

Human Disease Model Reports in FlyBase

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ABSTRACT The use of Drosophila melanogaster as a model for studying human disease is well established, reflected by the steady increase in both the number and proportion of fly papers describing human disease models in recent years. In order to improve both the visibility and accessibility of human disease model research, FlyBase has recently begun producing Human Disease Model Reports. These reports provide an integrated informational resource regarding specific diseases and fly disease models and their potential impacts on translational research.

The Integrated Human Disease Model Report

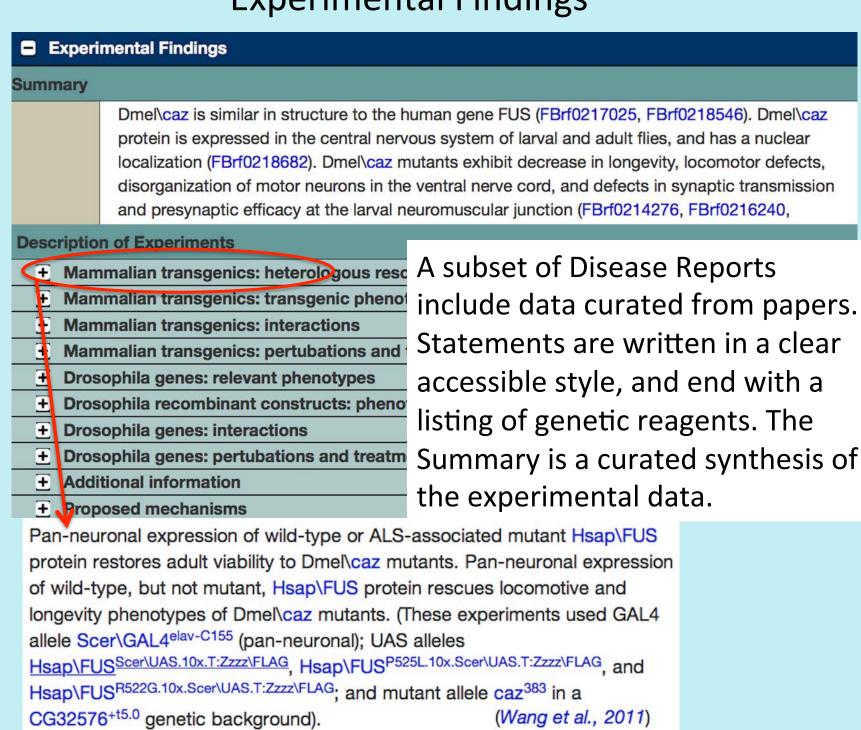
General Information						
Name	amyotrophic lateral sclerosis 8		FlyBase ID	FBhh0000020		
Disease	DOID:0050752		Parent	amyotrophic lateral sclerosis		
Ontology ID			Disease			
OMIM	AMYOTROPHI	CLATERAL	Parent	DOID:332		
	SCLEROSIS 8; ALS8		Disease DOID			
Overview						
This report describes amyotrophic lateral sclerosis 8 (ALS8), which is a subtype of amyotrophic lateral sclerosis. The human gene implicated in this disease is VAPB, which is a member of the vesicle-associated membrane protein (VAMP)-associated protein (VAP) family. This gene is also associated with the disease spinal muscular atrophy, late-onset, Finkel type (OMIM:182980, FBhh0000254). There is a single fly ortholog, Vap-33A, for which classical amorphic and hypomorphic alleles, RNAi-targeting constructs, and alleles caused by insertional mutagenesis have been generated. Disease Summary Information Disease Summary Information						
Ortholog Inform	₽ Ortholog Information		pecific Disease Summary: amyotrophic lateral sclerosis 8			
D. melanogaster Gene Informati		OMIM report	AMYOTROPHIC LATERAL SCLEROSIS 8; ALS8			
		Human gene(s)	VESICLE-ASSOCIATED MEMBRANE PROTEIN-ASSOCIATED			
Synthetic Gene(s) Used (0)		implicated	PROTEIN B; VAPB			
Experimental Findings		Symptoms and	characterized by fasciculations, cramps, and postural tremor			
Summary of Physical Interaction		phenotype				
♣ Alleles Reported to Model Huma			Charles and the second of the	Nishimura, et al., 2004, pubmed:15060112; Nishimura, et al., 2004, pubmed:15372378). [From OMIM:608627, 2015.12.16]		
Genetic Tools, Stocks and Reag Genetics		Genetics	ALS8 is caused by heterozygous mutation in the VAPB gene.			
References (16))		[from OMIM:608627, 20	015.02.12]		

Each Human Disease Model Report integrates information about a specific disease from many parts of FlyBase. The Disease Summary includes background information, primarily from OMIM (Online Mendelian Inheritance in Man).

