GEPHE SUMMARY

Gephebase Gene

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

Entry Status

Published

GepheID

GP00000846

Main curator

Martin

PHENOTYPIC CHANGE

Trait Category

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

Trait

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

Trait State in Taxon A

Pediculus capitis

Trait State in Taxon B

Pediculus capitis - 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

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

Common Name

human louse

Synonyms

human louse; body lice; head lice; human lice; Pediculus humanus Linnaeus, 1758

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Paraneoptera; Psocodea; Phthiraptera; Anoplura; Pediculidae; Pediculus

Parent

Pediculus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 121222)

NCBI Taxonomy ID

121225 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 121225)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

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

Common Name

human louse

Synonyms

human louse; body lice; head lice; human lice; Pediculus humanus Linnaeus, 1758

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Paraneoptera; Psocodea; Phthiraptera; Anoplura; Pediculidae; Pediculus

Parent

Pediculus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 121222)

NCBI Taxonomy ID

121225 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 121225)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

para

Synonyms

bas; bss; CG9907; Dmel\CG9907; DmNav; DmNav1; DmNa[[v]]; DmNa[[V]]; DmNa[[v]]1; l(1)14Da; l(1)ESHS48; lincRNA.S9469; Nav1; Ocd; olfD; par; sbl; sbl-1; Shu; Shudderer

String

7227.FBpp0303597 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 7227.FBpp0303597)

Sequence Similarities

Belongs to the sodium channel (TC 1.A.1.10) family. Para subfamily.

GO - Molecular Function

GO:0005509 : calcium ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005509)
GO:0005244 : voltage-gated ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005244)
GO:0005248 : voltage-gated sodium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005248)
GO:0005272 : sodium channel activity

UniProtKB Drosophila melanogaster

P35500 (http://www.uniprot.org/uniprot/P35500)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0005272)

GO - Biological Process

GO:0045433 : male courtship behavior, veined wing generated song production (https://www.ebi.ac.uk/QuickGO/term/GO:0045433)
GO:0001666 : response to hypoxia (https://www.ebi.ac.uk/QuickGO/term/GO:0001666)
GO:0009612 : response to mechanical stimulus (https://www.ebi.ac.uk/QuickGO/term/GO:0009612)
GO:0034765 : regulation of ion transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:0034765)
GO:0035725 : sodium ion transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:0035725)
GO:0007638 : mechanosensory behavior (https://www.ebi.ac.uk/QuickGO/term/GO:0007638)
GO:0060078 : regulation of postsynaptic membrane potential (https://www.ebi.ac.uk/QuickGO/term/GO:0060078)

GO - Cellular Component

GO:0005887 : integral component of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0001518 : voltage-gated sodium channel complex (https://www.ebi.ac.uk/QuickGO/term/GO:0001518)

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

M815I = M827I

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	-	-	-

Main Reference

Determination of knockdown resistance allele frequencies in global human head louse populations using the serial invasive signal amplification reaction. (2010) (https://pubmed.ncbi.nlm.nih.gov/20564731)

Authors

Hodgdon HE; Yoon KS; Previte DJ; Kim HJ; Aboelghar GE; Lee SH; Clark JM

Abstract

Pediculosis is the most prevalent parasitic infestation of humans. Resistance to pyrethrin- and pyrethroid-based pediculicides is due to knockdown (kdr)-type point mutations in the voltage-sensitive sodium channel alpha-subunit gene. Early detection of resistance is crucial for the selection of effective management strategies.

Kdr allele frequencies of lice from 14 countries were determined using the serial invasive signal amplification reaction. Lice collected from Uruguay, the United Kingdom and Australia had kdr allele frequencies of 100%, while lice from Ecuador, Papua New Guinea, South Korea and Thailand had kdr allele frequencies of 0%. The remaining seven countries investigated, including seven US populations, two Argentinian populations and populations from Brazil, Denmark, Czech Republic, Egypt and Israel, displayed variable kdr allele frequencies, ranging from 11 to 97%.

