



ADRC 2017

Reaching across the MODs: enhanced orthology data and future prospects



Cross-MOD resources

- Links to MOD gene reports from DIOPT/
FlyBase ortholog search
- Alliance of Genome Resources (AGR)
- Links from FlyBase to two new resources:
 - Gene2Function
 - MARRVEL

Orthology is the key approach for comparison of genes across organisms

- But determining orthology can be a tricky business
- Different methods:
 - Phylogenetic
 - Sequence comparison
 - Graph-based, other, combinations
- Different goals:
 - Exclusive (highly selective, high precision)
 - Inclusive (casts a wide net -- high sensitivity, high recall)
 - Intermediate (balancing act)

Determination of orthology: compilation of multiple algorithms

- No one best algorithm: different algorithms are appropriate for different applications.
- The result: a multitude of algorithms for making orthology calls.



- Flexible alternative: compilation of multiple algorithms (HCOP, DIOPT).

DIOPT multi-algorithm approach

DIOPT - DRSC Integrative
Ortholog Prediction Tool

<http://www.flyrnai.org/diopt>

- FlyBase has added data from DIOPT; a tool developed by the DRSC
- DIOPT uses a **scoring system**:
 - Number of algorithms that call a given ortholog pair
 - Compared to the number of algorithms that include those 2 species
- Link to DIOPT from the FlyBase 'Orthologs' query
 - Can access documentation from the DIOPT query page

DIOPT Documentation

Prediction Method	Source	Prediction Algorithm	Coverage	DIOPT Weight*	PMID
Compara	Ensembl	Phylogenetic approach	70 species (vs. 86)	0.931	19029536
Homologene	NCBI	Combination of BBH*, tree and synteny	21 species (vs. 68)	1	11125071
Inparanoid	Stockholm University, Sweden	BBH* approach to identify orthologs and in-paralogs	273 species (vs. 8)	1.005	11743721 25429972
Isobase	MIT	Sequence and PPI* network alignments	5 species (vs. 2, Nov. 2014)	0.957	21177658
OMA	CBRG, ETH Zurich	BBH*, global sequence alignments	1706 species (Oct 2014)	1.019	17545180
OrthoDB	University of Geneva	Phylogenetic approach	3027 species (vs. 9)	1.001	20972218 25428351


*BBH = Best Blast Hits


FlyBase home page: QuickSearch

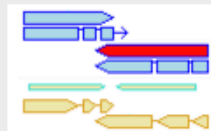
FB2017_01, released Feb 14, 2017

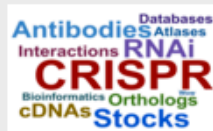
A Database of *Drosophila* Genes & Genomes


Home Tools Downloads Links Community Species About Help Archives Jump to Gene J2G

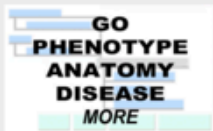
 FlyBase


 D.melanogaster
D.virilis
A.mellifera
BLAST


 GBrowse


 Databases
Antibodies
Interactions
RNAI
CRISPR
Bioinformatics
Orthologs
cDNAs
Stocks
Resources


 ON
OFF
RNA-Seq


 GO
PHENOTYPE
ANATOMY
DISEASE
MORE
Vocabularies


 ImageBrowse


 FIELD DATA
XML
sequence
Batch Download


 FAST-TRACK
YOUR PAPER


 FLY BOARD

 NEWS

 COMMUNITY

 MEETINGS

 COURSES

 COMMUNITY
ADVOCACY

QuickSearch

Human Disease Expression Phenotype GO References


Simple **Orthologs** Protein Domains Gene Groups Data Class

Species: include non-Dmel species

Enter text:

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

Commentary

 Databases
Antibodies
Interactions
RNAI
CRISPR
Bioinformatics
Orthologs
cDNAs
Stocks

Improved External Resources page Jan 14, 2016. The External Resources page has been updated and a prominent new button has been added to the FlyBase home page. This button replaces a link to the "Query Builder" field-specific search tool which can still be accessed via the navigation bar under [Tools](#) → [Query Tools and Portals](#) → [QueryBuilder](#). ... (More)

QuickSearch “Orthologs” tab

QuickSearch

[Human Disease](#) [Expression](#) [Phenotype](#) [GO](#) [References](#)

[Simple](#) **[Orthologs](#)** [Protein Domains](#) [Gene Groups](#) [Data Class](#)

Input:

Enter gene symbol(s) or ID(s), separated by spaces

Search

Species:

Gene(s):



Output:

MODEL ORGANISMS (via [DIOPT](#)) [instead [search OrthoDB orthology groups](#)]

- | | |
|--|---|
| <input checked="" type="checkbox"/> <i>H. sapiens</i> (Human) | <input checked="" type="checkbox"/> <i>D. melanogaster</i> (Fruit fly) |
| <input checked="" type="checkbox"/> <i>R. norvegicus</i> (Norway rat) | <input checked="" type="checkbox"/> <i>C. elegans</i> (Nematode, roundworm) |
| <input checked="" type="checkbox"/> <i>M. musculus</i> (Laboratory mouse) | <input checked="" type="checkbox"/> <i>S. cerevisiae</i> (Brewer's yeast) |
| <input checked="" type="checkbox"/> <i>X. tropicalis</i> (Western clawed frog) | <input checked="" type="checkbox"/> <i>S. pombe</i> (Fission yeast) |
| <input checked="" type="checkbox"/> <i>D. rerio</i> (Zebrafish) | |

un/check all:

QuickSearch “Orthologs” tab

QuickSearch

Human Disease Expression Phenotype GO References

Simple **Orthologs** Protein Domains Gene Groups Data Class

Input:

Enter gene symbol(s) or ID(s), separated by spaces

Search

Species: *D. melanogaster* ▾

Gene(s): e.g. Cdk1, CG5363, FBgn0004106, 34411

YouTube

Output:

MODEL ORGANISMS (via DIOPT) [instead [search OrthoDB orthology groups](#)]

- | | |
|--|---|
| <input checked="" type="checkbox"/> <i>H. sapiens</i> (Human) | <input checked="" type="checkbox"/> <i>D. melanogaster</i> (Fruit fly) |
| <input checked="" type="checkbox"/> <i>R. norvegicus</i> (Norway rat) | <input checked="" type="checkbox"/> <i>C. elegans</i> (Nematode, roundworm) |
| <input checked="" type="checkbox"/> <i>M. musculus</i> (Laboratory mouse) | <input checked="" type="checkbox"/> <i>S. cerevisiae</i> (Brewer's yeast) |
| <input checked="" type="checkbox"/> <i>X. tropicalis</i> (Western clawed frog) | <input checked="" type="checkbox"/> <i>S. pombe</i> (Fission yeast) |
| <input checked="" type="checkbox"/> <i>D. rerio</i> (Zebrafish) | |

un/check all:

QuickSearch “Orthologs” tab

QuickSearch

[Human Disease](#) [Expression](#) [Phenotype](#) [GO](#) [References](#)

[Simple](#) **Orthologs** [Protein Domains](#) [Gene Groups](#) [Data Class](#)

Input:

Enter gene symbol(s) or ID(s), separated by spaces

Species:

Gene(s):

Search

YouTube

Output:

MODEL ORGANISMS (via [DIOPT](#)) [instead [search OrthoDB orthology groups](#)]

- | | |
|--|---|
| <input checked="" type="checkbox"/> <i>H. sapiens</i> (Human) | <input checked="" type="checkbox"/> <i>D. melanogaster</i> (Fruit fly) |
| <input checked="" type="checkbox"/> <i>R. norvegicus</i> (Norway rat) | <input checked="" type="checkbox"/> <i>C. elegans</i> (Nematode, roundworm) |
| <input checked="" type="checkbox"/> <i>M. musculus</i> (Laboratory mouse) | <input checked="" type="checkbox"/> <i>S. cerevisiae</i> (Brewer's yeast) |
| <input checked="" type="checkbox"/> <i>X. tropicalis</i> (Western clawed frog) | <input checked="" type="checkbox"/> <i>S. pombe</i> (Fission yeast) |
| <input checked="" type="checkbox"/> <i>D. rerio</i> (Zebrafish) | |

un/check all:

QuickSearch “Orthologs” tab

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Human Disease Expression Phenotype GO References

Simple **Orthologs** Protein Domains Gene Groups Data Class

Input:

Enter gene symbol(s) or ID(s), separated by spaces

Search

Species: *D. melanogaster* ▾

Gene(s): e.g. Cdk1, CG5363, FBgn0004106, 34411



Output:

MODEL ORGANISMS [via DIOPT](#) [instead search OrthoDB orthology groups]

- | | |
|--|---|
| <input checked="" type="checkbox"/> <i>H. sapiens</i> (Human) | <input checked="" type="checkbox"/> <i>D. melanogaster</i> (Fruit fly) |
| <input checked="" type="checkbox"/> <i>R. norvegicus</i> (Norway rat) | <input checked="" type="checkbox"/> <i>C. elegans</i> (Nematode, roundworm) |
| <input checked="" type="checkbox"/> <i>M. musculus</i> (Laboratory mouse) | <input checked="" type="checkbox"/> <i>S. cerevisiae</i> (Brewer's yeast) |
| <input checked="" type="checkbox"/> <i>X. tropicalis</i> (Western clawed frog) | <input checked="" type="checkbox"/> <i>S. pombe</i> (Fission yeast) |
| <input checked="" type="checkbox"/> <i>D. rerio</i> (Zebrafish) | |

un/check all:

