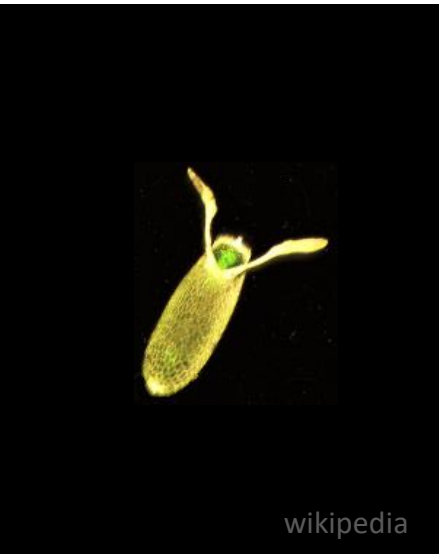
An introduction to the fruit fly, *Drosophila melanogaster*
- a century old model organism



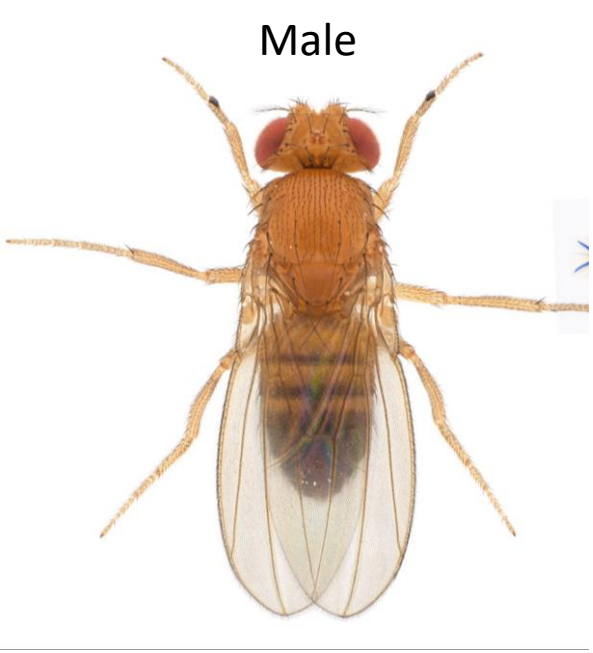
Presented by Imilce A. Rodriguez-Fernandez

