

GEPHE SUMMARY

	Gephebase Gene	GephelID
GSTe (https://www.gephebase.org/search-criteria?/and+Gene Gephebase="GSTe">#gephebase-summary-title)	GP00002455	
	Entry Status	Main curator
Published	Courtier	

PHENOTYPIC CHANGE

	Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category="Physiology">#gephebase-summary-title)	Trait		
Xenobiotic resistance (insecticide; DDT) (#gephebase-summary-title)	Trait State in Taxon A		
Anopheles funestus - sensitive	Trait State in Taxon B		
Anopheles funestus - resistant	Ancestral State		
Data not curated	Taxonomic Status		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status="Intraspecific">#gephebase-summary-title)			
Taxon A	Latin Name	Taxon B	Latin Name
Anopheles funestus (#gephebase-summary-title)		Anopheles funestus (#gephebase-summary-title)	
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
	Lineage		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		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	
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 Infraspecies?	No	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

GstE2	Generic Gene Name	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 ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^Unknown)

Molecular Type

Coding ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/and+Molecular+Type=^Coding)

Aberration Type

SNP ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/and+Aberration+Type=^SNP)

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

	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) ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/or+Taxon+ID=^62324^/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true)

Related Haplotypes

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

EXTERNAL LINKS

COMMENTS