

GEPHE SUMMARY

Gephebase Gene
beta-tubulin (ben-1)

Entry Status
Published

GepheID
GP00001847

Main curator
Courtier

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Xenobiotic resistance (benzimidazole)

Trait State in Taxon A
sensitive

Trait State in Taxon B
resistant

Ancestral State
Taxon A

Taxonomic Status
Intraspecific

	Taxon A	Taxon B
Latin Name	<i>Caenorhabditis elegans</i>	<i>Caenorhabditis elegans</i>
Common Name	-	-
Synonyms	roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900	roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900
Rank	species	species
Lineage	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Nematoda; Chromadorea; Rhabditida; Rhabditina; Rhabditomorpha; Rhabditoidea; Rhabditidae; Peloderinae; Caenorhabditis	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Nematoda; Chromadorea; Rhabditida; Rhabditina; Rhabditomorpha; Rhabditoidea; Rhabditidae; Peloderinae; Caenorhabditis
Parent	Caenorhabditis () - (Rank: genus)	Caenorhabditis () - (Rank: genus)
NCBI Taxonomy ID	6239	6239
is Taxon A an Intraspecies?	No	Yes

	Taxon A	Taxon B
Latin Name	<i>Caenorhabditis elegans</i>	<i>Caenorhabditis elegans</i>
Common Name	-	-
Synonyms	roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900	roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900
Rank	species	species
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Parent	Caenorhabditis () - (Rank: genus)	Caenorhabditis () - (Rank: genus)
NCBI Taxonomy ID	6239	6239
is Taxon B an Intraspecies?	Yes	Yes
Taxon B Description		WN2002

GENOTYPIC CHANGE

Generic Gene Name
TUB2

Synonyms
ARM10; SHE8; YFL037W

String
4932.YFL037W

Sequence Similarities
Belongs to the tubulin family.

GO - Molecular Function
GO:0005525 : GTP binding
GO:0003924 : GTPase activity
GO:0005200 : structural constituent of cytoskeleton

GO - Biological Process
GO:0007010 : cytoskeleton organization
GO:0000278 : mitotic cell cycle
GO:0000070 : mitotic sister chromatid segregation
GO:0007017 : microtubule-based process

UniProtKB *Saccharomyces cerevisiae* (strain ATCC 204508 / S288c)
P02557

GenebankID or UniProtKB

GO:0046677 : response to antibiotic
GO:0000226 : microtubule cytoskeleton organization
GO:0045143 : homologous chromosome segregation
GO:0030473 : nuclear migration along microtubule
GO:0090316 : positive regulation of intracellular protein transport

GO - Cellular Component

GO:0005737 : cytoplasm
GO:0005874 : microtubule
GO:0005816 : spindle pole body
GO:0005881 : cytoplasmic microtubule
GO:0005828 : kinetochore microtubule
GO:0005880 : nuclear microtubule
GO:0045298 : tubulin complex

Presumptive Null

Yes

Molecular Type

Coding

Aberration Type

SNP

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

	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)

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 β -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 β -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 β -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 β -tubulin gene. Furthermore, we used genome-editing to show that the most common parasitic nematode β -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 β -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

2 (GLC-1, str-217)

Related Haplotypes

26

EXTERNAL LINKS

COMMENTS