Search with a human gene

QuickSearch

[Human Disease](#) [Expression](#) [Phenotype](#) [GO](#) [References](#)

[Simple](#) **Orthologs** [Protein Domains](#) [Gene Groups](#) [Data Class](#)

Input:

Enter gene symbol(s) or ID(s), separated by spaces

Search

Species:

H. sapiens

Gene(s):

UBE3A

You
Tube

Output:

MODEL ORGANISMS (via [DIOPT](#))

- | | |
|--|---|
| <input checked="" type="checkbox"/> <i>H. sapiens</i> (Human) | <input checked="" type="checkbox"/> <i>D. melanogaster</i> (Fruit fly) |
| <input type="checkbox"/> <i>R. norvegicus</i> (Norway rat) | <input checked="" type="checkbox"/> <i>C. elegans</i> (Nematode, roundworm) |
| <input checked="" type="checkbox"/> <i>M. musculus</i> (Laboratory mouse) | <input checked="" type="checkbox"/> <i>S. cerevisiae</i> (Brewer's yeast) |
| <input checked="" type="checkbox"/> <i>X. tropicalis</i> (Western clawed frog) | <input type="checkbox"/> <i>S. pombe</i> (Fission yeast) |
| <input checked="" type="checkbox"/> <i>D. rerio</i> (Zebrafish) | |

un/check all:

Ortholog query output: human UBE3A

Search Term: **UBE3A** Species: *Homo sapiens* (Human) Gene: **UBE3A** Reports: [NCBI](#) [Ensembl](#) [HGNC](#) [OMIM](#) [Transgene In Fly](#)

Ortholog Gene	Ortholog Gene Reports	Via DIOPT (v6.0)			Source	Align
		Score	Best Score	Best Rev Score		
<i>Mus musculus</i> (Laboratory mouse)						
Ube3a	NCBI MGI	12 of 12	Yes	Yes (+)	Compara, eggNOG, HGNC, Homologene, Inparanoid, Isobase, OMA, orthoMCL, Panther, Phylome, RoundUp, TreeFam	(+)
Hectd2	NCBI MGI	2 of 12	No	No (+)	eggNOG, orthoMCL	(+)
Herc3	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
Herc4	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
Herc6	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
<i>Xenopus tropicalis</i> (Western clawed frog)						
ube3a	NCBI Xenbase	6 of 7	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, Phylome, TreeFam	(+)
herc3	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
herc4	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
herc6	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
<i>Danio rerio</i> (Zebrafish)						
ube3a	NCBI ZFIN	9 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, orthoMCL, Panther, Phylome, TreeFam, ZFIN	(+)
hectd2	NCBI ZFIN	2 of 11	No	No (+)	eggNOG, orthoMCL	(+)
herc3	NCBI ZFIN	1 of 11	No	No (+)	eggNOG	(+)
herc4	NCBI ZFIN	1 of 11	No	No (+)	eggNOG	(+)
<i>Drosophila melanogaster</i> (Fruit fly)						
Ube3a	NCBI FlyBase	10 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, Inparanoid, OMA, orthoMCL, Panther, Phylome, RoundUp, TreeFam	(+)
Sherpa	NCBI FlyBase	1 of 11	No	No (+)	eggNOG	(+)
<i>Caenorhabditis elegans</i> (Nematode, roundworm) - no orthologs found						
<i>Saccharomyces cerevisiae</i> (Brewer's yeast)						
HUL4	NCBI SGD	4 of 10	Yes	No (+)	Compara, eggNOG, orthoMCL, Panther	(+)

Ortholog query output: human UBE3A

Search Term: UBE3A Species: <i>Homo sapiens</i> (Human) Gene: UBE3A Reports: NCBI Ensembl HGNC OMIM Transcript					
Ortholog Gene	Ortholog Gene Reports	Via DIOPT (v6.0)			
		Score	Best Score	Best Rev Score	Source
<i>Mus musculus</i> (Laboratory mouse)					
Ube3a	NCBI MGI	12 of 12	Yes	Yes (+)	Compara, eggNOG, HGNC, Homologene, Inparanoid, Isobase, OMA, orthoMCL, Panther, Phylome, RoundUp, TreeFam
Hectd2	NCBI MGI	2 of 12	No	No (+)	eggNOG, orthoMCL
Herc3	NCBI MGI	1 of 12	No	No (+)	eggNOG
Herc4	NCBI MGI	1 of 12	No	No (+)	eggNOG
Herc6	NCBI MGI	1 of 12	No	No (+)	eggNOG
<i>Xenopus tropicalis</i> (Western clawed frog)					
ube3a	NCBI Xenbase	6 of 7	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, Phylome, TreeFam
herc3	NCBI Xenbase	1 of 7	No	No (+)	eggNOG
herc4	NCBI Xenbase	1 of 7	No	No (+)	eggNOG
herc6	NCBI Xenbase	1 of 7	No	No (+)	eggNOG
<i>Danio rerio</i> (Zebrafish)					
ube3a	NCBI ZFIN	9 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, orthoMCL, Panther, Phylome, TreeFam, ZFIN
hctd2	NCBI ZFIN	2 of 11	No	No (+)	eggNOG, orthoMCL
herc3	NCBI ZFIN	1 of 11	No	No (+)	eggNOG
herc4	NCBI ZFIN	1 of 11	No	No (+)	eggNOG

Ortholog query output: human UBE3A

Search Term: **UBE3A** Species: *Homo sapiens* (Human) Gene: **UBE3A** Reports: [NCBI](#) [Ensembl](#) [HGNC](#) [OMIM](#) [Transgene In Fly](#)

Ortholog Gene	Ortholog Gene Reports	Via DIOPT (v6.0)			Source	Align
		Score	Best Score	Best Rev Score		
<i>Mus musculus</i> (Laboratory mouse)						
Ube3a	NCBI MGI	12 of 12	Yes	Yes (+)	Compara, eggNOG, HGNC, Homologene, Inparanoid, Isobase, OMA, orthoMCL, Panther, Phylome, RoundUp, TreeFam	(+)
Hectd2	NCBI MGI	2 of 12	No	No (+)	eggNOG, orthoMCL	(+)
Herc3	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
Herc4	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
Herc6	NCBI MGI	1 of 12	No	No (+)	eggNOG	(+)
<i>Xenopus tropicalis</i> (Western clawed frog)						
ube3a	NCBI Xenbase	6 of 7	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, Phylome, TreeFam	(+)
herc3	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
herc4	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
herc6	NCBI Xenbase	1 of 7	No	No (+)	eggNOG	(+)
<i>Danio rerio</i> (Zebrafish)						
ube3a	NCBI ZFIN	9 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, OMA, orthoMCL, Panther, Phylome, TreeFam, ZFIN	(+)
hectd2	NCBI ZFIN	2 of 11	No	No (+)	eggNOG, orthoMCL	(+)
herc3	NCBI ZFIN	1 of 11	No	No (+)	eggNOG	(+)
herc4	NCBI ZFIN	1 of 11	No	No (+)	eggNOG	(+)
<i>Drosophila melanogaster</i> (Fruit fly)						
Ube3a	NCBI FlyBase	10 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, Inparanoid, OMA, orthoMCL, Panther, Phylome, RoundUp, TreeFam	(+)
Sherpa	NCBI FlyBase	1 of 11	No	No (+)	eggNOG	(+)
<i>Caenorhabditis elegans</i> (Nematode, roundworm) - no orthologs found						
<i>Saccharomyces cerevisiae</i> (Brewer's yeast)						
HUL4	NCBI SGD	4 of 10	Yes	No (+)	Compara, eggNOG, orthoMCL, Panther	(+)

Ube3a gene report

General Information

Symbol	DmelUbe3a	Species	<i>D. melanogaster</i>
Name	Ubiquitin protein ligase E3A	Annotation symbol	CG6190
Feature type	protein_coding_gene	FlyBase ID	FBgn0061469
Gene Model Status	Current	Stock availability	7 publicly available
Also Known As	dube3a, As		



Interactions and Pathways

Expression Data

Alleles and Phenotypes

Orthologs ←

Human Orthologs (via DIOPT v6) (5)

Model Organism Orthologs (via DIOPT v6) (31) ←

Orthologs (via OrthoDB v7) (34)

Human Disease Model Data

Gene Model and Products

Genomic Location and Detailed Mapping Data

Stocks and Reagents

Other Information

External Crossreferences and Linkouts

Synonyms and Secondary IDs (19)

References (63)

