GEPHE SUMMARY

Gephebase Gene

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

Entry Status

Published

GepheID

GP00001813

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

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

Trait

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

Trait State in Taxon A

rat - sensitive

Trait State in Taxon B

rat - tolerant

Ancestral State

Taxon A

Taxonomic Status

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

Taxon A

Latin Name

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

Common Name

Norway rat

Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

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; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Rattus

Parent

Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)

NCBI Taxonomy ID

10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

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

Common Name

Norway rat

Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

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; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Rattus

Parent

Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)

NCBI Taxonomy ID

10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)

is Taxon B an Infraspecies?

Yes

Taxon B Description

Han/Wistar (Kuopio) rat strain (H/W)

GENOTYPIC CHANGE

Generic Gene Name

Ahr

Synonyms

Ah; In; Ahh; Ahre; bHLHe76

String

10090.ENSMUSP00000112137 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 10090.ENSMUSP00000112137)

Sequence Similarities

-

GO - Molecular Function

GO:0042803 : protein homodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0042803)
GO:0003700 : DNA-binding transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0003700)
GO:0046982 : protein heterodimerization activity

UniProtKB Mus musculus

P30561 (http://www.uniprot.org/uniprot/P30561)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0046982)
GO:0043565 : sequence-specific DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043565)
GO:0008134 : transcription factor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
GO:0044212 : transcription regulatory region DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0044212)
GO:0003677 : DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003677)
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific
(https://www.ebi.ac.uk/QuickGO/term/GO:0000981)
GO:0004879 : nuclear receptor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0004879)
GO:0070888 : E-box binding (https://www.ebi.ac.uk/QuickGO/term/GO:0070888)
GO:1990837 : sequence-specific double-stranded DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:1990837)
GO:0051879 : Hsp90 protein binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051879)
GO:0051087 : chaperone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051087)
GO:0001223 : transcription coactivator binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0001223)
GO:0017162 : aryl hydrocarbon receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0017162)
GO:0035326 : enhancer binding (https://www.ebi.ac.uk/QuickGO/term/GO:0035326)
GO:0017025 : TBP-class protein binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0017025)
GO:0001094 : TFIID-class transcription factor complex binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0001094)

GO - Biological Process

GO:0045944 : positive regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0006357 : regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0006357)
GO:0006355 : regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0006355)
GO:0000122 : negative regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0045892 : negative regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045892)
GO:0045893 : positive regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045893)
GO:0035162 : embryonic hemopoiesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0035162)
GO:0001541 : ovarian follicle development
(https://www.ebi.ac.uk/QuickGO/term/GO:0001541)
GO:0030850 : prostate gland development
(https://www.ebi.ac.uk/QuickGO/term/GO:0030850)
GO:0032922 : circadian regulation of gene expression
(https://www.ebi.ac.uk/QuickGO/term/GO:0032922)
GO:0014070 : response to organic cyclic compound
(https://www.ebi.ac.uk/QuickGO/term/GO:0014070)
GO:0010468 : regulation of gene expression
(https://www.ebi.ac.uk/QuickGO/term/GO:0010468)
GO:0006805 : xenobiotic metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0006805)
GO:0008217 : regulation of blood pressure
(https://www.ebi.ac.uk/QuickGO/term/GO:0008217)
GO:0008015 : blood circulation (https://www.ebi.ac.uk/QuickGO/term/GO:0008015)
GO:0001974 : blood vessel remodeling
(https://www.ebi.ac.uk/QuickGO/term/GO:0001974)
GO:0006366 : transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0006366)
GO:0001889 : liver development (https://www.ebi.ac.uk/QuickGO/term/GO:0001889)
GO:0048608 : reproductive structure development
(https://www.ebi.ac.uk/QuickGO/term/GO:0048608)
GO:0043010 : camera-type eye development
(https://www.ebi.ac.uk/QuickGO/term/GO:0043010)
GO:0048745 : smooth muscle tissue development
(https://www.ebi.ac.uk/QuickGO/term/GO:0048745)
GO:0000902 : cell morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0000902)
GO:0050880 : regulation of blood vessel size
(https://www.ebi.ac.uk/QuickGO/term/GO:0050880)
GO:0030183 : B cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030183)
GO:0045793 : positive regulation of cell size
(https://www.ebi.ac.uk/QuickGO/term/GO:0045793)
GO:0071320 : cellular response to cAMP
(https://www.ebi.ac.uk/QuickGO/term/GO:0071320)
GO:0009636 : response to toxic substance
(https://www.ebi.ac.uk/QuickGO/term/GO:0009636)
GO:0007049 : cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0007049)