The newly developed and validated SISAR method is suitable for accurate monitoring of kdr allele frequencies in head lice. Proactive management is needed where kdr-type resistance is not yet saturated. Based on sodium channel insensitivity and its occurrence in louse populations resistant to pyrethrin- and pyrethroid-based pediculicides, the T917I mutation appears to be a key marker for resistance. Results from the Egyptian population, however, indicate that phenotypic resistance of lice with single or double mutations (M815I and/or L920F) should also be determined.

Additional References

Molecular biology of insect sodium channels and pyrethroid resistance. (2014) (https://pubmed.ncbi.nlm.nih.gov/24704279)
Sodium channel mutations associated with knockdown resistance in the human head louse, Pediculus capitis (De Geer) . (2003) (https://pubmed.ncbi.nlm.nih.gov/00000000.000024)

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

T929I (ACC to ATC or ATA) = L932F

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 molecular interactions of pyrethroid insecticides with insect and mammalian sodium channels. (2001) (https://pubmed.ncbi.nlm.nih.gov/11695180)

Authors

Vais H; Williamson MS; Devonshire AL; Usherwood PN

Abstract

Recent progress in the cloning of alpha (para) and beta (TipE) Na channel sub-units from Drosophila melanogaster (fruit fly) and Musca domestica (housefly) have facilitated functional expression studies of insect Na channels in Xenopus laevis oocytes, assayed by voltage clamp techniques. The effects of Type I and Type III pyrethroids on the biophysical properties of these channels are critically reviewed. Pyrethroid resistance mutations (termed kdr and super-kdr) that reduce the sensitivity of the insect Na channel to pyrethroids have been identified in a range of insect species. Some of these mutations (e.g. L1014F, M918T and T929I) have been incorporated into the para Na channel of Drosophila, either individually or in combination, to investigate their effects on the sensitivity of this channel to pyrethroids. The kdr mutation (L1014F) shifts the voltage dependence of both activation and steady-state inactivation by approximately 5 mV towards more positive potentials and facilitates Na channel inactivation. Incorporation of the super-kdr mutation (M918T) into the Drosophila Na channel also increases channel inactivation and causes a > 100-fold reduction in deltamethrin sensitivity. These effects are shared by T929I, an alternative mutation that confers super-kdr-like resistance. Parallel studies have been undertaken using the rat IIA Na channel to investigate the molecular basis for the low sensitivity of mammalian brain Na channels to pyrethroids. Rat IIA channels containing the mutation L1014F exhibit a shift in their mid-point potential for Na activation, but their overall sensitivity to permethrin remains similar to that of the wild-type rat channel (i.e. both are 1000-fold less sensitive than the wild-type insect channel). Mammalian neuronal Na channels have an isoleucine rather than a methionine at the position (874) corresponding to the super-kdr (M918) residue of the insect channel. Replacement of the isoleucine of the wild-type rat IIA Na channel with a methionine (I874M) increases deltamethrin sensitivity 100-fold. In this way, studies of wild-type and mutant Na channels of insects and mammals are providing a molecular understanding of kdr and super-kdr resistance in insects, and of the low pyrethroid sensitivity of most mammalian Na channels. They are also giving valuable insights into the binding sites for pyrethroids on these channels.

Additional References

Mutations in DIIS5 and the DIIS4-S5 linker of Drosophila melanogaster sodium channel define binding domains for pyrethroids and DDT. (2007) (https://pubmed.ncbi.nlm.nih.gov/17991435)
Molecular biology of insect sodium channels and pyrethroid resistance. (2014) (https://pubmed.ncbi.nlm.nih.gov/24704279)

Mutation #3

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

L920F

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

Determination of knockdown resistance allele frequencies in global human head louse populations using the serial invasive signal amplification reaction. (2010) (https://pubmed.ncbi.nlm.nih.gov/20564731)

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Additional References

Molecular biology of insect sodium channels and pyrethroid resistance. (2014) (https://pubmed.ncbi.nlm.nih.gov/24704279)

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

1 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^para (kdr)^/and+Taxon ID=^121225^/or+Gene Gephebase=^para (kdr)^/and+Taxon ID=^121225^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SuccessiveMutationsAtSameCodon