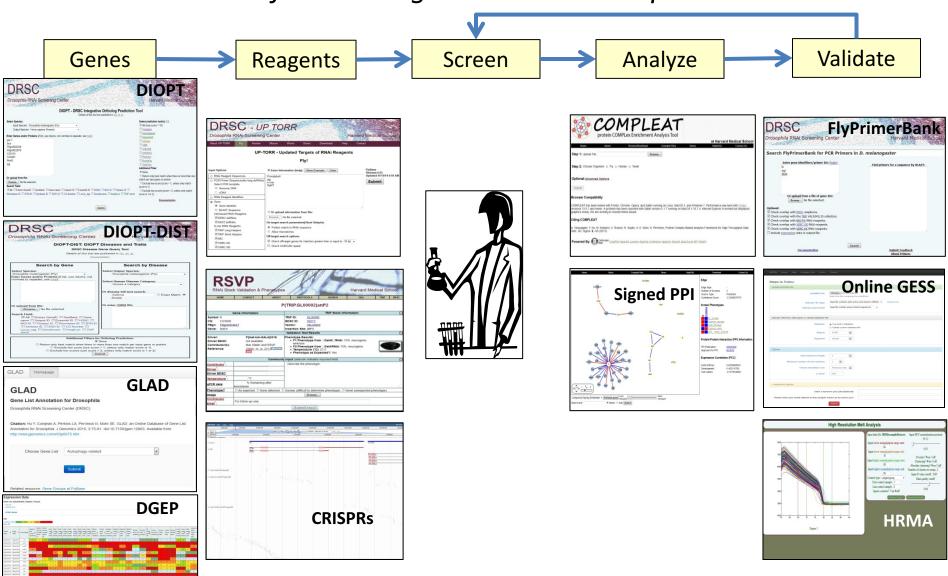
DRSC/TRiP Informatics Tools for Functional Genomics Studies - 2018 Update

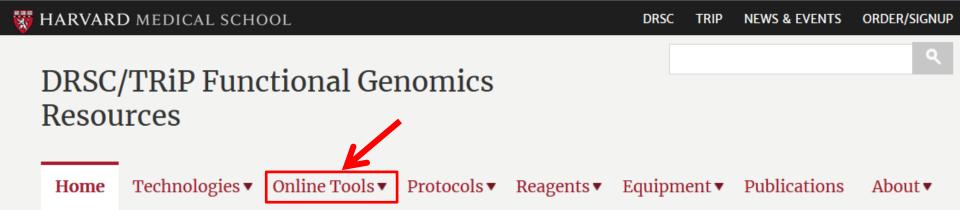
Claire Yanhui Hu April 13th 2018

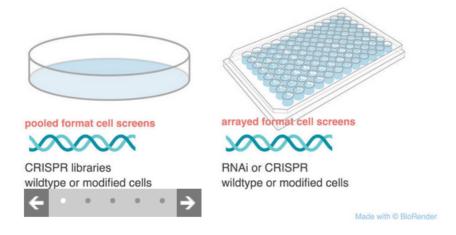
DRSC/TRiP Informatics Tools

GSA functional genomics workshop 2015



New Look of DRSC/TRiP Web Site





DRSC/TRiP Functional Genomics Resources

The DRSC/TRIP-FGR site joins the *Drosophila* RNAi Screening Center (DRSC) and Transgenic RNAi Project (TRiP). Check out our *Technologies*, *Online Tools*, and other pages to learn more.

Quick *direct* links to our most popular online search tools:

- DIOPT ortholog search tool
- Gene Lookup search of DRSC/TRiP reagents, data, etc.
- UP-TORR batch search all public fly RNAi reagents
- RSVP search of in vivo fly RNAi data
- Find CRISPR gRNA search
- <u>Search and Nominate</u> genes for TRiP-CRISPR fly stocks
- Nominate genes for CRIMIC production

http://www.flyrnai.org -> https://fgr.hms.harvard.edu/

Topics

New features of old tools

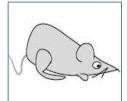
DIOPT

New tools

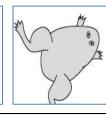
- Gene2Function
- MIST
- iProteinDB

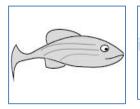


Or unload from file:











User Submission

ZFIN

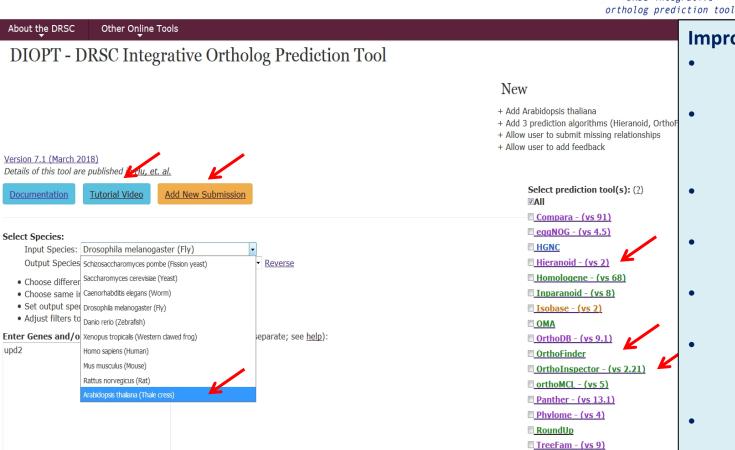




DRSC/TRiP Functional Genomics Resources

10 species, 17 algorithms





Improvements

- Add tutorial video
- Add species eg.
 Arabidopsis
 thaliana
- Add prediction algorithms
- Add paralog search
- Add all species search
- Allow user to submit missing relationships
- Allow user to add feedback

DRSC/TRiP Functional Genomics Resources

(2 of 9)



12)

14)

16)

(1 of 15)

ortholog prediction tool About the DRSC Other Online Tools DIOPT - DRSC Integrative Ortholog Prediction Tool New + Add Arabidopsis thaliana + Add 3 prediction algorithms (Hieranoid, OrthoFinder, OrthoInspector) + Allow user to submit missing relationships + Allow user to add feedback Version 7.1 (March 2018) Details of this tool are published Mu, et. Select prediction tool(s): (?) Tutorial Video **Documentation** Add New Submission ■ Compara - (vs 91) eggNOG - (vs 4.5) Select Species: HGNC Input Species: Drosophila melanogaster (Fly) ■ Hieranoid - (vs 2) Output Species | Schizosaccharomyces pombe (Fission yeast) Reverse Saccharomyces cerevisiae (Yeast) ■ Homologene - (vs 68) · Choose differer • Choose same ir Caenorhabditis elegans (Worm) ■ Inparanoid - (vs 8) • Set output spe Drosophila melanogaster (Fly) ■ Isobase - (vs 2) • Adjust filters to Danio rerio (Zebrafish) ■ OMA Enter Genes and/o Xenopus tropicalis (Western clawed frog) separate; see help): □ OrthoDB - (vs 9.1) upd2 Homo sapiens (Human) Search Fission **Budding** Thale Cress Worm Fly Zebrafish Frog Rat Mouse Human Term yeast yeast ATG1 AT3G61960 atg1 ATG1 unc-51 Atg1 ulk1b ulk1 Ulk1 Ulk1 NA (6 of 9) (9 of 12) (10 of (11 of (13 of 15) (11 of 15) (6 of (14 of (16 of 15) 15) 12) 14) 16) ATP2B1 ACA4, ACA11 SPAPB2B4.04c PMC1 **PMCA** atp2b1a atp2b2 Atp2b1 NA mca-3 Atp2b1 (8 of 9) (10 of 12) (12 of (11 of (13 of 15) (15 of 15) (4 of (11 of (13 ofOr unload from file 15) 15) 12) 14) 16) AT4G24480, Raf **BRAF** lin-45 braf braf Braf Braf NA (14 of 15) (14 of 15) CTR1 (11 of (8 of (9 of (14 of (2 of 9)15) 12) 14) 16) BRCA1 BARD1, SPCC548.05c CBF2 brc-1 CG10916, Sce, nopo, lnx1, lnx2b, rnf2, si:ch211-165g14.1, Brca1 Brca1 NA brca1 BRCA1 (1 of 12) (1 of (3 of CG44271, CG5098 bard1, ftr73, LOC101882614 (3 of(13 of (13 of

(1 of 15)

15)

15)



Drosophila Cytokine Unpaired 2 Regulates Physiological Homeostasis by Remotely Controlling Insulin Secretion

Akhila Rajan1,* and Norbert Perrimon1,2,*

¹Department of Genetics

²Howard Hughes Medical Institute

Harvard Medical School, 77 Avenue Louis Pasteur, Boston, MA 02115, USA

*Correspondence: akhila@genetics.med.harvard.edu (A.R.), perrimon@receptor.med.harvard.edu (N.P.)

http://dx.doi.org/10.1016/j.cell.2012.08.019

SUMMARY

In Drosophila, the fat body (FB), a functional analog of the vertebrate adipose tissue, is the nutrient sensor that conveys the nutrient status to the insulin-producing cells (IPCs) in the fly brain to release Drosophila insulin-like peptides (Dilps). Dilp secretion in turn regulates energy balance and promotes systemic growth. We identify Unpaired 2 (Upd2), a protein with similarities to type I cytokines, as a secreted factor produced by the FB in the fed state. When upd2 function is perturbed specifically in the FB, it results in a systemic reduction in growth and alters energy metabolism. Upd2 activates JAK/ STAT signaling in a population of GABAergic neurons that project onto the IPCs. This activation relieves the inhibitory tone of the GABAergic neurons on the IPCs resulting in the secretion of Dilps Strikingly

we find that human Leptin can rescue the *upd2* mutant phenotypes, suggesting that Upd2 is the functional homolog of Leptin.

About the DRSC Other Online Tools

DIOPT - DRSC Integrative Ortholog Prediction Tool

Version 7.1 (March 201

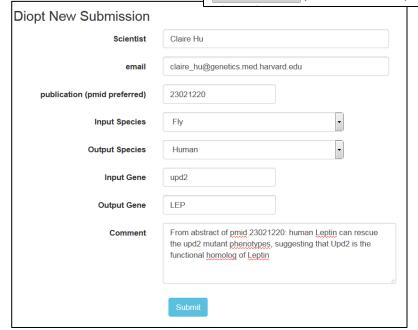
Details of this tool are published in Hu, et. al.

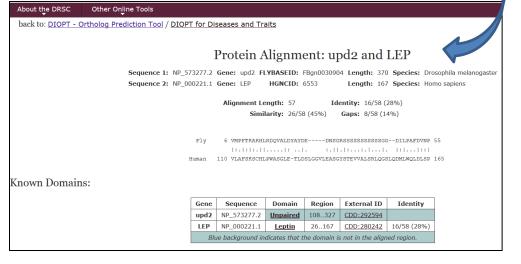
Your 1 query symbols mapped to 1 genes.

Download the Results (as a tab-delimitted text file, named as ".xls").

Input Order	Search Term	Fly GeneID	FlyBaseID	Fly Symbol	Species 2	Human GeneID	Human Species Gene ID	Human Symbol	DIOPT Score	Weighted Score	Rank	Best Score	Best Score Reverse	Prediction Derived From	Alignment & Scores	Feedback
1	upd2	32805	FBgn0030904	upd2	Human	<u>3952</u>	6553	LEP	1	1	low	Yes	Yes	User_Submission	View	(1) <u>Show</u> <u>Add</u>

Download the Results (as a tab-delimitted text file, named as ".xls").





Topics

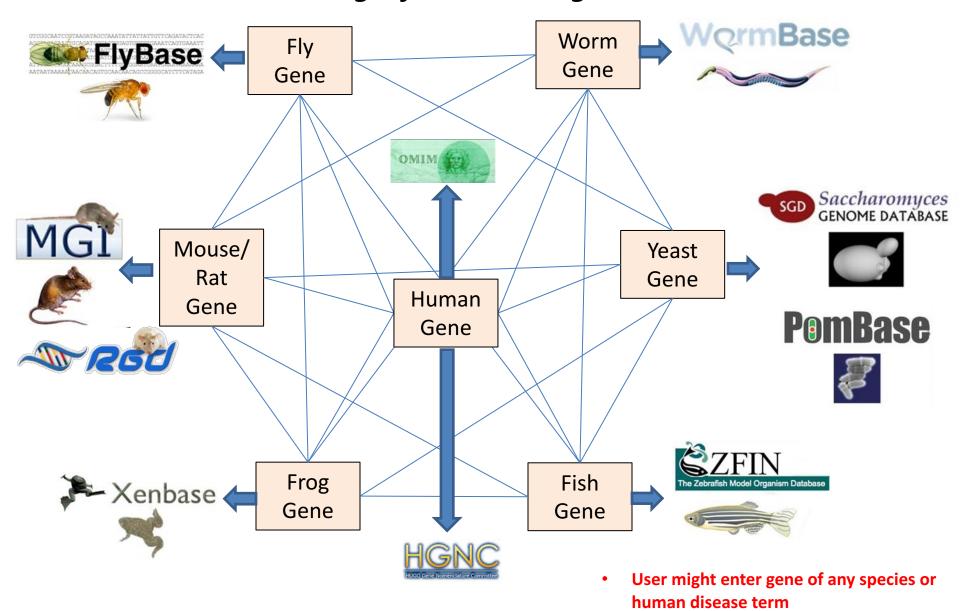
New features of old tools

DIOPT

New tools

- Gene2Function
- MIST
- iProteinDB

Gene2Function: highly integrated system using DIOPT as hub to bring information together

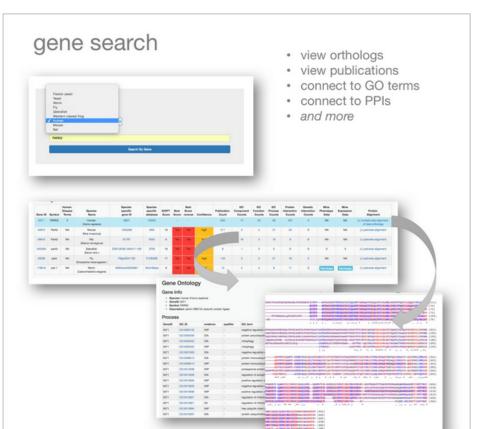


Blue edges are DIOPT relationships

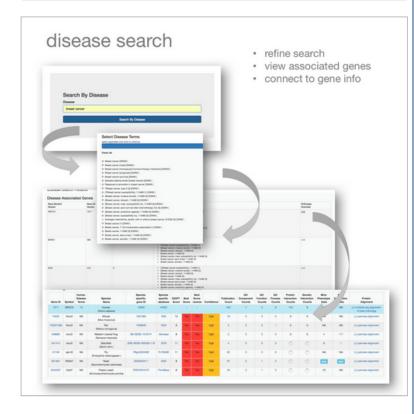
Gene 2. Function

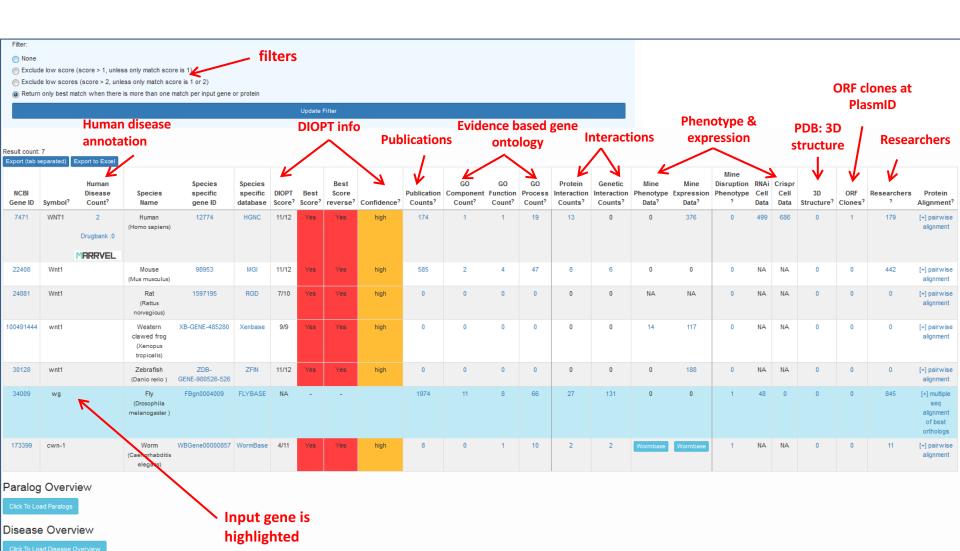






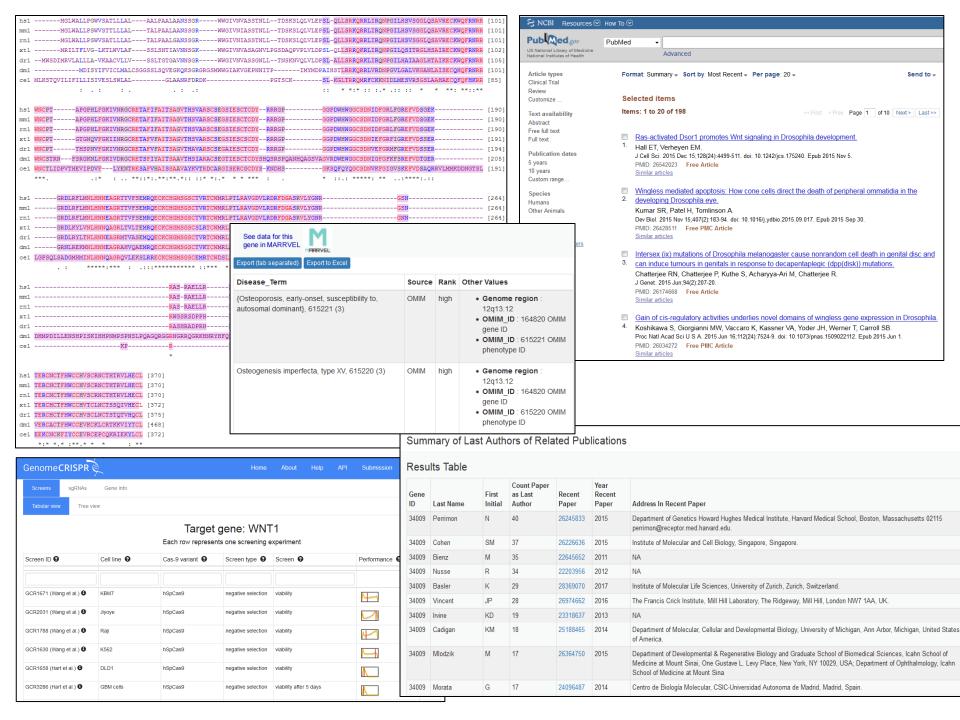
Search by Disease Disease Disease Name Search By Disease