Related Diseases spinal muscular atrophy, late onset, Finkel type Related human health report(s) elated Specific Diseases **OMIM** phenotypic Amyotrophic lateral sclerosis Frontotemporal dementia and/or Amyotrophic Lateral Sclerosis Drosophila model Human gene(s) Drosophila ALS1 SOD1 amyotrophic lateral sclerosis 1 ALS4 SETX ALS5 SPG11 ALS6 **FUS** amyotrophic lateral sclerosis 6 y The Related Diseases section allows for easy

navigation to disease subtypes, or to diseases caused by the same gene or mechanism.

Experimental Findings



Orthologs and Promoted Data

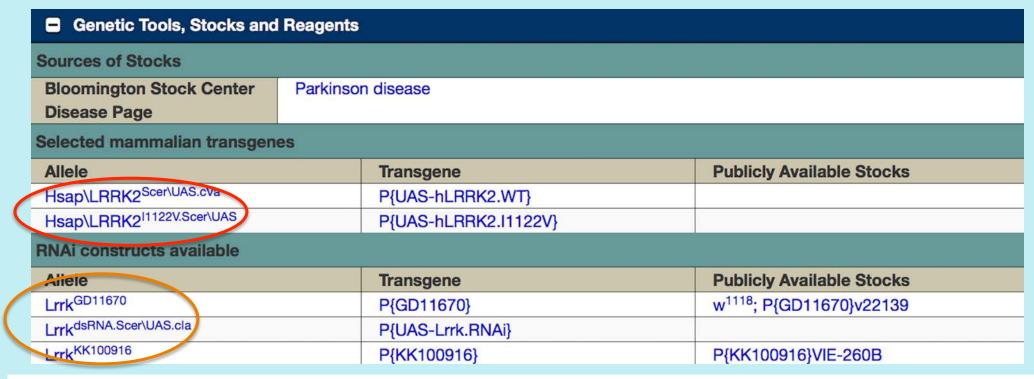


In the Ortholog Information section we associate the human gene identified as the cause of the disease, whether it has been transgenically expressed in flies, and its orthologous fly gene. These gene associations allow us to promote data from elsewhere in FlyBase.

Disease Ontology Allele Annotation

Lrrk						
Models						
Allele	Disease	Evidence	References			
Lrrk ^{e03680}	model of Parkinson's disease	inferred from mutant phenotype	(Lin et al., 2015)			
LrrkRC.Scer\UAS.T:Zzzz\FLAG	model of Parkinson's disease	inferred from mutant phenotype	(Godena et al., 2014)			
+ Interactions						
Hsap\LRRK2						
± Models						
☐ Interactions						
Allele	Disease	Interaction	References			
Hsap\LRRK2 ^{Scer\UAS.cVa}	model of Parkinson's disease	is ameliorated by Hsap\PARK7 ^{Scer\UAS.cYa}	(Venderova et al., 2009)			

Thus, we can display Disease Ontology annotations of alleles of both the fly and human genes. Other promoted data types include physical interactions, and genetic tools, stocks and reagents.



In the Genetic Tools, Stocks and Reagents section we include a link to the relevant BDSC disease page, and indicate whether a stock is available from a public stock repository.

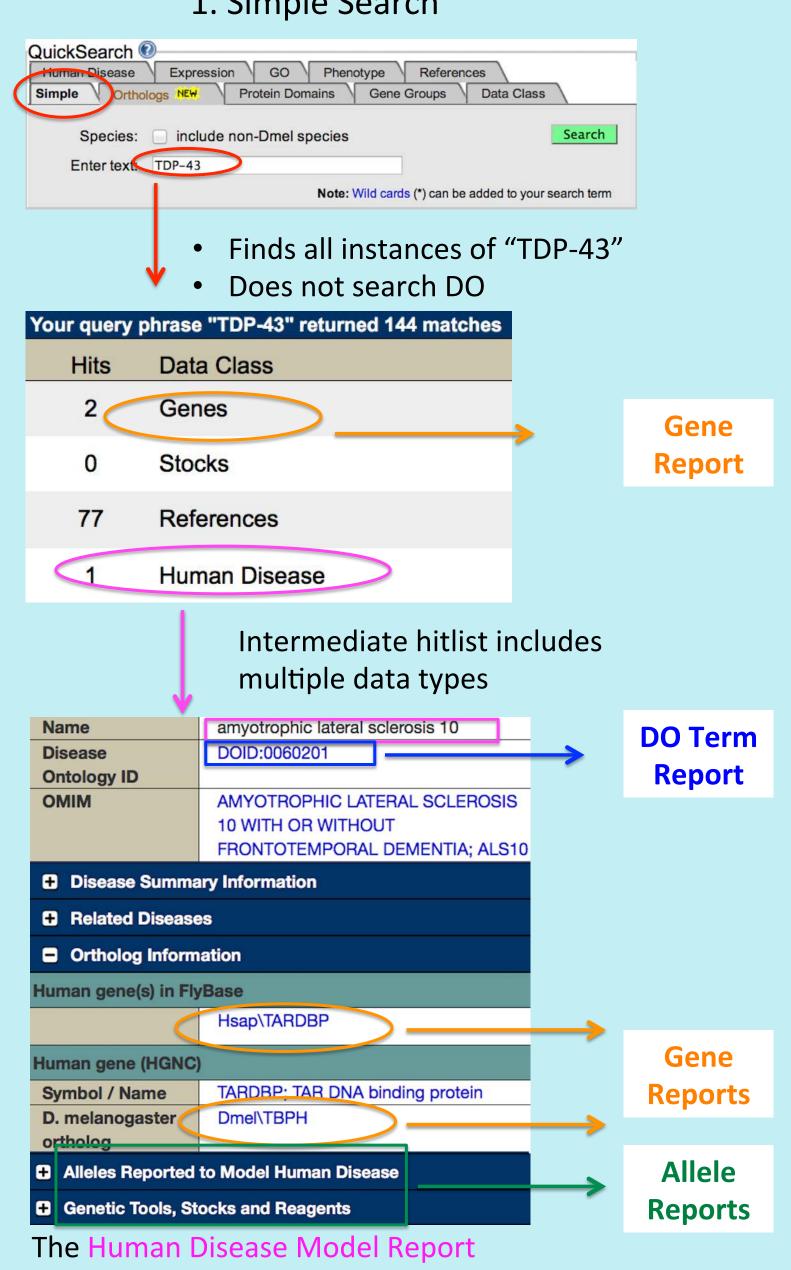
Searching for Disease Model Information

The QuickSearch tool on the FlyBase front page offers three options to search for human disease information:

- (1) The Simple tab searches exact text strings.
- (2) The dedicated Human Disease tab searches the Disease Ontology (DO).
- (3) The Human Disease tab also includes a link to a browseable list of Human Disease Model Reports.

Disease model information in FlyBase is organized using a "you can get there from here" philosophy. A user may locate a bit of disease model information in a disease model report, a gene report, or a DO term report. Each of these reports includes links to the other reports.

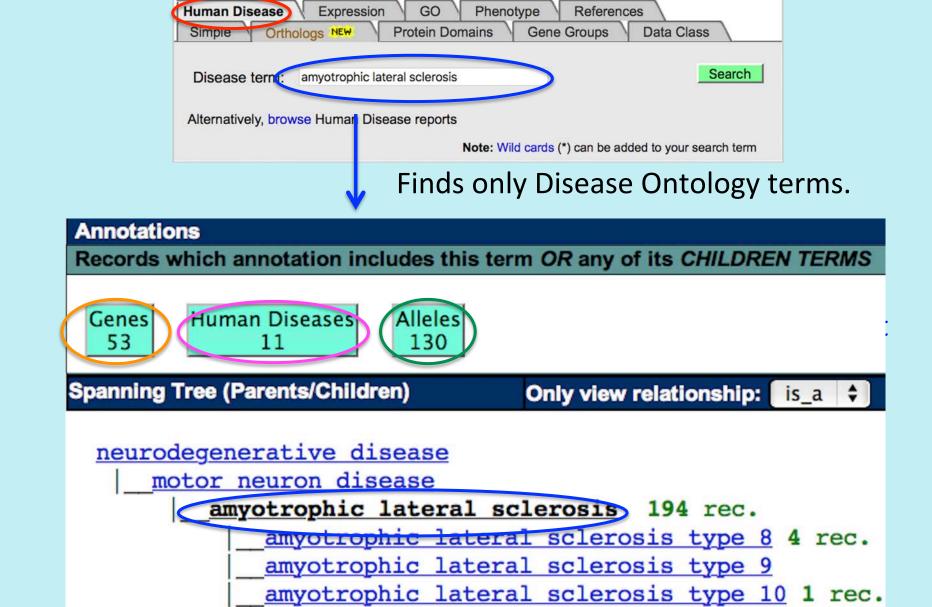
1. Simple Search



links to DO, Gene and Allele Reports

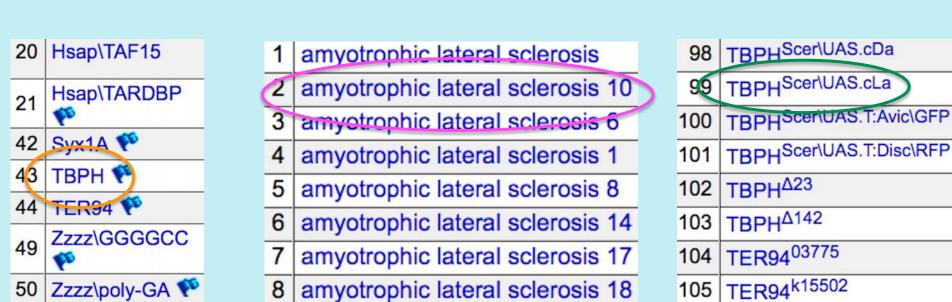
2. Human Disease Tab

QuickSearch (

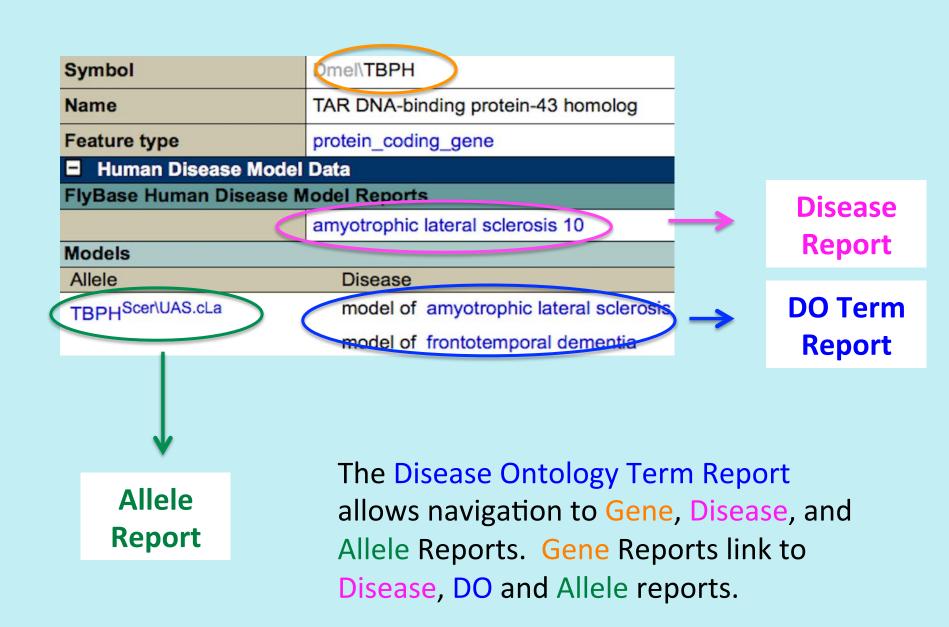


- Spanning tree allows browsing of DO hierarchy.
- Aqua buttons correspond to Genes, Alleles or Disease Reports to which a DO term or one of its children is attached.

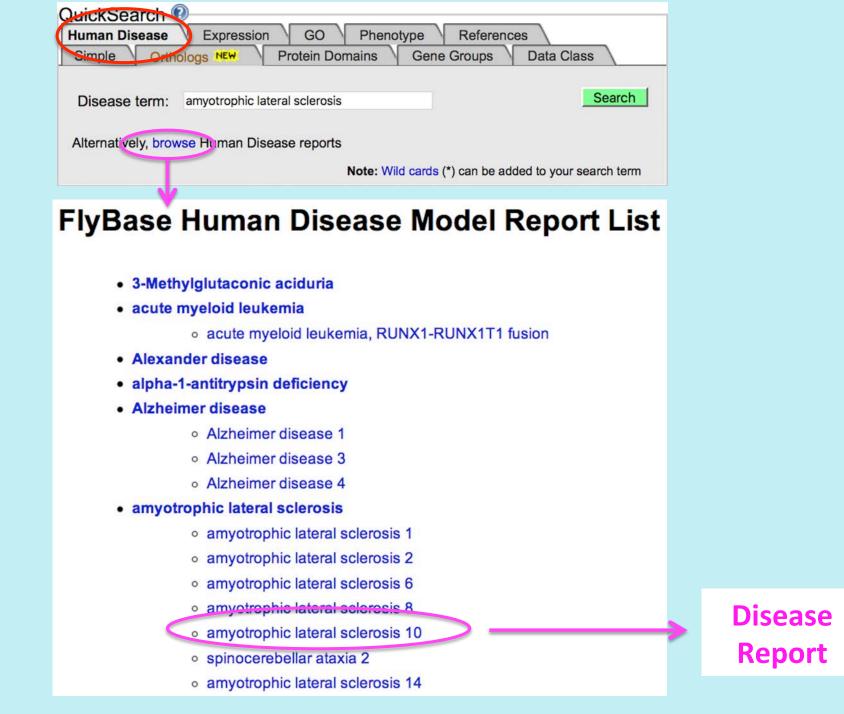
amyotrophic lateral sclerosis type 11



Buttons lead to hit lists of Genes, Disease Reports, and Alleles. Genes may include fly genes, human transgenes (Hsap), or artificial genes (Zzzz).



3. Browseable List

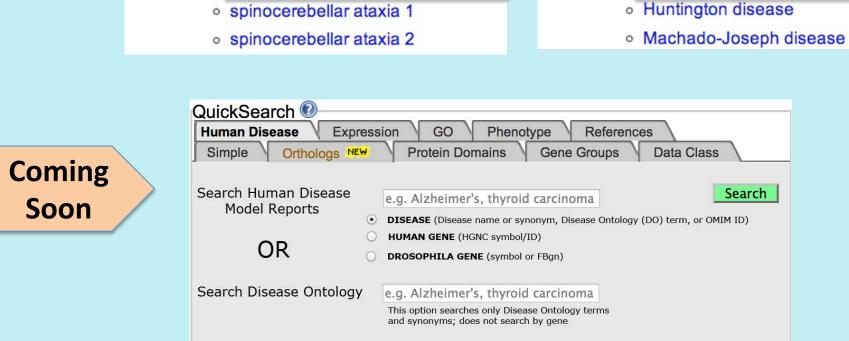


The Human Disease Model Report List consists of links to those reports. Some reports are redundantly listed; in the example below, dentatorubro-pallidoluysian atrophy is both a subtype of spinocerebellar ataxia, and is a disease caused by polyglutamine repeat expansion.

polyglutamine diseases

Note: Wild cards (*) can be added to your search term

dentatorubro-pallidoluysian atrophy



spinocerebellar ataxia

dentatorubro-pallidoluysian atrophy

An integrated Human Disease tab will allow searching by disease, human gene, or Drosophila gene.

Citation: Millburn, G.H., Crosby, M.A., Gramates, L.S., Tweedie, S., FlyBase Consortium, (2016). FlyBase portals to human disease research using Drosophila models. Dis. Model Mech. 9(3): 245--252.

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