GEPHE SUMMARY

Gephebase Gene

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

Entry Status

Published

GepheID

GP00001811

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

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

Trait

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

Trait State in Taxon A

Gallus gallus - sensitive

Trait State in Taxon B

Sterna hirundo - tolerant

Ancestral State

Taxon A

Taxonomic Status

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

Taxon A

Latin Name

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

Common Name

chicken

Synonyms

Gallus gallus domesticus; chicken; bantam; chickens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Archelosauria; Archosauria; Dinosauria; Saurischia; Theropoda; Coelurosauria; Aves; Neognathae; Galloanserae; Galliformes; Phasianidae; Phasianinae; Gallus

Parent

Gallus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9030)

NCBI Taxonomy ID

9031 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9031)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

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

Common Name

-

Synonyms

Sterna hirundo hirundo Linnaeus, 1758

Rank

subspecies

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Archelosauria; Archosauria; Dinosauria; Saurischia; Theropoda; Coelurosauria; Aves; Neognathae; Charadriiformes; Laridae; Sterna; Sterna hirundo

Parent

() - (Rank:) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 108405NULL)

NCBI Taxonomy ID

1471880 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 1471880)

is Taxon B an Infraspecies?

No

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)

Mutation #1

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

Nonsynonymous

Molecular Details of the Mutation

V325I and A381S substitutions in the tern AHR converted the ligand-binding and transactivation abilities of the tern AHR to those of a chicken AHR- each substitution tested individually has an effect

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Val	Ile	325

Main Reference

The molecular basis for differential dioxin sensitivity in birds: role of the aryl hydrocarbon receptor. (2006) (https://pubmed.ncbi.nlm.nih.gov/16606854)

Authors

Karchner SI; Franks DG; Kennedy SW; Hahn ME

Abstract

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and related halogenated aromatic hydrocarbons (HAHs) are highly toxic to most vertebrate animals, but there are dramatic differences in sensitivity among species and strains. Aquatic birds including the common tern (Sterna hirundo) are highly exposed to HAHs in the environment, but are up to 250-fold less sensitive to these compounds than the typical avian model, the domestic chicken (Gallus gallus). The mechanism of HAH toxicity involves altered gene expression subsequent to activation of the aryl hydrocarbon receptor (AHR), a basic helix-loop-helix-PAS transcription factor. AHR polymorphisms underlie mouse strain differences in sensitivity to HAHs and polynuclear aromatic hydrocarbons, but the role of the AHR in species differences in HAH sensitivity is not well understood. Here, we show that although chicken and tern AHRs both exhibit specific binding of [3H]TCDD, the tern AHR has a lower binding affinity and exhibits a reduced ability to support TCDD-dependent transactivation as compared to AHRs from chicken or mouse. We further show through use of chimeric AHR proteins and site-directed mutagenesis that the difference between the chicken and tern AHRs resides in the ligand-binding domain and that two amino acids (Val-325 and Ala-381) are responsible for the reduced activity of the tern AHR. Other avian species with reduced sensitivity to HAHs also possess these residues. These studies provide a molecular understanding of species differences in sensitivity to dioxin-like compounds and suggest an approach to using the AHR as a marker of dioxin susceptibility in wildlife.

Additional References

Key amino acids in the aryl hydrocarbon receptor predict dioxin sensitivity in avian species. (2008) (https://pubmed.ncbi.nlm.nih.gov/18939598)

Mutation #2

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

Nonsynonymous

Molecular Details of the Mutation

V325I and A381S substitutions in the tern AHR converted the ligand-binding and transactivation abilities of the tern AHR to those of a chicken AHR- each substitution tested individually has an effect

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Ala	Ser	381

Main Reference

The molecular basis for differential dioxin sensitivity in birds: role of the aryl hydrocarbon receptor. (2006) (https://pubmed.ncbi.nlm.nih.gov/16606854)

Authors

Karchner SI; Franks DG; Kennedy SW; Hahn ME

Abstract

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and related halogenated aromatic hydrocarbons (HAHs) are highly toxic to most vertebrate animals, but there are dramatic differences in sensitivity among species and strains. Aquatic birds including the common tern (Sterna hirundo) are highly exposed to HAHs in the environment, but are up to 250-fold less sensitive to these compounds than the typical avian model, the domestic chicken (Gallus gallus). The mechanism of HAH toxicity involves altered gene expression subsequent to activation of the aryl hydrocarbon receptor (AHR), a basic helix-loop-helix-PAS transcription factor. AHR polymorphisms underlie mouse strain differences in sensitivity to HAHs and polynuclear aromatic hydrocarbons, but the role of the AHR in species differences in HAH sensitivity is not well understood. Here, we show that although chicken and tern AHRs both exhibit specific binding of [3H]TCDD, the tern AHR has a lower binding affinity and exhibits a reduced ability to support TCDD-dependent transactivation as compared to AHRs from chicken or mouse. We further show through use of chimeric AHR proteins and site-directed mutagenesis that the difference between the chicken and tern AHRs resides in the ligand-binding domain and that two amino acids (Val-325 and Ala-381) are responsible for the reduced activity of the tern AHR. Other avian species with reduced sensitivity to HAHs also possess these residues. These studies provide a molecular understanding of species differences in sensitivity to dioxin-like compounds and suggest an approach to using the AHR as a marker of dioxin susceptibility in wildlife.

Additional References

Key amino acids in the aryl hydrocarbon receptor predict dioxin sensitivity in avian species. (2008) (https://pubmed.ncbi.nlm.nih.gov/18939598)

RELATED GEPHE

Related Genes

1 (SCN9A (Nav1.7)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9031^/and+Trait=Xenobiotic resistance/or+Taxon ID=^1471880^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Mutation in AHR2 is protective of toxicity in killifish, tomcod and mice Ala-381 in the tern AHR is homologous to (i.e. at the equivalent position as) Ala-375 of the high-affinity mouse Ahbâ^'1 protein and Val-375 and Val-380 of the lower-affinity mouse Ahd and human AHR proteins; respectively - Val > Ala > Ser at this position appear to form a series of substitutions leading to increasing stability of TCDD interaction with the AHR @& taxonID did not fetch species name