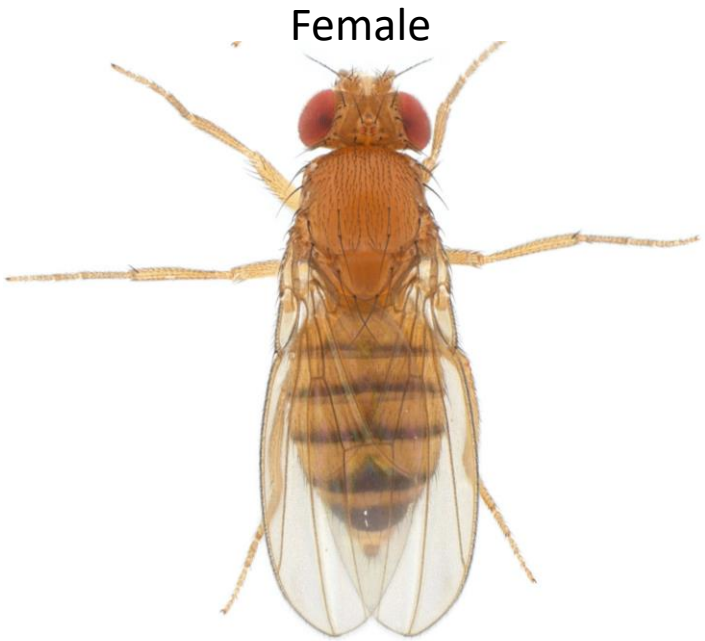
Postdoctoral Fellow at Henri Jasper lab

Buck Institute for Research on Aging

5.31.17

The fruit fly, *Drosophila melanogaster*



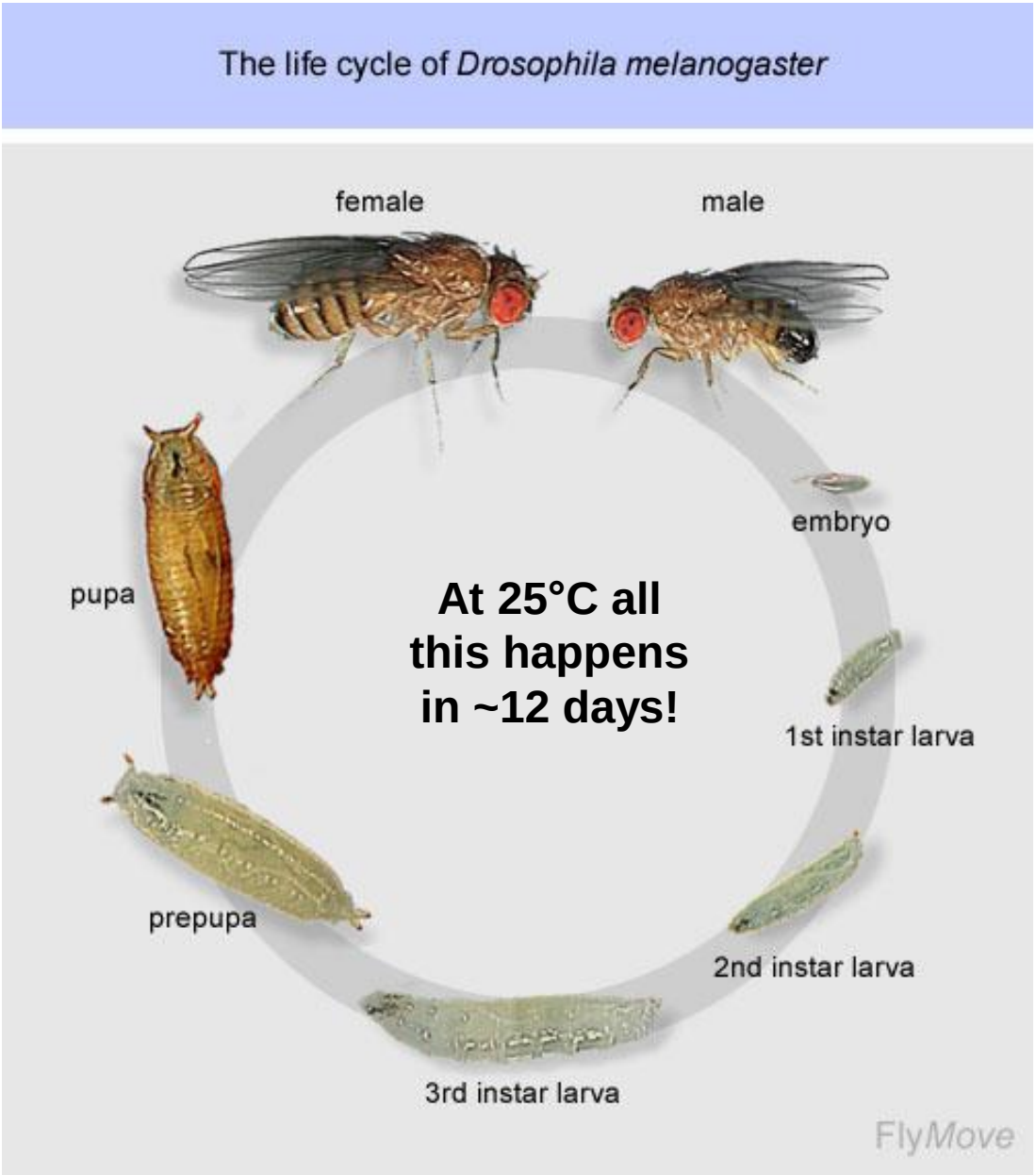


- Sexually dimorphic
- ~2-4 mm long
- Weight ~1 mg
- Originally from equatorial Africa
- First introduced as a model organism in 1900s
- Currently used by >2000 researchers worldwide

Images from Atlas of *Drosophila* phenotypes flystuff.com and easternct.edu

Some of many reasons why *Drosophila* is a good model organism

Reason 1: Short life cycle



- Temperature affects their development
  - 25°C = 10-12 days
  - 18°C = ~19 days

- Under crowded conditions development time increases

Reason 2: Reproduce quickly and have large numbers of offspring

- One females can lay 100s of eggs
- Females are capable of mating 8 hours after emerging from pupae and are *polyandrous*
  - can retain sperm from multiple males

Virgin female

Images from PLoS Biology, course.bio.Indiana.edu, theYORF

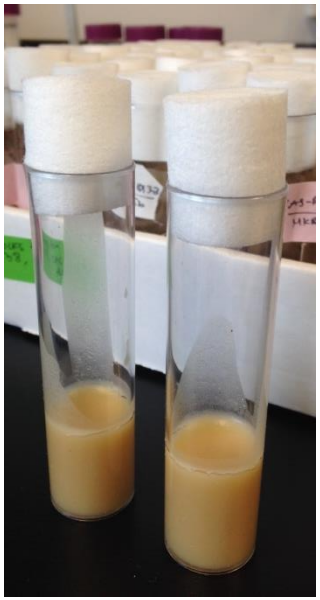
Reason 3: Easy to maintain in a lab

Culturing conditions:

