

## GEPHE SUMMARY

|  |                |            |              |
|--|----------------|------------|--------------|
|  | Gephebase Gene |            | GepheID      |
| beta-tubulin (ben-1) ( <a href="https://www.gephebase.org/search-criteria?/and+Gene">https://www.gephebase.org/search-criteria?/and+Gene</a> ) |                | GP00001848 |              |
| Gephebase="beta-tubulin (ben-1)"#gephebase-summary-title)  |                |            | Main curator |
|  | Entry Status   | Courtier   |              |
| Published  |                |            |              |

## PHENOTYPIC CHANGE

|   |                             |  |                             |
|---|-----------------------------|--|-----------------------------|
|   | Trait Category              |  |                             |
| Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait">https://www.gephebase.org/search-criteria?/and+Trait</a> )  |                             |  |                             |
| Category="Physiology"#gephebase-summary-title)  | Trait                       |  |                             |
| Xenobiotic resistance (benzimidazole) ( <a (benzimidazole)"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=" resistance="" xenobiotic="">https://www.gephebase.org/search-criteria?/and+Trait="Xenobiotic resistance (benzimidazole)"#gephebase-summary-title</a> ) |                             |  |                             |
|   | Trait State in Taxon A      |  |                             |
| sensitive   |                             |  |                             |
|   | Trait State in Taxon B      |  |                             |
| resistant   |                             |  |                             |
|   | Ancestral State             |  |                             |
| Taxon A   |                             |  |                             |
|   | Taxonomic Status            |  |                             |
| Intraspecific ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic">https://www.gephebase.org/search-criteria?/and+Taxonomic</a> )   |                             |  |                             |
| Status="Intraspecific"#gephebase-summary-title)   |                             |  |                             |
|   | Taxon A                     | Taxon B  |                             |
|   | Latin Name                  |  | Latin Name                  |
| Caenorhabditis elegans  |                             | Caenorhabditis elegans   |                             |
| ( <a caenorhabditis="" elegans"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Caenorhabditis elegans"#gephebase-summary-title</a> )  |                             | ( <a caenorhabditis="" elegans"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Caenorhabditis elegans"#gephebase-summary-title</a> ) |                             |
|   | Common Name                 |  | Common Name                 |
| -   |                             | -  |                             |
|   | Synonyms                    |  | Synonyms                    |
| roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900   |                             | roundworm; Rhabditis elegans; Caenorhabditis elegans (Maupas, 1900); Rhabditis elegans Maupas, 1900  |                             |
|   | Rank                        |  | Rank                        |
| species   |                             | species  |                             |
|   | Lineage                     |  | 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                      |  | Parent                      |
| Caenorhabditis () - (Rank: genus)   |                             | Caenorhabditis () - (Rank: genus)  |                             |
| ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237</a> )   |                             | ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6237</a> )  |                             |
|   | NCBI Taxonomy ID            |  | NCBI Taxonomy ID            |
| 6239  |                             | 6239   |                             |
| ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239</a> )   |                             | ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6239</a> )  |                             |
|   | is Taxon A an Intraspecies? |  | is Taxon B an Intraspecies? |
| No  |                             | Yes  |                             |
|   |                             |  | Taxon B Description         |
|   |                             | ED3012   |                             |

## GENOTYPIC CHANGE

|   |                         |  |   |
|---|-------------------------|--|---|
|   | Generic Gene Name       |  | UniProtKB Saccharomyces cerevisiae (strain ATCC 204508 / S288c) |
| TUB2  |                         | P02557 ( <a href="http://www.uniprot.org/uniprot/P02557">http://www.uniprot.org/uniprot/P02557</a> ) |   |
|   | Synonyms                |  | GenebankID or UniProtKB   |
| ARM10; SHE8; YFL037W  |                         | 0  |   |
|   | String                  |  |   |
| 4932.YFL037W  |                         |  |   |
| ( <a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier= 4932.YFL037W">http://string-db.org/newstring.cgi/show_network_section.pl?identifier= 4932.YFL037W</a> ) |                         |  |   |
|   | Sequence Similarities   |  |   |
| Belongs to the tubulin family.  |                         |  |   |
|   | GO - Molecular Function |  |   |
| GO:000525 : GTP binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:000525">https://www.ebi.ac.uk/QuickGO/term/GO:000525</a> )   |                         |  |   |
| GO:0003924 : GTPase activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0003924">https://www.ebi.ac.uk/QuickGO/term/GO:0003924</a> )  |                         |  |   |
| GO:0005200 : structural constituent of cytoskeleton   |                         |  |   |
| ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005200">https://www.ebi.ac.uk/QuickGO/term/GO:0005200</a> )   |                         |  |   |
|   | GO - Biological Process |  |   |
| GO:0007010 : cytoskeleton organization  |                         |  |   |

(<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

Deletion (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~Deletion~#gephebase-summary-title>)

Deletion Size

1-9 bp

Molecular Details of the Mutation

Del\_3540300\_3540301 â€” 1bp deletion in coding exon 2

Experimental Evidence

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

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  $\beta$ -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  $\beta$ -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  $\beta$ -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  $\beta$ -tubulin gene. Furthermore, we used genome-editing to show that the most common parasitic nematode  $\beta$ -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  $\beta$ -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 Gephbase=~beta-tubulin \(ben-1\)~/and+Taxon ID=~6239~/or+Gene Gephbase=~beta-tubulin \(ben-1\)~/and+Taxon ID=~6239~#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephbase=~beta-tubulin (ben-1)~/and+Taxon ID=~6239~/or+Gene Gephbase=~beta-tubulin (ben-1)~/and+Taxon ID=~6239~#gephebase-summary-title))

EXTERNAL LINKS

