

GEPHE SUMMARY

GST e (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+^GSTe^#gephebase-summary-title)	Gephebase Gene	GP00002455	GepheID
Published	Entry Status	Courtier	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category+^Physiology^#gephebase-summary-title)	Trait Category
Xenobiotic resistance (insecticide; DDT) (https://www.gephebase.org/search-criteria?/and+Trait+^Xenobiotic+resistance+(insecticide;+DDT)^#gephebase-summary-title)	Trait
Anopheles funestus - sensitive	Trait State in Taxon A
Anopheles funestus - resistant	Trait State in Taxon B
Data not curated	Ancestral State
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status+^Intraspecific^#gephebase-summary-title)	Taxonomic Status

Taxon A	Latin Name	Taxon B	Latin Name
Anopheles funestus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+^Anopheles+funestus^#gephebase-summary-title)	Anopheles funestus	Anopheles funestus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+^Anopheles+funestus^#gephebase-summary-title)	Anopheles funestus
African malaria mosquito	Common Name	African malaria mosquito	Common Name
African malaria mosquito; Anopheles funestus Giles, 1900	Synonyms	African malaria mosquito; Anopheles funestus Giles, 1900	Synonyms
species	Rank	species	Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Nematocera; Culicomorpha; Culicoidea; Culicidae; Anophelinae; Anopheles; Cellia; Myzomyia; funestus group; funestus subgroup	Lineage	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Nematocera; Culicomorpha; Culicoidea; Culicidae; Anophelinae; Anopheles; Cellia; Myzomyia; funestus group; funestus subgroup	Lineage
funestus subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62323)	Parent	funestus subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62323)	Parent
62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62324)	NCBI Taxonomy ID	62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62324)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

GENOTYPIC CHANGE

GstE2	Generic Gene Name	Q7JYZ9 (http://www.uniprot.org/uniprot/Q7JYZ9)	UniProtKB Drosophila melanogaster
CG17523; Dmel\CG17523; DmGSTE2; gste2; GSTE2; Dmel_CG17523	Synonyms	()	GenebankID or UniProtKB
7227.FBpp0085851 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=7227.FBpp0085851)	String		
-	Sequence Similarities		
GO:0004364 : glutathione transferase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004364)	GO - Molecular Function		
GO:0006749 : glutathione metabolic process (https://www.ebi.ac.uk/QuickGO/term/GO:0006749)	GO - Biological Process		
	GO - Cellular Component		

GO:0005737 : cytoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005737>)

Presumptive Null

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

L119F. The resistant allele is more efficient at metabolizing DDT than the susceptible one.

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	Leu	Phe	119

Main Reference

A single mutation in the GSTe2 gene allows tracking of metabolically based insecticide resistance in a major malaria vector. (2014) (<https://pubmed.ncbi.nlm.nih.gov/24565444>)

Authors

Riveron JM; Yunta C; Ibrahim SS; Djouaka R; Irving H; Menze BD; Ismail HM; Hemingway J; Ranson H; Albert A; Wondji CS

Abstract

Metabolic resistance to insecticides is the biggest threat to the continued effectiveness of malaria vector control. However, its underlying molecular basis, crucial for successful resistance management, remains poorly characterized.

Here, we demonstrate that the single amino acid change L119F in an upregulated glutathione S-transferase gene, GSTe2, confers high levels of metabolic resistance to DDT in the malaria vector *Anopheles funestus*. Genome-wide transcription analysis revealed that GSTe2 was the most over-expressed detoxification gene in DDT and permethrin-resistant mosquitoes from Benin. Transgenic expression of GSTe2 in *Drosophila melanogaster* demonstrated that over-transcription of this gene alone confers DDT resistance and cross-resistance to pyrethroids. Analysis of GSTe2 polymorphism established that the point mutation is tightly associated with metabolic resistance to DDT and its geographical distribution strongly correlates with DDT resistance patterns across Africa. Functional characterization of recombinant GSTe2 further supports the role of the L119F mutation, with the resistant allele being more efficient at metabolizing DDT than the susceptible one. Importantly, we also show that GSTe2 directly metabolizes the pyrethroid permethrin. Structural analysis reveals that the mutation confers resistance by enlarging the GSTe2 DDT-binding cavity, leading to increased DDT access and metabolism. Furthermore, we show that GSTe2 is under strong directional selection in resistant populations, and a restriction of gene flow is observed between African regions, enabling the prediction of the future spread of this resistance.

This first DNA-based metabolic resistance marker in mosquitoes provides an essential tool to track the evolution of resistance and to design suitable resistance management strategies.

Additional References

RELATED GEPHE

Related Genes

3 (CYP6P9 cluster (CYP6P9a and CYP6P9b), CYP6P9; CYP6P4 cluster, resistance to dieldrin) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=^62324^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

1 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^GSTe^/and+Taxon ID=^62324^/or+Gene Gephebase=^GSTe^/and+Taxon ID=^62324^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS