WormQTL^{HD}

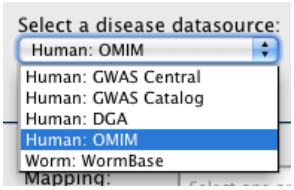
- Tool tutorial

Tool 1: Disease2QTL

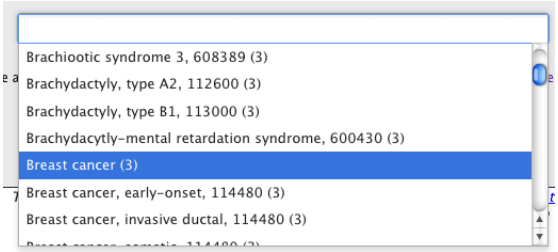
Disease2QTL is a tool for human geneticists to explore novel causal genes for a specific human disease by using worm QTL findings. Using a selection of one or multiple human diseases (from OMIM, DGA, NHGRI GWAS Catalogue, or GWAS Central), a 'shopping' page is presented with worm gene expression probes 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



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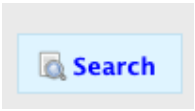
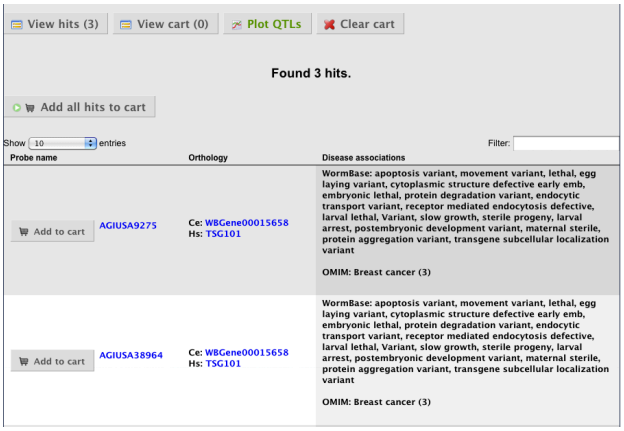
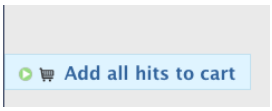
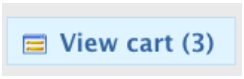
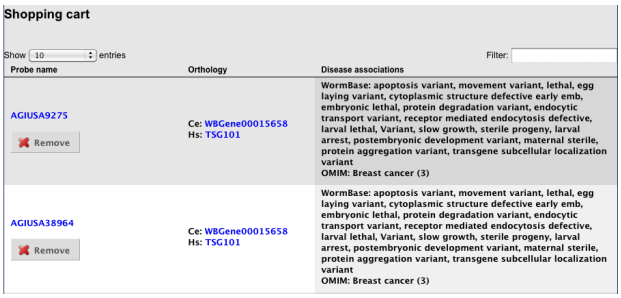




Add to cart







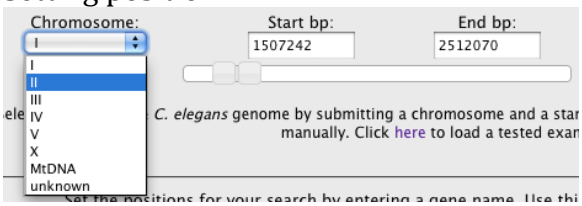
QTL Plot

Tool 2: Region2disease

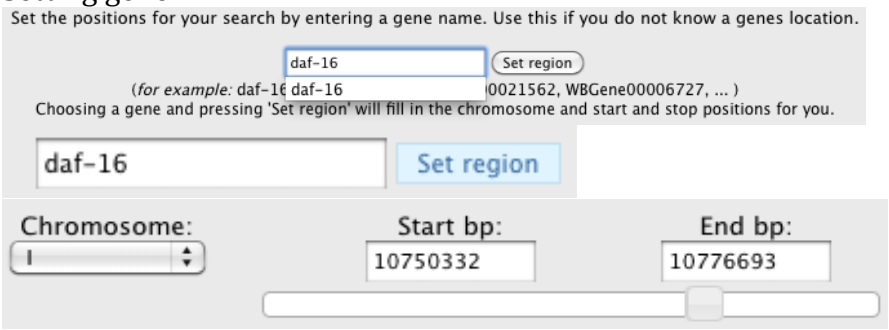
Researchers can link worm genomic regions to human diseases. This approach starts by selecting a region in the worm genome, e.g. a known 'eQTL hotspot', where a number of eQTLs are located. The region is selected by providing the chromosome name, start- and end base pair positions. If a gene is known 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



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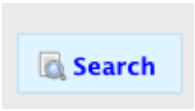
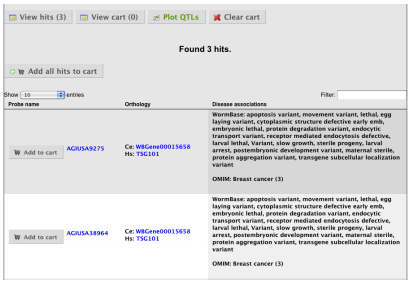
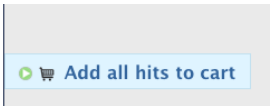
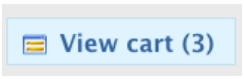
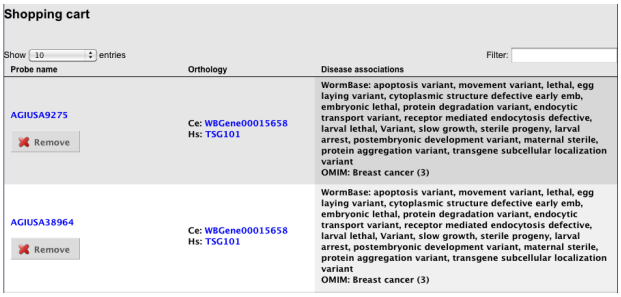




