

Kimchi-Sarfaty C; Oh JM; Kim IW; Sauna ZE; Calcagno AM; Ambudkar SV; Gottesman MM

Abstract

Synonymous single-nucleotide polymorphisms (SNPs) do not produce altered coding sequences, and therefore they are not expected to change the function of the protein in which they occur. We report that a synonymous SNP in the Multidrug Resistance 1 (MDR1) gene, part of a haplotype previously linked to altered function of the MDR1 gene product P-glycoprotein (P-gp), nonetheless results in P-gp with altered drug and inhibitor interactions. Similar mRNA and protein levels, but altered conformations, were found for wild-type and polymorphic P-gp. We hypothesize that the presence of a rare codon, marked by the synonymous polymorphism, affects the timing of cotranslational folding and insertion of P-gp into the membrane, thereby altering the structure of substrate and inhibitor interaction sites.

Additional References

RELATED GEPHE

Related Genes

4 (alcohol dehydrogenase (ADH1B), CYP2C9, CYP4F2, Vkorc1) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9606^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Synonymous mutation