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

## Published

## PHENOTYPIC CHANGE

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

Taxon A
Taxonomic Status
Intergeneric or Higher (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^^ntergeneric 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

Gallus gallus domesticus; chicken; bantam; chickens

## species

Lineage 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

Gallus 0 - (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)

$$
\text { is Taxon } A \text { an Infraspecies? }
$$

No

## GENOTYPIC CHANGE

| Ahr | Generic Gene Name |
| :--- | ---: |
| Ah; In; Ahh; Ahre; bHLHe76 | Synonyms |
| 10090.ENSMUSP00000112137 |  |
| (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= |  |
| 10090.ENSMUSPo0000112137) |  |
| - Sequence Similarities |  |

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
(https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (dioxins; Trait State in Taxon A

Trait State in Taxon B

Ancestral State


## String

10090.ENSMUSP00000112137
10090.ENSMUSP00000112137)

Sequence Similarities

GO - Molecular Function

## 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
subspecies
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
0-(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

## UniProtKB Mus musculus

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

0
(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 Componen

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)

V325l 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 $\quad$ Taxon B Position

| Codon | - | - | - |
| ---: | :---: | :---: | :---: |
| Amino-acid | Val | lle | 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)

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 $[3 H] T C D D$, 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 ligandbinding 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

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

Presumptive Null
No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^\#gephebase-summary-title)
Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^\#gephebase-summary-title)
SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^\#gephebase-summary-title)

## 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= ${ }^{\wedge}$ Candidate Gene ${ }^{\wedge}$ \#gephebase-summary-title)
Taxon A Taxon B Position

| Codon | - | - | - |
| ---: | :---: | :---: | :---: |
| Amino-acid | Ala | Ser | 381 |

The molecular basis for differential dioxin sensitivity in birds: role of the aryl hydrocarbon receptor. (2006) (https://pubmed.ncbi.nlm.nih.gov/16606854)
Karchner SI; Franks DG; Kennedy SW; Hahn ME
KarchnerSI, Frans DG, Kenedy 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 ligandbinding 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)

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

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