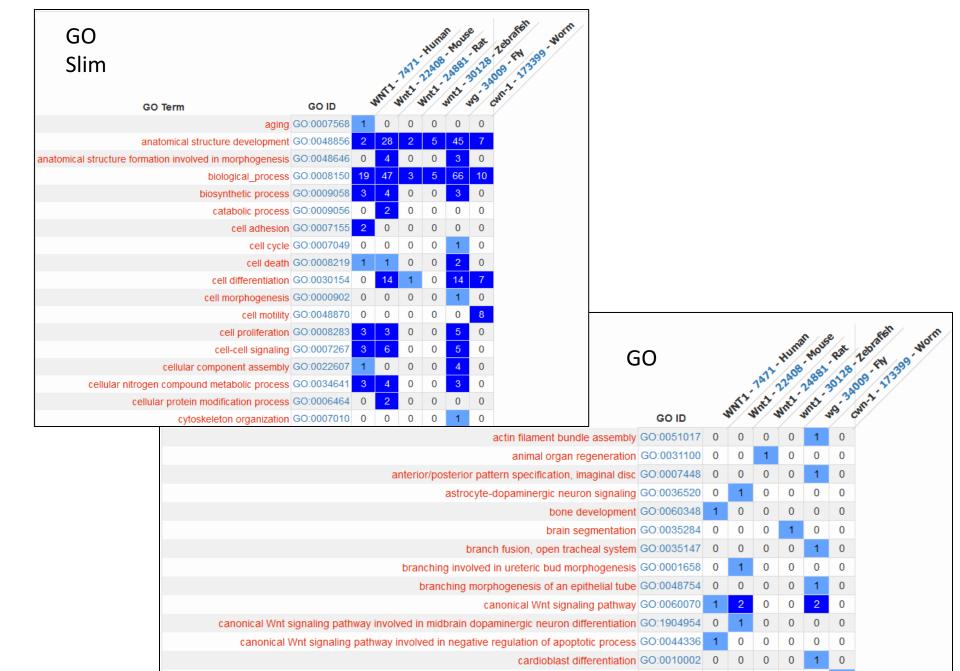
Gene Annotation Overview

Click To Load Go Annotation Overvi



Paralo	g Over	view																						
		Export to Ex	pel .																					
NCBI Gene ID	Symbol?	Human Disease Count?	Species Name	Species specific gene ID	Species specific database	DIOPT Score?	Best Score?	Best Score reverse?	Confidence?	Publication Counts?	GO Component Count?	GO Function Count?	GO Process Count?	Protein Interaction Counts?	Genetic Interaction Counts?	Mine Phenotype Data?	Mine Expression Data?	Mine Disruption Phenotype ?	RNAi Cell Data	Crispr Cell Data	3D Structure?	ORF Clones?	Researchers	Protein Alignment?
34009	wg		Fly (Drosophila melanogaster)	FBgn0284084	FLYBASE	NA	-	-		1974	11	8	66	25	131	1306	0	1	48	0	0	0	832	[+] multiple seq alignment of best orthologs
35975	Wnt2		Fly (Drosophila melanogaster)	FBgn0004360	FLYBASE	4/10	Yes	Yes	high	56	0	1	3	10	6	128	104	0	36	0	0	0	43	[+] pairwise alignment
34010	Wnt6		Fly (Drosophila melanogaster)	FBgn0031902	FLYBASE	4/10	Yes	Yes	high	16	0	0	1	15	2	15	104	0	33	0	0	1	18	[+] pairwise alignment
Click To L																								
Go S	Slim	Vertical						ogene	\$*/															





cell fate specification GO:0001708

cell proliferation in midbrain GO:0033278 0

0

Examples Using G2F

Genev	GWAS Traits	GWAS publications	Publications Gene Ontology	Information about orthologs	Suggested species for follow up
IGSF9B	Schizophrenia	25056061	0/0	higher expression in the nervous system in worm and fly. 34 fly paper and 2 mouse paper. Disruption neuronal phenotype in fly	fly mouse worm
NT5DC2	Bipolar disorder Schizophrenia	21926972 25056061 23974872	0/0	expressed in the nervous system in frog, fish and fly. Partially lethal in fly. 3 fly papers, 2 mouse papers and 1 rat paper	fly mouse fish rat
PPDPF	Prostate cancer	23535732	0/0	fish: GO-cell proliferation. 4 fish papers	fish
COQ10B	Schizophrenia	25056061	0/0	yeast (S.c.): GO-mitochondrion/ubiquinone binding. rich genetic-interaction data in yeast	yeast (sc)
NTN5	Bipolar disorder diarrhoeal disease at age 1 diarrhoeal disease at age 2	21926972 27559109 27559109	0/0	100 fly papers, 36 worm papers and 2 fish papers	fly worm fish
SAMD10	Prostate cancer	23535732	0/0	fly: GO - EGFR pathway; regulates Ras protein signal transduction; compound eye cone cell differentiation; positive regulation of ERK1 and ERK2 cascade. 5 fly papers	fly
ABHD16B	Prostate cancer	23535732	0/0	fly paper: A genetic screen in Drosophila identifying novel components of the hedgehog signaling pathway.	fly
C2orf69	Schizophrenia	23974872	0/0	fly: expressed in the nervous system and rich in PPI data	fly
FAM26D	Pelvic organ prolapse (moderate/severe)	26545240	0/0	worm: disruption phenotype - Uncoordinated locomotion with mutants showing reduced forward velocity, muscle force and power production	worm
ASPHD1	Schizophrenia	25056061	0/0	expressed in nervous system in fish, fly and worm. 5 fly papers	fish fly Worm
ACBD7	Hippocampal sclerosis	25188341	0/0	yeast (S.c.): rich interaction data; GO:chronological cell aging/long-chain fatty acid transport	yeast (sc)
NDUFC2-KCTD14	Pelvic organ prolapse	26545240	0/0	rat: NADH dehydrogenase (ubiquinone) activity; fly: phenotype-partial lethal; mouse-paper (mitochondria)	rat fly mouse

Topics

New features of old tools

DIOPT

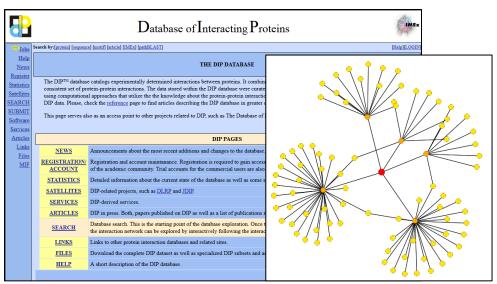
New tools

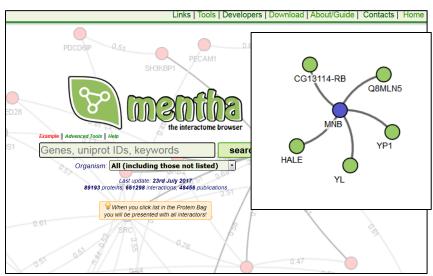
- Gene2Function
- MIST
- iProteinDB

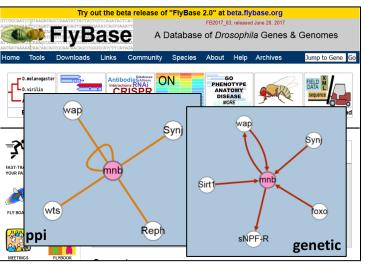
Public resources

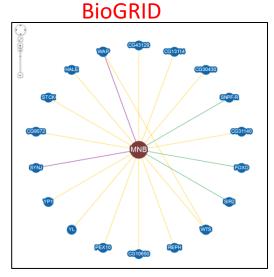
- using Drosophila gene mnb as example

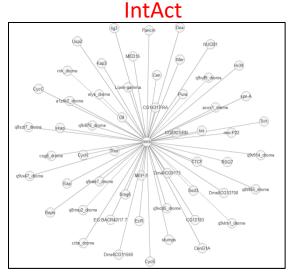
DIP mentha







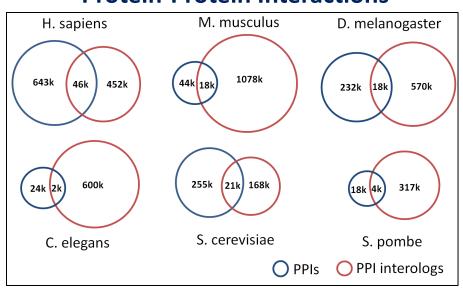




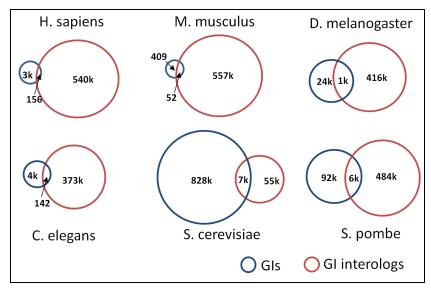
MIST (Molecular Interaction Search Tool)

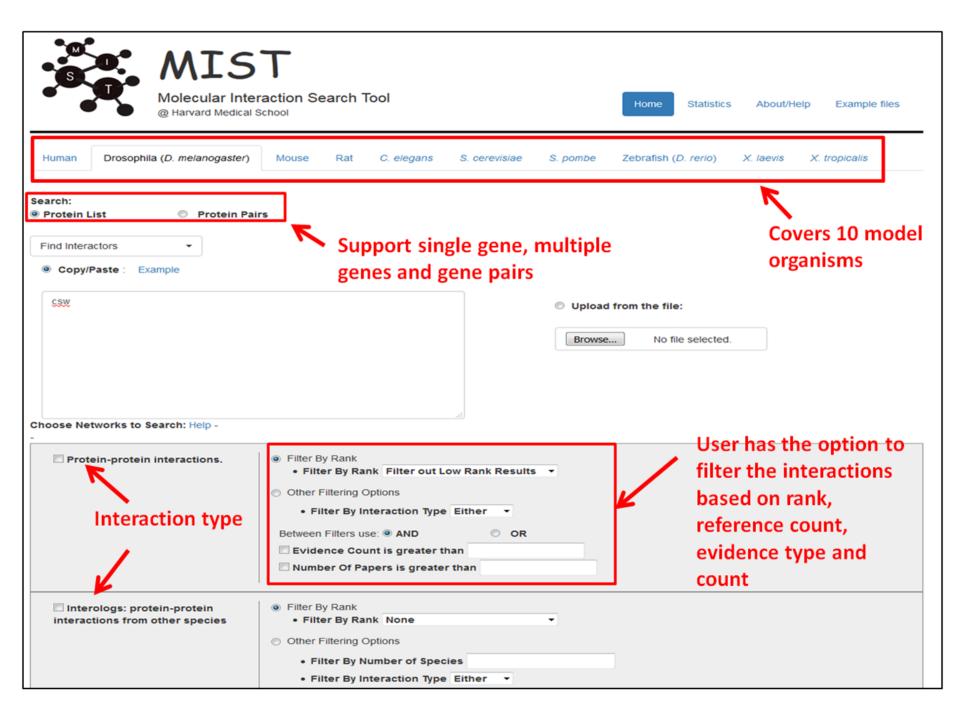
			PPI-	Genetic-	Batch	Pair-		Functional
Data Source	PPI	Genetic	interolog	interolog	search	search	Filters	prediction
DIP	Yes							
DroID	Yes	Yes	Yes					
BioGrid	Yes	Yes						
IntAct	Yes	Yes						
FlyBase	Yes	Yes						
HPRD	Yes							
PomBase	Yes							
mentha	Yes							
HumanMAPK	Yes							
MIST	Yes	Yes	Yes	Yes	Yes	Yes	Yes	

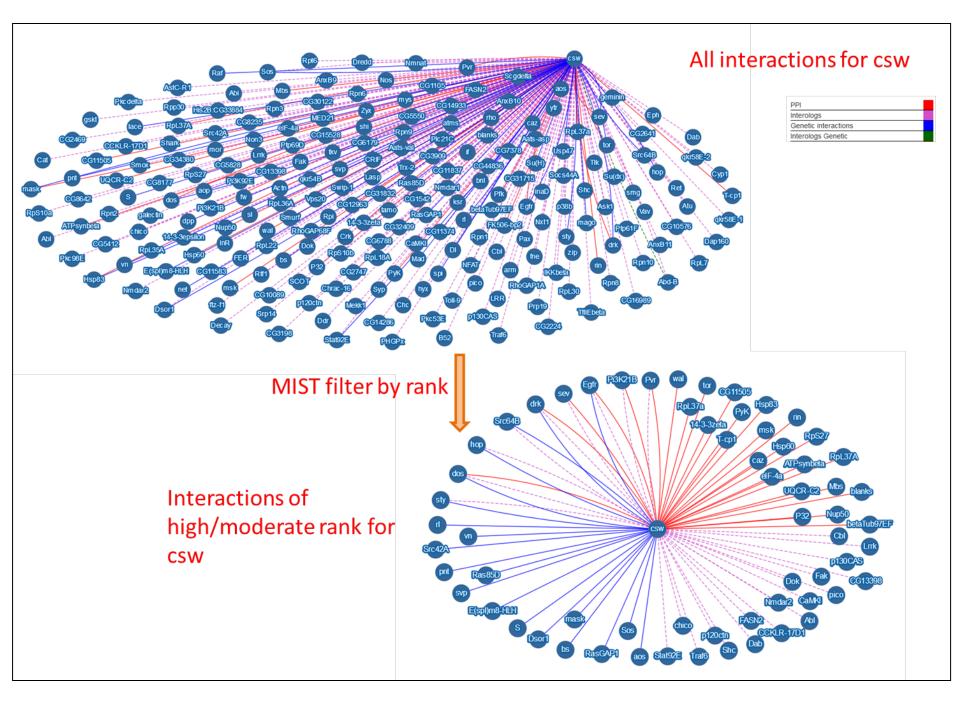
Protein-Protein Interactions

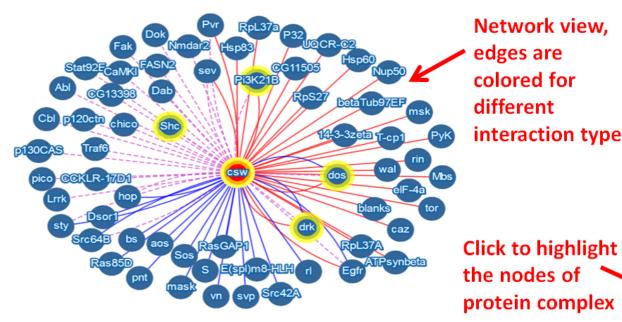


Genetic Interactions









Network view, edges are colored for different interaction type

Interologs Genetic interactions Interologs Genetic Kinase Substrate Phospho Correlation Exp. Correlation Phenotype Correl.

Change Layout -

Search Graph Search

Complex Groups

- p130Cas-ER-alpha-cSrc-kinase- Pl3-kinase p85-subunit complex
- Ternary complex (Abl1, Dok1, Nck1)
- SHC3-GAB1 complex
- · Cd2ap-Fyn complex
- cRET-Shc-Grb2-Gab2-P85Pl3K-Shp2 complex
- . CNK1-SRC-RAF1 complex
- · Shc-Grb2-mSos1 complex, EGF stimulated
- · PLC-gamma-2-SLP-76-Lyn-Grb2 complex
- EGF-Ncore
- ITGA6-ITGB4-FYN complex
- PSD95-FYN-NR2A complex

SI P.76.Chl.Grh?.Sho compley. Fo recentor remme.P1 etimulated

Go to Mapping table

Protein Protein Interactions

Export interaction tables

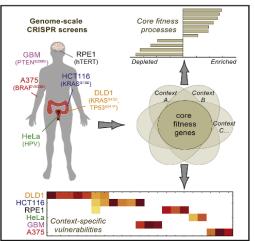
Show 10 →	entries						Sea	arch:	
Entrez GeneID ^ A	Symbol \$	Entrez \$ GeneID B	Symbol B	PubMed \$	† Rank	Source Databases	Direct	 Indirect	
45278	csw	32039	sev	9582352	high	BioGrid, DroID, FlyBase, mentha		western blot(MI:0113) affinity chromatography technology(MI:0004) anti bait coimmunoprecipitation(MI:0006)	_
45278	csw	32045	Hsp60	22028469	high	DroID, FlyBase		anti tag coimmunoprecipitation(MI:0007) peptide massfingerprinting(MI:0082)	
45278	csw	32446	RpL37a	22028469	high	DroID, FlyBase		anti tag coimmunoprecipitation(MI:0007) peptide massfingerprinting(MI:0082)	

List view with detailed information

Cell

High-Resolution CRISPR Screens Reveal Fitness Genes and Genotype-Specific Cancer Liabilities

Graphical Abstract



Authors

Traver Hart, Megha Chandrashekhar, Michael Aregger, ..., Daniel Durocher, Stephane Angers, Jason Moffat

Resource

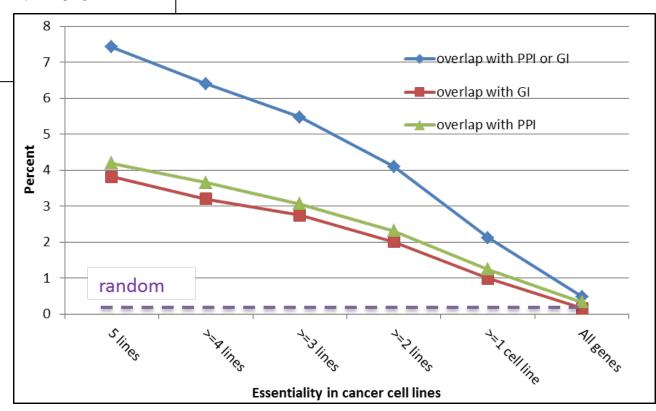
Correspondence

i.moffat@utoronto.ca

In Brief

CRISPR knockout screens for essential genes reveal oncogenic drivers specific to different cancer cell lines as well as unexpected metabolic and signaling dependencies that may guide future therapeutic targeting.

- Higher confident hits in the screens are more likely to interact with each other
- MIST can help set a cutoff as well as helps prioritize hits
- MIST can help generate hypotheses about the biological mechanisms for functionally related genes



Topics

New features of old tools

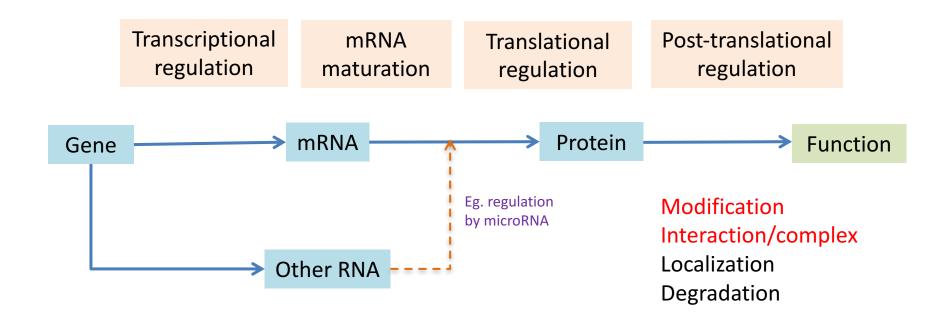
DIOPT

New tools

- Gene2Function
- MIST
- iProteinDB

iProteinDB (<u>i</u>ntegrated <u>Protein</u> <u>D</u>ata<u>B</u>ase)

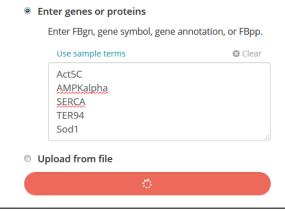
- a resource for post-translational modification



INTEGRATED PROTEIN DATABASE OF PTM FOR DROSOPHILA GENES

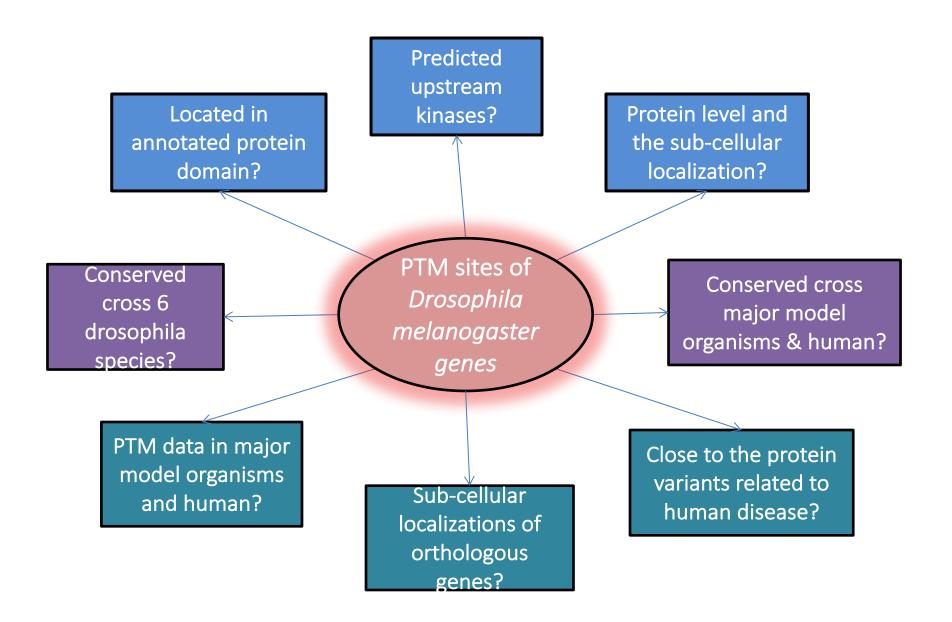
iProteinDB is an online integrated protein database and resource tool for providing information on post-translational modifications (PTMs) in *Drosophila melanogaster*. Comparative analysis is available with 5 other Drosophila species (*D. ananassae*, *D. pseudoobscura*, *D. simulans*, *D. virilis*, and *D. yakuba*), as well as the major model organisms and human.

SFARCH



- Different IDs are supported: gene identifiers (FBgn), gene symbol and protein identifiers (FBpp)
- 2. Batch search is possible

iProteinDB Online Features



iProteinDB will be available soon at DRSC/TRiP website, stay tuned!