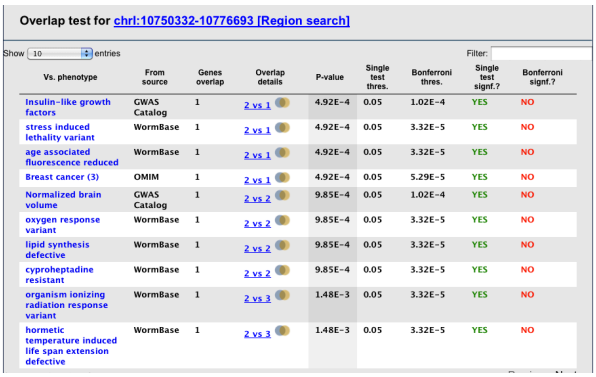
Add to cart



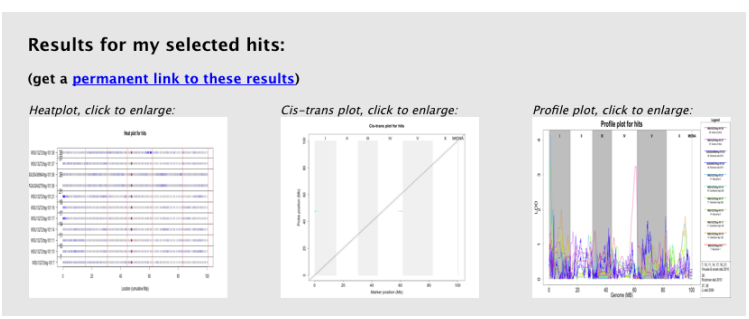




Disease enrichment



QTL plot

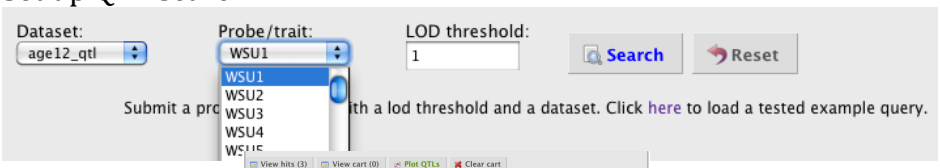


Tool 3: QTL2disease

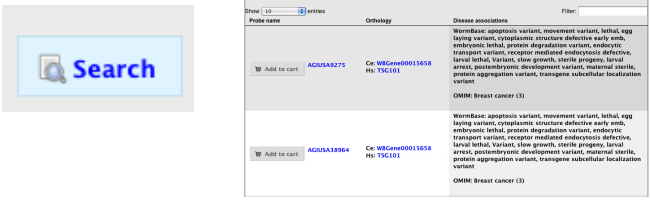
Researchers can start by selecting a QTL/eQTL in worm to find potential relationships with human diseases. You can select QTLs of interest based on three criteria: a selected experiment, a certain threshold for significance (LOD score), and a specific gene expression probe with a suspected QTL. If there 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

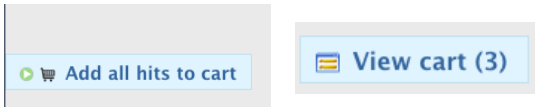
Set up QTL search

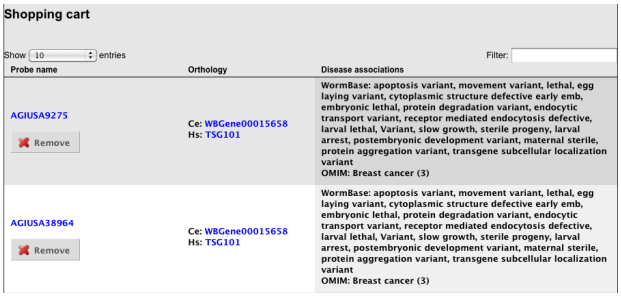


Search

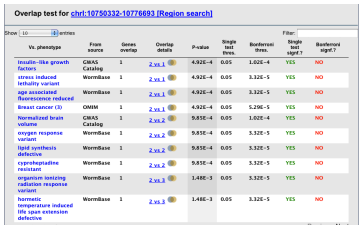


Add to cart





Disease enrichment

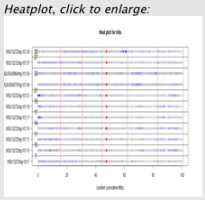


QTL plot

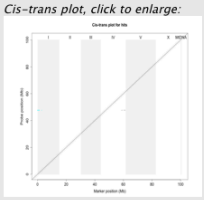
Results for my selected hits:

(get a permanent link to these results)

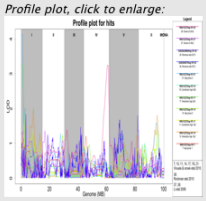
Heatplot, click to enlarge:



Cis-trans plot, click to enlarge:



Profile plot, click to enlarge:

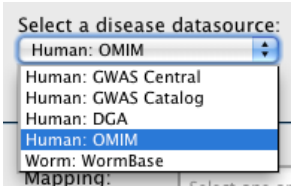


Tool 4: ComparePheno

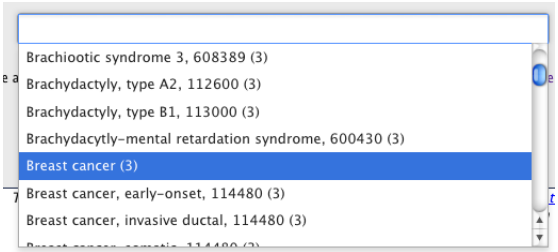
WormQTLHD also provides a tool that links human diseases to classical worm phenotypes (and vice versa) to discover phenologs in a systematic way. Users begin by selecting one or more human diseases and clicking on 'Compare'. The genes associated with the selected disease are tested for enrichment against 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



Compare