GEPHE SUMMARY

Gephebase Gene
beta-tubulin (ben-1) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^beta-tubulin (ben-1)^#gephebase-summary-title)

GepheID
GP00001847

Entry Status
Published

Main curator
Courtier

PHENOTYPIC CHANGE

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

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

Trait State in Taxon A
sensitive

Trait State in Taxon B
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
Caenorhabditis elegans (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Caenorhabditis elegans^#gephebase-summary-title)

Common Name
-

Synonyms
roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Nematoda; Chromadorea; Rhabditida; Rhabditina; Rhabditomorpha; Rhabditoidea; Rhabditidae; Peloderinae; Caenorhabditis

Parent
Caenorhabditis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237)

NCBI Taxonomy ID
6239 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Caenorhabditis elegans (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Caenorhabditis elegans^#gephebase-summary-title)

Common Name
-

Synonyms
roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Nematoda; Chromadorea; Rhabditida; Rhabditina; Rhabditomorpha; Rhabditoidea; Rhabditidae; Peloderinae; Caenorhabditis

Parent
Caenorhabditis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237)

NCBI Taxonomy ID
6239 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239)

is Taxon B an Infraspecies?
Yes

Taxon B Description
WN2002

GENOTYPIC CHANGE

Generic Gene Name
TUB2

Synonyms
ARM10; SHE8; YFL037W

String
4932.YFL037W (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 4932.YFL037W)

Sequence Similarities
Belongs to the tubulin family.

GO - Molecular Function
GO:0005525 : GTP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005525)
GO:0003924 : GTPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0003924)
GO:0005200 : structural constituent of cytoskeleton (https://www.ebi.ac.uk/QuickGO/term/GO:0005200)

GO - Biological Process
GO:0007010 : cytoskeleton organization

UniProtKB Saccharomyces cerevisiae (strain ATCC 204508 / S288c)
P02557 (http://www.uniprot.org/uniprot/P02557)

GenebankID or UniProtKB
()

(https://www.ebi.ac.uk/QuickGO/term/GO:0007010)
GO:0000278 : mitotic cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0000278)
GO:0000070 : mitotic sister chromatid segregation
(https://www.ebi.ac.uk/QuickGO/term/GO:0000070)
GO:0007017 : microtubule-based process
(https://www.ebi.ac.uk/QuickGO/term/GO:0007017)
GO:0046677 : response to antibiotic (https://www.ebi.ac.uk/QuickGO/term/GO:0046677)
GO:0000226 : microtubule cytoskeleton organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0000226)
GO:0045143 : homologous chromosome segregation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045143)
GO:0030473 : nuclear migration along microtubule
(https://www.ebi.ac.uk/QuickGO/term/GO:0030473)
GO:0090316 : positive regulation of intracellular protein transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0090316)

GO - Cellular Component

GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005874 : microtubule (https://www.ebi.ac.uk/QuickGO/term/GO:0005874)
GO:0005816 : spindle pole body (https://www.ebi.ac.uk/QuickGO/term/GO:0005816)
GO:0005881 : cytoplasmic microtubule
(https://www.ebi.ac.uk/QuickGO/term/GO:0005881)
GO:0005828 : kinetochore microtubule
(https://www.ebi.ac.uk/QuickGO/term/GO:0005828)
GO:0005880 : nuclear microtubule (https://www.ebi.ac.uk/QuickGO/term/GO:0005880)
GO:0045298 : tubulin complex (https://www.ebi.ac.uk/QuickGO/term/GO:0045298)

Presumptive Null

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

missense_variant_MODERATE_c.392A>T_3540187 â€“ comment from Steffen Hahnel: The amino acid change is Q131L. This strain was excluded from the original screen because it was slow growing. We re-phenotyped it later (see Sup Fig. 9)

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	CAA	CTA	3540187
Amino-acid	Gln	Leu	131

Main Reference

Extreme allelic heterogeneity at a Caenorhabditis elegans beta-tubulin locus explains natural resistance to benzimidazoles. (2018) (https://pubmed.ncbi.nlm.nih.gov/30372484)

Authors

Hahnel SR; Zdraljevic S; Rodriguez BC; Zhao Y; McGrath PT; Andersen EC

Abstract

Benzimidazoles (BZ) are essential components of the limited chemotherapeutic arsenal available to control the global burden of parasitic nematodes. The emerging threat of BZ resistance among multiple nematode species necessitates the development of novel strategies to identify genetic and molecular mechanisms underlying this resistance. All detection of parasitic helminth resistance to BZ is focused on the genotyping of three variant sites in the orthologs of the Î²-tubulin gene found to confer resistance in the free-living nematode Caenorhabditis elegans. Because of the limitations of laboratory and field experiments in parasitic nematodes, it is difficult to look beyond these three sites to identify additional mechanisms that might contribute to BZ resistance in the field. Here, we took an unbiased genome-wide mapping approach in the free-living nematode species C. elegans to identify the genetic underpinnings of natural resistance to the commonly used BZ, albendazole (ABZ). We found a wide range of natural variation in ABZ resistance in natural C. elegans populations. In agreement with known mechanisms of BZ resistance in parasites, we found that a majority of the variation in ABZ resistance among wild C. elegans strains is caused by variation in the Î²-tubulin gene ben-1. This result shows empirically that resistance to ABZ naturally exists and segregates within the C. elegans population, suggesting that selection in natural niches could enrich for resistant alleles. We identified 25 distinct ben-1 alleles that are segregating at low frequencies within the C. elegans population, including many novel molecular variants. Population genetic analyses indicate that ben-1 variation arose multiple times during the evolutionary history of C. elegans and provide evidence that these alleles likely occurred recently because of local selective pressures. Additionally, we find purifying selection at all five Î²-tubulin genes, despite predicted loss-of-function variants in ben-1, indicating that BZ resistance in natural niches is a stronger selective pressure than loss of one Î²-tubulin gene. Furthermore, we used genome-editing to show that the most common parasitic nematode Î²-tubulin allele that confers BZ resistance, F200Y, confers resistance in C. elegans. Importantly, we identified a novel genomic region that is correlated with ABZ resistance in the C. elegans population but independent of ben-1 and the other Î²-tubulin loci, suggesting that there are multiple mechanisms underlying BZ resistance. Taken together, our results establish a population-level resource of nematode natural diversity as an important model for the study of mechanisms that give rise to BZ resistance.

Additional References

RELATED GEPHE

Related Genes

3 (acetyl-CoA carboxylase (ACC), GLC-1, str-217) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^6239^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

26 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^beta-tubulin (ben-1)^/and+Taxon ID=^6239^/or+Gene Gephebase=^beta-tubulin (ben-1)^/and+Taxon

ID=^6239^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS