

WormQTL^{HD}

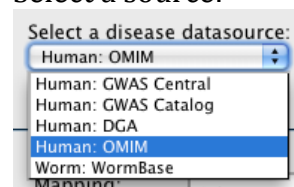
- Tool tutorial

Tool 1: Disease2QTL

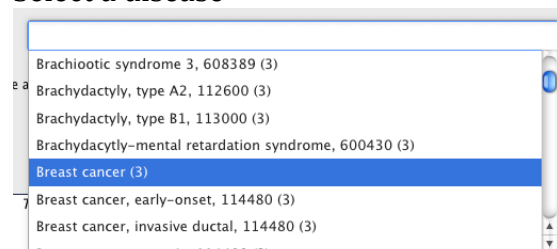
Disease2QTL is a tool for human geneticists to explore novel causal genes for a specific human disease by using worm QTL findings. Using a selection of one or multiple human diseases (from OMIM, DGA, NHGRI GWAS Catalogue, or GWAS Central), a 'shopping' page is presented with worm gene expression probes and their human disease association. More information about the gene orthology mapping and association studies can be browsed. Users can put individual probes, or all probes at once, into the 'shopping cart'. Subsequently, they can explore the genetic variation of those genes across the different experiments and studies that are stored in the WormQTL^{HD} database. The shopping cart is a central place in WormQTL^{HD} where users can see the various worm gene probes that they have selected, and create QTL/eQTL visualizations from the items in the shopping cart using 'Plot QTLs'. Using the 'Plot QTLs' function, researchers can test if genes associated with the selected diseases have any QTLs and if they map to a common genomic region. Alternatively, users can also select worm phenotypes (1,504 total) instead of human diseases as a starting point. The shopping window is presented in exactly the same way as before, so users can browse human diseases from a worm phenotype perspective instead, or simply shop for probes of choice for a given worm phenotype and plot their QTLs, without considering any human disease relation.

How to do it

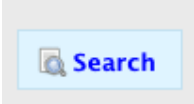
Select a source:



Select a disease



Search



View hits (3)

View cart (0)

Plot QTLs

Clear cart

Found 3 hits.

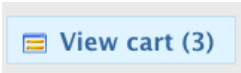
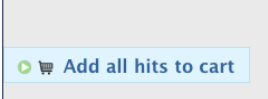
Add all hits to cart

Show 10 entries

Filter:

Probe name	Orthology	Disease associations
<div><div>Add to cart</div><div>AGIUSA9275</div></div>	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)
<div><div>Add to cart</div><div>AGIUSA3864</div></div>	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)

Add to cart



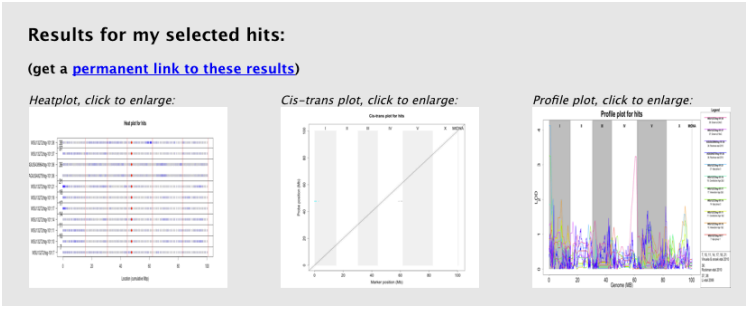
Shopping cart

Show 10 entries

Filter:

Probe name	Orthology	Disease associations
<div><div>Remove</div><div>AGIUSA9275</div></div>	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)
<div><div>Remove</div><div>AGIUSA3864</div></div>	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)

QTL Plot



Tool 2: Region2disease

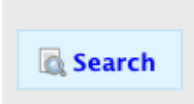
Researchers can link worm genomic regions to human diseases. This approach starts by selecting a region in the worm genome, e.g. a known 'eQTL hotspot', where a number of eQTLs are located. The region is selected by providing the chromosome name, start- and end base pair positions. If a gene is known but the region is not, a region can be set by inputting the name of the gene. The database then returns all worm gene expression probes that are annotated in this region. From the probes, the corresponding worm genes are gathered, plus their human orthologs. The user is presented with a table containing the human-worm orthology and disease/phenotype associations in man and worm. After shopping for some or all of the relevant probes, users can choose to visualize eQTL results for them (similar to Tool 1), or perform a disease enrichment test. The hypergeometric gene overlap test to discover phenologs (phenotype orthologs) can be performed by clicking on 'Disease enrichment'. All probes in the region are linked to their corresponding genes in worm, and a test is performed whether this entire group of genes is significantly 'enriched' for one or more human diseases by overlapping orthologous groups and worm- and human genes. The statistical significance of phenologs (P-value) is listed in an output table. A significant result means that the input genomic region shares a significantly larger set of orthologous genes with a human disease than would be expected at random, even if the expressed phenotype in worm appears very different from the human disease phenotype (e.g. breast cancer and fertility). This tool can provide novel interpretation of genomic regions of interest.

