Online Bioinformatics Resources at DRSC/TRiP

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June 11th 2020

Boston Area Drosophila Meeting
DRSC/TRiP Functional Genomics Resources

publications & data
view recent publications and data sets

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:

- iProteinDB - post translational modification tool
- 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 pRNA search
- Search and Nominate genes for TRIP-CRISPR fly stocks
- Nominate genes for CRIMIC production

https://fgr.hms.harvard.edu/
https://flyrnai.org/
### Online tools

#### Multi-Species

- **DIOPT**
  - Ortholog search
  - 10 species, 18 algorithms
  - [Demo Video](https://flyrnai.org/)

- **Gene2Function**
  - Orthologs & gene info summaries
  - (orthologs, GO, publications, & more)

- **BioLitMine**
  - Literature mining tool
  - (genes, pathways, people, MeSH terms)

- **MIST**
  - Protein-protein & genetic interactions
  - (multi-source)
  - [Demo Video](https://flyrnai.org/)

- **MARRVEL**
  - Connect human gene variants to ortholog info (multi-source)

- **DIOPT-DIST**
  - Connect disease genes to ortholog info or vice versa (OMIM & GWAS)

#### Fly CRISPR

- **fly sgRNA database/LIMS**
  - Trip sgRNA LIMS
  - Nominate or track
  - Trip-KO & -OE fly stock production

- **Find CRISPRs**
  - Trip sgRNA design with genome view

- **CRISPR 3**
  - Find CRISPRs
  - Find CRISPRs 3
  - Nominate for GDP gene trap fly stocks

- **SNP CRISPR**
  - Design allele-specific sgRNA for major model organisms

#### Fly RNAi

- **UP-TORR**
  - Cell and in vivo RNAi reagent search

- **SnapDragon**
  - Design dsRNAs for fly cell RNAi

- **RSVP Plus**
  - In vivo CRISPR & RNAi phenotype data

- **Screen Summary**
  - Browse DRSC cell RNAi screen data sets

- **GeneLookup**
  - Search DRSC & Trip reagents by gene

- **Trip Batch Query**
  - Make a Trip fly stock list from a g

[https://flyrnai.org/](https://flyrnai.org/)
DIOPT and Gene2Function

Examples of gene focused tools
## DIOPT - DRSC Integrative Ortholog Prediction Tool

### Usage:
101,769 (6 month)

### Model organism Aggregated Resources for Rare Variant Exploration

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<th>FlyBaseID</th>
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[https://www.flyrnai.org/diopt/](https://www.flyrnai.org/diopt/)
Gene2Function

Problem: Lots of info but separate databases, formats, etc.

Solution: Highly integrated and standardized resource

User Input

Connects to orthologs

For any given ortholog:

Gene or Disease

Human

Mouse

Fish

Frog

Fly

Worm

Yeasts

Gene Info

Protein Info

Interactions

Expression

Publications

GO

etc.
Option 1: search by gene

Gene2Function

Search by Gene
- Step 1: select species
- Step 2: enter gene symbol

Search by Disease
- Disease: Breast cancer

Filters
- None
- Exclude low score (score > 1, unless only match score is 1)
- Exclude low scores (score > 2, unless only match score is 1 or 2)
- Return only best match when there is more than one match per input gene or protein

http://www.gene2function.org/
G2F Gene Search Result

- Orthologous genes, conservation, annotation, data and reagents

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<th>Gene ID</th>
<th>Symbol</th>
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Paralog Overview

Disease Overview

Gene Annotation Overview

http://www.gene2function.org/
Link to summary of last authors of all publications

http://www.gene2function.org/
### GO Slim

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<th>GO Term</th>
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<th>Wnt1 - 22488 - Rat</th>
<th>wg1 - 30128 - Zebrafish</th>
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http://www.gene2function.org/
Biological Literature Mining Tool for Human and Model Organisms

Find relationships between genes, MeSH terms, pathways, and people from PubMed literature

Single Term Search

Step 1 - what do you want to find?
Gene to MeSH Terms

Step 2 - select organism
Select organism

Step 3 - enter search term (case-insensitive)
Enter gene name, symbol, or Entrez gene ID

[+] Filter Options

Search

Reset

https://www.flyrnai.org/tools/biolitmine/
## Gene: wg → MeSH Terms

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<th>Descriptor ID</th>
<th>MeSH Categories</th>
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<td>Photoreceptor Cells, Invertebrate</td>
<td>26384554, 23119900, 23025917, 23582303, 24961795, 24781183, 22352597, 22055063, 26004573, 19233440</td>
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<td>Cell Membrane</td>
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<td>Central Nervous System</td>
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[https://www.flyrnai.org/tools/biolitmine/](https://www.flyrnai.org/tools/biolitmine/)
<table>
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<tr>
<th>Descriptor ID</th>
<th>MeSH Categories</th>
<th>MeSH Term</th>
<th>RecentPublications (max. 10)</th>
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<td>Wings, Animal</td>
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<td>272, 142, 99, 95, 82, 71, 58, 58, 57, 53, 53</td>
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</table>
Find CRISPR Tool

Examples of reagent focused tools
**DRSC Find CRISPRs**

To find CRISPRs, enter the gene ID, symbol, or chromosome/location. Then select tracks and click the ‘Submit’ button. This will take you to the JBrowse view. If you want to change tracks or search for another gene in JBrowse, type a gene ID, symbol, or chromosome/location over the coordinates directly in JBrowse. In the upper left-hand corner of the JBrowse view, click “Select Tracks” to change your track selections.

**Version 1.0.2 (Jan 2017)**

**NEW** features:
- Based on Fly Genome Assembly 9
- Added a "seedScore" to each CRISPR (ranging from 12 to 15). This number indicates the uniqueness of the bp-end of a CRISPR excluding PAM. For example, a seed score of 12 means that CRISPR has an unique 12-bp end excluding PAM, whereas a seed score of 13 means that CRISPR has an unique 13-bp end excluding PAM.
- Bug fix: gene names on the mitochondrion genome show more than just "mt".

1. Enter Gene ID, Symbol, or Chromosome:Location
   - esg

2. Select Tracks
   - Targets CDS, No Predicted Off-Targets (preferred)
   - Targets UTR, No Predicted Off-Targets (preferred)
   - Targets Introns, No Predicted Off-Targets (preferred)
   - Targets UTR/CDS Boundary or Intron/Exon Boundary, No Predicted Off-Targets (preferred)
   - Targets Intergenic Region, No Predicted Off-Targets (preferred)
   - Targets CDS, UTR, Boundary, Intron, or Intergenic Region, One to Three Predicted Non-CDS Off-Targets
   - Targets CDS, UTR, Boundary, Intron, or Intergenic Region, One to Three Predicted CDS Off-Targets
   - Targets CDS, UTR, Boundary, Intron, or Intergenic Region, More than Three Predicted Off-Targets

3. Select mismatch stringency for off-targets
   - 5 Mismatches (most stringent)
   - 4 mismatches
   - 3 mismatches (least stringent)

Submit

https://www.flyrnai.org/crispr/
Find CRISPRs

» Search by gene
To find CRISPRs within a gene, enter the gene symbol, select tracks of interest, then click the 'Submit' button.

» Search by sequence
If you have a sequence and want to find nearby CRISPRs, enter the sequence into the textbox to BLAST it before viewing it on JBrowse. If the sequence is a significant hit, it will show as a highlight.

Both search functions will take you to a summary page with a table and embedded JBrowse view. If you want to zoom in or shift the location on the genome, click on “Full-screen view.”

**NEW** features:
- Variant Search (data sources below)
- Summary table of all CRISPRs within gene/location of interest
- Searching by design sequence
- Batch search by gene
- "seedScore" available for each CRISPR (ranging from 12 to 15), indicating its unique bp-end excluding PAM
- Machine Learning based efficiency prediction?
- Updated JBrowse to version 1.13.0
- Updated FlyBase release 6.14.3 to 6.24

Search by gene

1. Enter Gene ID or Symbol

2. Select Tracks
- CDS
- UTR
- Intron
- UTR/CDS Boundary or Intron/Exon Boundary
- Intergenic Region

1-3 Predicted Off-Targets
- CDS, UTR, Boundary, Intron, or Intergenic Region (Non-CDS Off-Targets)
- CDS, UTR, Boundary, Intron, or Intergenic Region (CDS Off-Targets)

>3 Predicted Off-Targets
- CDS, UTR, Boundary, Intron, or Intergenic Region

3. Select Mismatch Stringency
- 5 Mismatches (most stringent)
- 4 mismatches
- 3 mismatches (least stringent)

Search

Batch search by gene

1. Enter one Gene ID or Symbol per line

2. Select Tracks
- No Predicted Off-Targets (preferred)
- CDS
- UTR

https://www.flyrnai.org/crispr3/
Browser: click to view each sgRNA design

Filters: Genome location, Exon name/isoform, Various scores

Table: Info of all relevant sgRNA designs synchronized with browser, Searchable, exportable

https://www.flyrnai.org/crispr3/
# SNP Annotation

<table>
<thead>
<tr>
<th>FBgn</th>
<th>CRISPR Sequence</th>
<th>Housden Efficiency Score</th>
<th>Machine Learning Efficiency Score</th>
<th>Frameshift Score</th>
<th>Seed Region</th>
<th>Off Target Score</th>
<th>U6 Terminator</th>
<th>Chr</th>
<th>Start</th>
<th>End</th>
<th>Strand</th>
<th>Cut Frame</th>
<th>Start Codon Distance</th>
<th>Domains</th>
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</thead>
<tbody>
<tr>
<td>FBgn0003731</td>
<td>GGGCCGAAAAGCTGCGGTATAGG</td>
<td>4.97</td>
<td>0.45</td>
<td>52.77</td>
<td>12</td>
<td>0</td>
<td>none</td>
<td>2R</td>
<td>21547758</td>
<td>21547800</td>
<td>-</td>
<td>Egrr-PB: 2</td>
<td>170</td>
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<td>12</td>
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<td>2R</td>
<td>21554881</td>
<td>21554903</td>
<td>+</td>
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<td>218, 365</td>
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<td>CTAAGGCTCAATGCTCGG</td>
<td>6.55</td>
<td>0.24</td>
<td>48.39</td>
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<td>21554952</td>
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</table>

### SNP info:
- TRiP Cas9 injection stocks
- S2R+ cell line
- CRiMIC injection stocks

[https://www.flyrnai.org/crispr3/](https://www.flyrnai.org/crispr3/)
CRISPR GuideXpress for Anopheles gambiae

**NEW** features:
- Search for orthologous genes between Drosophila Melanogaster and Anopheles gambiae
- Search for Anopheles gambiae CRISPR designs
- Batch search by gRNA sequences
- Machine Learning based efficiency prediction
- CRISPR Distance to Start Codon + % Coverage
- CRISPR Transcript Isoform Hits

CRISPR design in Drosophila Melanogaster: https://www.flyrnai.org/crispr3

Ortholog Search

Fly ⇒ Mosquito
Enter one ID per line.
FBgn(s) or Gene Name(s):
Ortholog Prediction Tools: All
Search

Mosquito ⇒ Fly
Enter one ID per line.
VectorBase ID(s):
Ortholog Prediction Tools: All
Search

CRISPR Search

Search by Gene
Search by gene location.
VectorBase ID:
Search

Search by Location
Search by genomic location.
Chromosome:
Start: Stop:
Search

CRISPR Batch Search

Search by Gene
Enter one VectorBase ID per line.
Search

https://www.flyrnai.org/tools/fly2mosquito/
Examples of data focused tools
Public resources
- using Drosophila gene mnb as example

DIP

mentha

BioGRID

IntAct
Network view, edges are colored for different interaction type.

Click to highlight the nodes of protein complex.

Export interaction tables.

List view with detailed information.

https://fgrtools.hms.harvard.edu/MIST/
Digestive system 20-day adult

https://fgrtools.hms.harvard.edu/MIST/
Single-Cell RNA-seq

Welcome to the single-cell RNA-seq data portal of DRSC/Perrimon lab

Drosophila Data Sets

- Gut Datasets
- Blood Datasets
- Abdomen Datasets

https://www.flyrnai.org/scRNA
Draw dot plot for genes of interest

Compare the expression of any 2 genes

Get the statistics for genes of interest

Select tSNE or uMap

Select one or all samples

Plot distribution

Search up to 5 genes

https://www.flyrnai.org/scRNA
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Aram Comjean
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Yifang Liu
Yue Gao

https://fgr.hms.harvard.edu/
https://flyrnai.org/