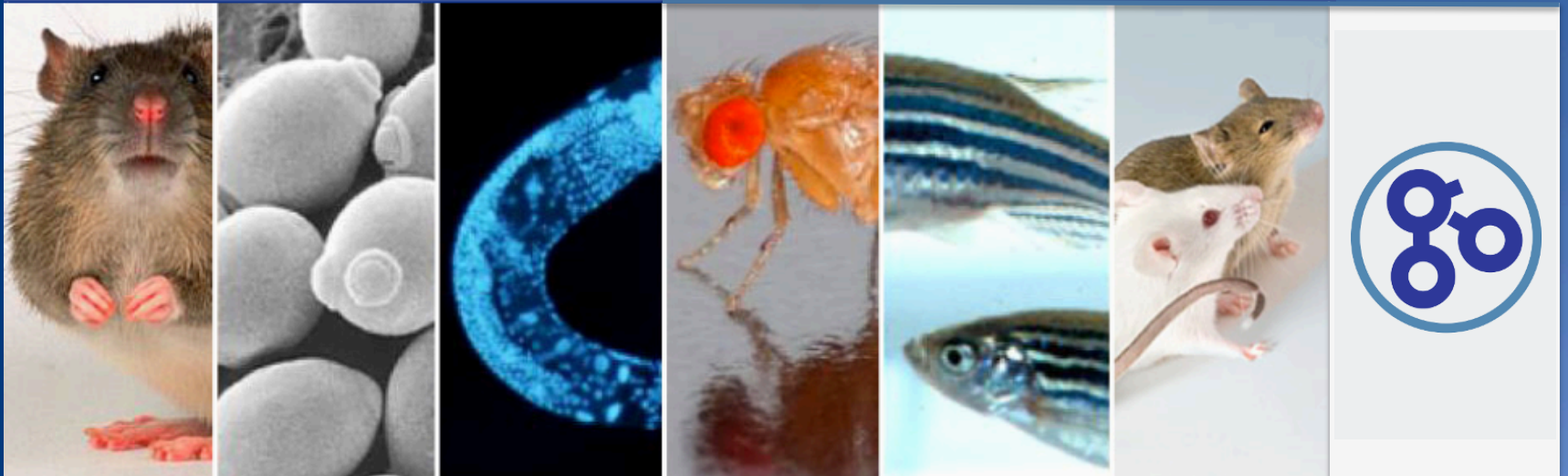
Ortholog table in Ube3a gene report

Model Organism Orthologs (via DIOPT v6) (31)																				
Homo sapiens (Human)																				
Species\Gene Symbol	NCBI Gene	Score	Best score	Best reverse score	Source	Compara	eggNOG	Homologene	Inparanoid	Isobase	OMA	OrthoDB	orthoMCL	Panther	Phylome	RoundUp	TreeFam	ZFIN	Align	Transgene in Fly
Hsap\UBE3A	7337	10 of 11	Yes	Yes		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		Yes
Hsap\HECTD2	143279	2 of 11	No	Yes		<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Hsap\HERC6	55008	1 of 11	No	No		<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Hsap\HERC4	26091	1 of 11	No	No		<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Xenopus tropicalis (Western clawed frog)																				
Species\Gene Symbol	NCBI Gene	Score	Best score	Best reverse score	Source	Compara	eggNOG	Homologene	Inparanoid	Isobase	OMA	OrthoDB	orthoMCL	Panther	Phylome	RoundUp	TreeFam	ZFIN	Align	Transgene in Fly
Xtro\ube3a	407881	7 of 7	Yes	Yes		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Xtro\herc6Xtro\herc6	100487734	1 of 7	No	No		<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Xtro\herc4	100036667	1 of 7	No	No		<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Saccharomyces cerevisiae (Brewer's yeast)																				
Species\Gene Symbol	NCBI Gene	Score	Best score	Best reverse score	Source	Compara	eggNOG	Homologene	Inparanoid	Isobase	OMA	OrthoDB	orthoMCL	Panther	Phylome	RoundUp	TreeFam	ZFIN	Align	Transgene in Fly
Scer\HUL4	853494	5 of 10	Yes	Yes		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

Cross-MOD resources

- Links to MOD gene reports from DIOPT/
FlyBase ortholog search
- Alliance of Genome Resources (AGR)
- Links from FlyBase to two new resources:
 - Gene2Function
 - MARRVEL

COMING SOON:
Alliance of
Genome
Resources (AGR)



AGR proposed gene report

Common report format for all
(model organisms plus human)

GAK











Symbol	GAK
Name	cyclin G associated kinase
Synonyms	DNAJC26, auxilin-2, FLJ40395, FLJ16629, DNAJ26, OTTHUMP00000217314, OTTHUMP00000147520, MGC99654, cyclin-G-associated kinase
Biotype	protein coding gene
Description	In all eukaryotes, the cell cycle is governed by cyclin-dependent protein kinases (CDKs), whose activities are regulated by cyclins and CDK inhibitors in a diverse array of mechanisms that involve the control of phosphorylation and dephosphorylation of Ser,
Genomic Resources	Ensembl: ENSG00000178950 NCBIGene: 2580 UniProtKB: B4DS37 UniProtKB: D6RAQ7

Species	<i>Homo sapiens</i>
Primary Source	HGNC:4113

AGR gene report: ortholog table

Simplifies navigation between species

Orthology

Species	Gene symbol	Score	Best score	Best reverse score	Method	Align
					        R  	
Homo sapiens	GAK [NCBI]	11 of 11	Yes	Yes	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>	View
Homo sapiens	DNAJC6 [NCBI]	7 of 11	No	Yes	<input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>	View
Mus musculus	Gak [NCBI]	11 of 11	Yes	Yes	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>	View
Rattus norvegicus	Gak [NCBI]	8 of 8	Yes	Yes	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>	View
Mus musculus	Dnajc6 [NCBI]	7 of 11	No	Yes	<input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>	View
Danio rerio	Gak [NCBI]	7 of 11	Yes	Yes	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>	View
Danio rerio	Dnajc6 [NCBI]	5 of 11	No	Yes	<input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	View
Caenorhabditis elegans	tag-257 [NCBI]	5 of 11	Yes	Yes	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>	View
Caenorhabditis elegans	dnj-25 [NCBI]	5 of 11	No	Yes	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	View
Saccharomyces cerevisiae	SWA2 [NCBI]	2 of 11	Yes	Yes	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	View

Cross-MOD resources

- Links to MOD gene reports from DIOPT/
FlyBase ortholog search
- Alliance of Genome Resources (AGR)
- Links from FlyBase to two new resources:
 - Gene2Function
 - MARRVEL
- **Feedback welcome!**

New links from the home page: G2F and MARRVEL

Multi-species mining:



Gene 2 Function Mar 28, 2017.

The DRSC and FlyBase announce the release of Gene2Function (G2F). The primary goal of G2F is to facilitate the development of new hypotheses regarding the function of a given gene based on what is known about the function of orthologs of that gene in other species.

Gene2Function



<http://www.gene2function.org>

Same species that are included in DIOPT

Search By Gene

Species

Mouse

Gene

Ube3a

Search By Gene

Search By Disease

Disease

Disease Name

Search By Disease

- View orthologs & alignments
- View publications
- Connect to GO terms, PPIs, and more

- Refine search
- View associated genes
- Connect to gene info

Gene2Function gene output is based on the DIOPT ortholog table

Gene ID	Symbol	Human Disease Terms	Species Name	Species specific gene ID	Species specific database	DIOPT Score	Best Score	Best Score reverse	Confidence
7337	UBE3A	4	Human (Homo sapiens)	12496	HGNC	12	Yes	Yes	high
22215	Ube3a	NA	Mouse (Mus musculus)	105098	MGI		-	-	
361585	Ube3a	NA	Rat (Rattus norvegicus)	1306361	RGD	10	Yes	Yes	high
407881	ube3a	NA	Western clawed frog (Xenopus tropicalis)	XB-GENE-948557	Xenbase	7	Yes	Yes	high
792398	ube3a	NA	Zebrafish (Danio rerio)	ZDB-GENE-041114-190	ZFIN	10	Yes	Yes	high
39266	Ube3a	NA	Fly (Drosophila melanogaster)	FBgn0061469	FLYBASE	11	Yes	Yes	high



G2F gene output: extended ortholog table

- Provides links to protein function data and related info
- Includes model organisms plus human

Symbol	Human Disease Terms	Species Name	Publication Count	GO Component Counts	GO Function Counts	GO Process Counts	Protein Interaction Counts	Protein Alignment
UBE3A	4	Human (Homo sapiens)	203	0	3	5	161	[+] pairwise alignment
Ube3a	NA	Mouse (Mus musculus)	130	2	3	9	3	[+] multiple seq alignment of best orthologs
Ube3a	NA	Rat (Rattus norvegicus)	4	0	0	0	1	[+] pairwise alignment
ube3a	NA	Western clawed frog (Xenopus tropicalis)	2	0	0	0	0	[+] pairwise alignment
ube3a	NA	Zebrafish (Danio rerio)	2	0	0	0	0	[+] pairwise alignment
Ube3a	NA	Fly (Drosophila melanogaster)	33	1	1	11	1	[+] pairwise alignment

G2F: Human disease terms include data from OMIM and GWAS Catalog

Symbol	Human Disease Terms	Species Name	Publication Count	GO Component Counts	GO Function Counts	GO Process Counts	Protein Interaction Counts	Protein Alignment
UBE3A	4	Human (Homo sapiens)	203	0	3	5	161	[+] pairwise alignment
Ube3a	NA	Mouse (Mus musculus)	130	2	3	9	3	[+] multiple seq alignment of best orthologs
Ube3a	NA	Rat (Rattus norvegicus)	4	0	0	0	1	[+] pairwise alignment
ube3a	NA	Western clawed frog (Xenopus tropicalis)	2	0	0	0	0	[+] pairwise alignment
ube3a	NA	Zebrafish (Danio rerio)	2	0	0	0	0	[+] pairwise alignment
Ube3a	NA	Fly (Drosophila melanogaster)	33	1	1	11	1	[+] pairwise alignment

MARRVEL (<http://marrvel.org/>)

Model organism **A**ggregated **R**esources for **R**are **V**ariant **E**xp**L**oration

- Human gene reports: compilation of data from multiple sources; information on protein domains
- Emphasis on disease, natural variants, and variants associated with disease



MARRVEL β

? Human Gene
Symbol:

Please use official HGNC Gene Symbol. E.g. FBXL4

Human Variant
(hg19):

E.g. 6:99365567 T>C

Example: [6:99365567 T>C / FBXL4](#) or [6:99365567 T>C](#) or [FBXL4](#)

MARRVEL gene page includes model organisms in the Gene Function Table

Gene Function Table
UBE3A

Show only best DIOPT v6 score gene

+ multi-protein sequence alignments

	Homolog	DIOPT Score	Expression	Molecular function	Cellular component	Biological process
Human	UBE3A PubMed	NA	<ul style="list-style-type: none"> adrenal gland appendix breast bronchus 	<ul style="list-style-type: none"> ubiquitin-protein transferase activity 	No term based on experiment	<ul style="list-style-type: none"> positive regulation of protein ubiquitination regulation of circadian rhythm protein autoubiquitination
Rat	Ube3a PubMed	10	Show all (10)	No term based on experiment	No term based on experiment	No term based on experiment
Mouse	Ube3a PubMed	12	<ul style="list-style-type: none"> embryo ectoderm nervous system visual system Open on MGI	<ul style="list-style-type: none"> transcription coactivator activity protein binding ubiquitin protein ligase activity 	<ul style="list-style-type: none"> nucleus cytosol 	<ul style="list-style-type: none"> ovarian follicle development ubiquitin-dependent protein catabolic process positive regulation of phosphatidylinositol 3-kinase signaling
Drosophila	Ube3a PubMed	10	<ul style="list-style-type: none"> Eye Brain Thoracic-Abdominal Ganglion Malpighian Tubules 	<ul style="list-style-type: none"> ubiquitin protein ligase activity 	<ul style="list-style-type: none"> cell cortex cytoplasm 	<ul style="list-style-type: none"> circadian rhythm dendrite morphogenesis locomotion long-term memory

MARRVEL by default shows only best hit or hits

Gene Function Table ×

UBE3A

Show only best DIOPT score gene

	Homolog	DIOPT Score	Expression	Molecular function	Cellular component	Biological process
Human	UBE3A PubMed	NA	<ul style="list-style-type: none"> adrenal gland appendix breast bronchus 	<ul style="list-style-type: none"> ubiquitin-protein transferase activity 	No term based on experiment	<ul style="list-style-type: none"> positive regulation of protein ubiquitination regulation of circadian rhythm protein autoubiquitination
Rat	Ube3a PubMed	10	Show all (10)	No term based on experiment	No term based on experiment	No term based on experiment
Mouse	Ube3a PubMed	12	<ul style="list-style-type: none"> embryo ectoderm nervous system visual system Open on MGI	<ul style="list-style-type: none"> transcription coactivator activity protein binding ubiquitin protein ligase activity 	<ul style="list-style-type: none"> nucleus cytosol 	<ul style="list-style-type: none"> ovarian follicle development ubiquitin-dependent protein catabolic process positive regulation of phosphatidylinositol 3-kinase signaling
Drosophila	Ube3a PubMed	10	<ul style="list-style-type: none"> Eye Brain Thoracic-Abdominal Ganglion Malpighian Tubules 	<ul style="list-style-type: none"> ubiquitin protein ligase activity 	<ul style="list-style-type: none"> cell cortex cytoplasm 	<ul style="list-style-type: none"> circadian rhythm dendrite morphogenesis locomotion long-term memory

DIOPT: a note concerning filters

- FlyBase – no filtering (yet)
- DIOPT – removes hits of score = 1* (can override)
- Gene2Function – removes hits = 1 or 2*
- MARRVEL – shows only best hit or hits (can override)
- Alliance – will filter

* Unless no higher score

Good example: human **ACTB**

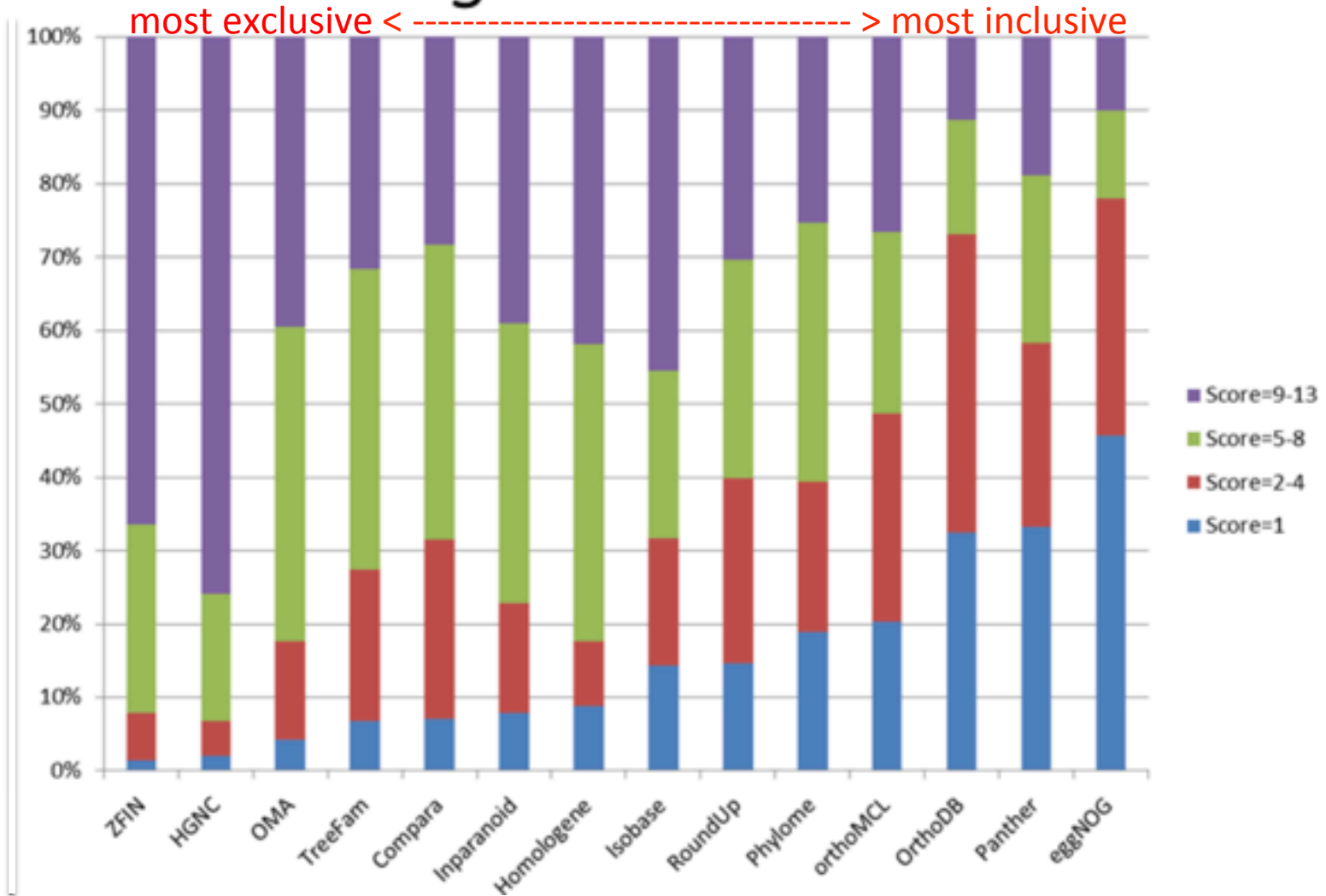
Thank you!

Fly Gdap1 has two high-scoring human orthologs

Search Term: Gdap1 Species: <i>Drosophila melanogaster</i> (Fruit fly) Gene: Gdap1 Reports: NCBI FlyBase					
Ortholog Gene	Ortholog Gene Reports	Via DIOPT (v6.0)			
		Score	Best Score	Best Rev Score	Source
<i>Homo sapiens</i> (Human)					
GDAP1	NCBI Ensembl HGNC OMIM	10 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, Inparanoid, OMA, OrthoDB, orthoMCL, Phylome, RoundUp, TreeFam
GDAP1L1	NCBI Ensembl HGNC	7 of 11	No	Yes (+)	Compara, eggNOG, Inparanoid, OrthoDB, Phylome, RoundUp, TreeFam
EEF1G	NCBI Ensembl HGNC OMIM	1 of 11	No	No (+)	Panther
GSTT2	NCBI Ensembl HGNC OMIM	1 of 11	No	No (+)	Phylome
<i>Mus musculus</i> (Laboratory mouse)					
Gdap1	NCBI MGI	10 of 11	Yes	Yes (+)	Compara, eggNOG, Homologene, Inparanoid, OMA, OrthoDB, orthoMCL, Phylome, RoundUp, TreeFam
Gdap1l1	NCBI MGI	6 of 11	No	Yes (+)	Compara, eggNOG, Inparanoid, Phylome, RoundUp, TreeFam
Eef1g	NCBI MGI	1 of 11	No	No (+)	Panther
Gstt2	NCBI MGI	1 of 11	No	No (+)	Phylome

DIOPT Documentation

Ortholog score distributions



Benchmarking of ortholog algorithms

- Quest for Orthologs: Altenhoff *et al.* (2016) Standardized benchmarking in the quest for orthologs. *Nat. Methods* 13:425-30.
- DIOPT: Hu *et al.* (2011) An integrative approach to ortholog prediction for disease-focused and other functional studies. *BMC Bioinformatics* 12:357.