GO:0009410 : response to xenobiotic stimulus
(https://www.ebi.ac.uk/QuickGO/term/GO:0009410)
GO:0001568 : blood vessel development
(https://www.ebi.ac.uk/QuickGO/term/GO:0001568)
GO:0001782 : B cell homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0001782)
GO:0001922 : B-1 B cell homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0001922)
GO:0048514 : blood vessel morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0048514)
GO:0001569 : branching involved in blood vessel morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0001569)
GO:0019933 : cAMP-mediated signaling
(https://www.ebi.ac.uk/QuickGO/term/GO:0019933)
GO:0003214 : cardiac left ventricle morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0003214)
GO:1904613 : cellular response to 2,3,7,8-tetrachlorodibenzodioxine
(https://www.ebi.ac.uk/QuickGO/term/GO:1904613)
GO:1904682 : cellular response to 3-methylcholanthrene
(https://www.ebi.ac.uk/QuickGO/term/GO:1904682)
GO:1904322 : cellular response to forskolin
(https://www.ebi.ac.uk/QuickGO/term/GO:1904322)
GO:0003243 : circumferential growth involved in left ventricle morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0003243)
GO:0061009 : common bile duct development
(https://www.ebi.ac.uk/QuickGO/term/GO:0061009)
GO:0048732 : gland development (https://www.ebi.ac.uk/QuickGO/term/GO:0048732)
GO:0072102 : glomerulus morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0072102)
GO:0002376 : immune system process
(https://www.ebi.ac.uk/QuickGO/term/GO:0002376)
GO:0060993 : kidney morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0060993)
GO:0002260 : lymphocyte homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0002260)
GO:0060547 : negative regulation of necrotic cell death
(https://www.ebi.ac.uk/QuickGO/term/GO:0060547)
GO:0003085 : negative regulation of systemic arterial blood pressure
(https://www.ebi.ac.uk/QuickGO/term/GO:0003085)
GO:0045906 : negative regulation of vasoconstriction
(https://www.ebi.ac.uk/QuickGO/term/GO:0045906)
GO:0040010 : positive regulation of growth rate
(https://www.ebi.ac.uk/QuickGO/term/GO:0040010)
GO:0045899 : positive regulation of RNA polymerase II transcriptional preinitiation complex
assembly (https://www.ebi.ac.uk/QuickGO/term/GO:0045899)
GO:0035166 : post-embryonic hemopoiesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0035166)
GO:0030888 : regulation of B cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030888)
GO:0060420 : regulation of heart growth
(https://www.ebi.ac.uk/QuickGO/term/GO:0060420)
GO:0048536 : spleen development (https://www.ebi.ac.uk/QuickGO/term/GO:0048536)
GO:0043029 : T cell homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0043029)
GO:0060841 : venous blood vessel development
(https://www.ebi.ac.uk/QuickGO/term/GO:0060841)

GO - Cellular Component

GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005634 : nucleus (https://www.ebi.ac.uk/QuickGO/term/GO:0005634)
GO:0005667 : transcription factor complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0005667)
GO:0032991 : protein-containing complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0032991)
GO:0034751 : aryl hydrocarbon receptor complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0034751)
GO:0034752 : cytosolic aryl hydrocarbon receptor complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0034752)
GO:0034753 : nuclear aryl hydrocarbon receptor complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0034753)

Presumptive Null

Yes (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^Yes^#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

-

Molecular Details of the Mutation

point mutation in the exon/intron 10 boundary in AHR genomic structure that leads to use of 3 alternative cryptic splice sites; potentially creating 3 alternative transcripts and 2 protein products. At the protein level the mutation leads to a total loss of either 43 or 38 amino acids (with altered sequence for the last seven amino acids in the latter case) toward the carboxyl-terminal end in the trans-activation domain of the AhR. H/W rats also harbor a point mutation in exon 10 that will cause a Val-to-Ala substitution in codon 497, but this occurs in a variable region of the AhR

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

Main Reference

The AH receptor and a novel gene determine acute toxic responses to TCDD: segregation of the resistant alleles to different rat lines. (1999) (https://pubmed.ncbi.nlm.nih.gov/10036220)

Authors

Tuomisto JT; Viluksela M; Pohjanvirta R; Tuomisto J

Abstract

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD),12 the most toxic congener of dioxins, exhibits wide sensitivity differences between a sensitive Long-Evans (L-E) rat and a resistant Han/Wistar (H/W) rat. The sensitivity is determined probably by two autosomal genes and it is highly end point dependent. The difference is more than 1000-fold for acute toxicity and negligible for CYP1A1 induction. The rat strains were recently shown to have differences in the size of AH receptor (AHR), which mediates most effects of TCDD. In the present study, the rat strains were crossed and the resistant alleles of genes determining TCDD sensitivity were segregated to new rat lines. Selection was based on AHR phenotype determined by Western blot and resistance to TCDD lethality. Two genes determining resistance were found: the Ahr and a novel gene designated "B." In homozygous rats, the H/W type Ahrhw allele prevented TCDD lethality up to 2000 microg/kg or more, and the H/W type "Bhw" allele also increased resistance to TCDD lethality but to a lesser extent. Heterozygous rats were only slightly more resistant to acute lethality than the respective sensitive homozygous rats. CYP1A1 induction was similar irrespective of the Ahr and "B" genotypes, but a substantial increase in serum bilirubin seen after low doses in sensitive rats occurred only after large doses in "Bhw/hw" and not at all in Ahrhw/hw rats. In conclusion, the Ahrhw allele is a major determinant of the exceptional resistance of H/W rats to TCDD lethality. There is also an additional gene, whose function remains to be characterized, conferring limited resistance to TCDD toxicity. These two H/W rat-derived alleles are separately expressed in the new rat lines created.

Additional References

Aryl hydrocarbon receptor splice variants in the dioxin-resistant rat: tissue expression and transactivational activity. (2007) (https://pubmed.ncbi.nlm.nih.gov/17636048)
Point mutation in intron sequence causes altered carboxyl-terminal structure in the aryl hydrocarbon receptor of the most 2,3,7,8-tetrachlorodibenzo-p-dioxin-resistant rat strain. (1998) (https://pubmed.ncbi.nlm.nih.gov/9658193)

RELATED GEPHE

Related Genes

2 (Vkorc1, Na/K-ATPase alpha-subunit) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^10116^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

@Splicing - Mutation in AHR2 is protective of toxicity in mice, killifish, tomcod, etc.