How to do it

Setting position

Setting gene

Search



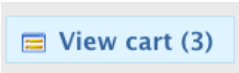
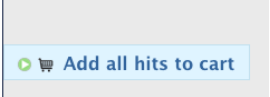
View hits (3) View cart (0) Plot QTLs Clear cart

Found 3 hits.

Add all hits to cart

Probe name	Orthology	Disease associations
AGUSA9275	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)
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Add to cart



Shopping cart

Show 10 entries

Probe name	Orthology	Disease associations
AGUSA9275	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)
AGUSA3864	Ce: WBGene00015658 Hs: TSG101	WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant OMIM: Breast cancer (3)

Disease enrichment

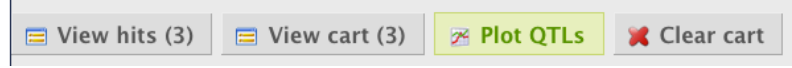


Overlap test for chr1:10750332-10776693 [Region search]

Show 10 entries

Vs. phenotype	From source	Genes overlap	Overlap details	P-value	Single test thres.	Bonferroni thres.	Single test signif.?	Bonferroni signif.?
Insulin-like growth factors	GWAS Catalog	1	2 vs 1	4.92E-4	0.05	1.02E-4	YES	NO
stress induced lethality variant	WormBase	1	2 vs 1	4.92E-4	0.05	3.32E-5	YES	NO
age associated fluorescence reduced	WormBase	1	2 vs 1	4.92E-4	0.05	3.32E-5	YES	NO
Breast cancer (3)	OMIM	1	2 vs 1	4.92E-4	0.05	5.29E-5	YES	NO
Normalized brain volume	GWAS Catalog	1	2 vs 2	9.85E-4	0.05	1.02E-4	YES	NO
oxygen response variant	WormBase	1	2 vs 2	9.85E-4	0.05	3.32E-5	YES	NO
lipid synthesis defective	WormBase	1	2 vs 2	9.85E-4	0.05	3.32E-5	YES	NO
cisplatin resistant	WormBase	1	2 vs 2	9.85E-4	0.05	3.32E-5	YES	NO
organism ionizing radiation response variant	WormBase	1	2 vs 3	1.48E-3	0.05	3.32E-5	YES	NO
hormetic temperature induced life span extension defective	WormBase	1	2 vs 3	1.48E-3	0.05	3.32E-5	YES	NO

QTL plot



Researchers can start by selecting a QTL/eQTL in worm to find potential relationships with human diseases. You can select QTLs of interest based on three criteria: a selected experiment, a certain threshold for significance (LOD score), and a specific gene expression probe with a suspected QTL. If there is a QTL with a LOD score above the threshold, we automatically select the closest 50 probes on both sides of the highest peak marker. These probes are presented and available for browsing, shopping and plotting of QTLs, or can be the input for the disease enrichment test to find phenologs.


How to do it

Set up QTL search

Dataset: Probe/trait: LOD threshold:


Submit a probe with a lod threshold and a dataset. Click [here](#) to load a tested example query

Search



Search

Show: 10 1 entries

Protein name	Orthology	Disease associations
 <p style="text-align: right; margin-top: 10px;">ACUAS8275</p> <p style="text-align: right; margin-top: 10px;">Add to cart</p>	<p>Wormlike, apoptosis variant, movement variant, lethal, egg laying variant, synaptonemal structure defective early embryo, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variants: some growth, vitelline progeny, larval arrest, postembryonic development variant, maternal sterility, protein aggregation variant, transgene subcellular localizatio</p>	<p>OMIM: Breast cancer (3)</p>
 <p style="text-align: right; margin-top: 10px;">ACUAS18964</p> <p style="text-align: right; margin-top: 10px;">Add to cart</p>	<p>Wormlike, apoptosis variant, movement variant, lethal, egg laying variant, synaptonemal structure defective early embryo, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variants: some growth, vitelline progeny, larval arrest, postembryonic development variant, maternal sterility, protein aggregation variant, transgene subcellular localizatio</p>	<p>OMIM: Breast cancer (3)</p>

Add to cart

[Add all hits to cart](#)
[View cart \(3\)](#)

Shopping cart

Show 10 entries		Orthology	Disease associations
AGIUAS9275		Ce: WBGene00015658 Hs: TSGC101	<p>WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant</p> <p>OMIM: Breast cancer (3)</p>
AGUISA38964		Ce: WBGene00015658 Hs: TSGC101	<p>WormBase: apoptosis variant, movement variant, lethal, egg laying variant, cytoplasmic structure defective early emb, embryonic lethal, protein degradation variant, endocytic transport variant, receptor mediated endocytosis defective, larval lethal, Variant, slow growth, sterile progeny, larval arrest, postembryonic development variant, maternal sterile, protein aggregation variant, transgene subcellular localization variant</p> <p>OMIM: Breast cancer (3)</p>

Disease enrichment

[View hits \(7\)](#)
[View cart \(10\)](#)
[Plot QTLs](#)
[Disease enrichment](#)
[Clear cart](#)

[illegible]

QTL plot

 View hits (3)

 View cart (3)

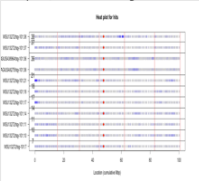
 Plot QTLs

 Clear cart

Results for my selected hits:

(get a [permanent link to these results](#))

Heatplot, click to enlarge:



Cis-trans plot, click to enlarge:



Profile plot, click to enlarge:



Tool 4: ComparePheno

WormQTLHD also provides a tool that links human diseases to classical worm phenotypes (and vice versa) to discover phenologs in a systematic way. Users begin by selecting one or more human diseases and clicking on ‘Compare’. The genes associated with the selected disease are tested for enrichment against all sets of known associated genes for worm phenotypes. The result reveals functionally coherent, evolutionarily conserved gene networks. Alternatively, users can also start by selecting worm phenotypes, which are tested against human diseases. In addition to cross-species testing, results of within-species disease enrichment are also available (e.g. to find the closest related human disease for another input human disease).

How to do it

Select a source:

Select a disease datasource:


- Human: OMIM
- Human: GWAS Central
- Human: GWAS Catalog
- Human: DGA
- Human: OMIM
- Worm: WormBase
- Mammal: Mammal

Select a disease

Brachiootic syndrome 3, 608389 (3)
Brachydactyly, type A2, 112600 (3)
Brachydactyly, type B1, 113000 (3)
Brachydactyly-mental retardation syndrome, 600430 (3)
Breast cancer (3)
Breast cancer, early-onset, 114480 (3)
Breast cancer, invasive ductal, 114480 (3)

Breast cancer (3) ✕

Compare

 **Compare**

Overlap test for [Breast cancer \(3\)](#) [\[OMIM\]](#)

Show entries

Vs. phenotype	From source	Genes overlap	Overlap details	P-value	Single test thresh.	Bonferroni thresh.	Filter: <div>Single test signif.? Bonferroni signif.?</div>
Breast cancer (3)	OMIM	1	1 vs 1	2.46E-4	0.05	5.29E-5	<div>YESNO</div>
cytoplasmic structure defective early emb	WormBase	1	1 vs 6	1.48E-3	0.05	3.32E-5	<div>YESNO</div>
movement variant	WormBase	1	1 vs 19	4.68E-3	0.05	3.32E-5	<div>YESNO</div>
endocytic transport variant	WormBase	1	1 vs 20	4.92E-3	0.05	3.32E-5	<div>YESNO</div>
apoptosis variant	WormBase	1	1 vs 93	2.29E-2	0.05	3.32E-5	<div>YESNO</div>
protein degradation variant	WormBase	1	1 vs 116	2.86E-2	0.05	3.32E-5	<div>YESNO</div>
egg laying variant	WormBase	1	1 vs 228	5.61E-2	0.05	3.32E-5	<div>NONO</div>
receptor mediated endocytosis defective	WormBase	1	1 vs 418	1.03E-1	0.05	3.32E-5	<div>NONO</div>
protein aggregation variant	WormBase	1	1 vs 515	1.27E-1	0.05	3.32E-5	<div>NONO</div>
transgene subcellular localization variant	WormBase	1	1 vs 854	2.1E-1	0.05	3.32E-5	<div>NONO</div>

Showing 1 to 10 of 19 entries

PreviousNext