- 12-hour light and 12-hour dark cycle
- 25°C or 18°C
- ~60% Humidity

Food:

- Mix of cornmeal, molasses, agar, sugar, yeast, and water

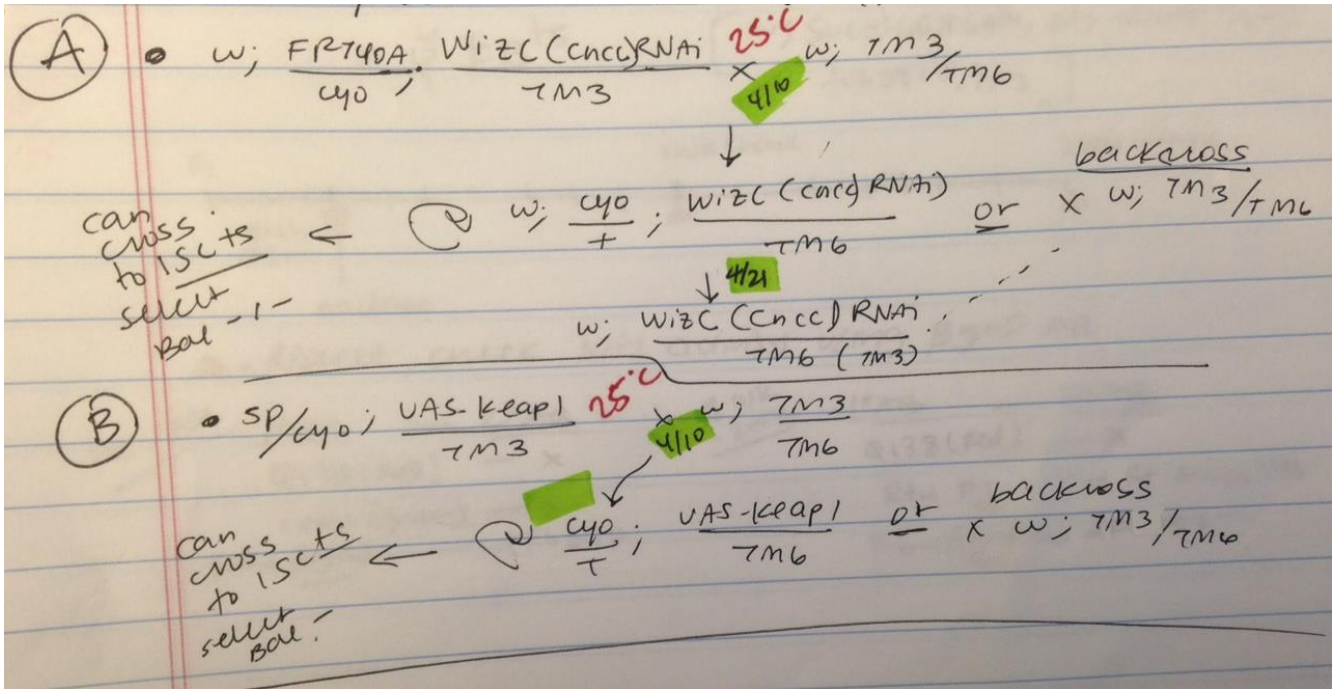


Handling

- Easily anesthetized by CO_2 or cold
- Need relatively inexpensive equipment
  - Dissecting microscope
  - Brushes
  - CO_2 tank connected to a porous plastic pad
  - Bottles or vials with food
  - Bottle with ethanol to discard unwanted flies

A typical day in the Jasper fly room…

Example of a cross



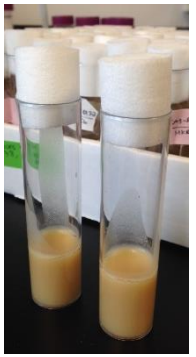
A typical day in the Jasper fly room…

Repeat steps 1-4, infinite times

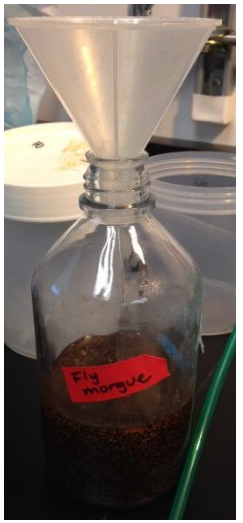
1. Collect flies from crosses

2. Sort the flies

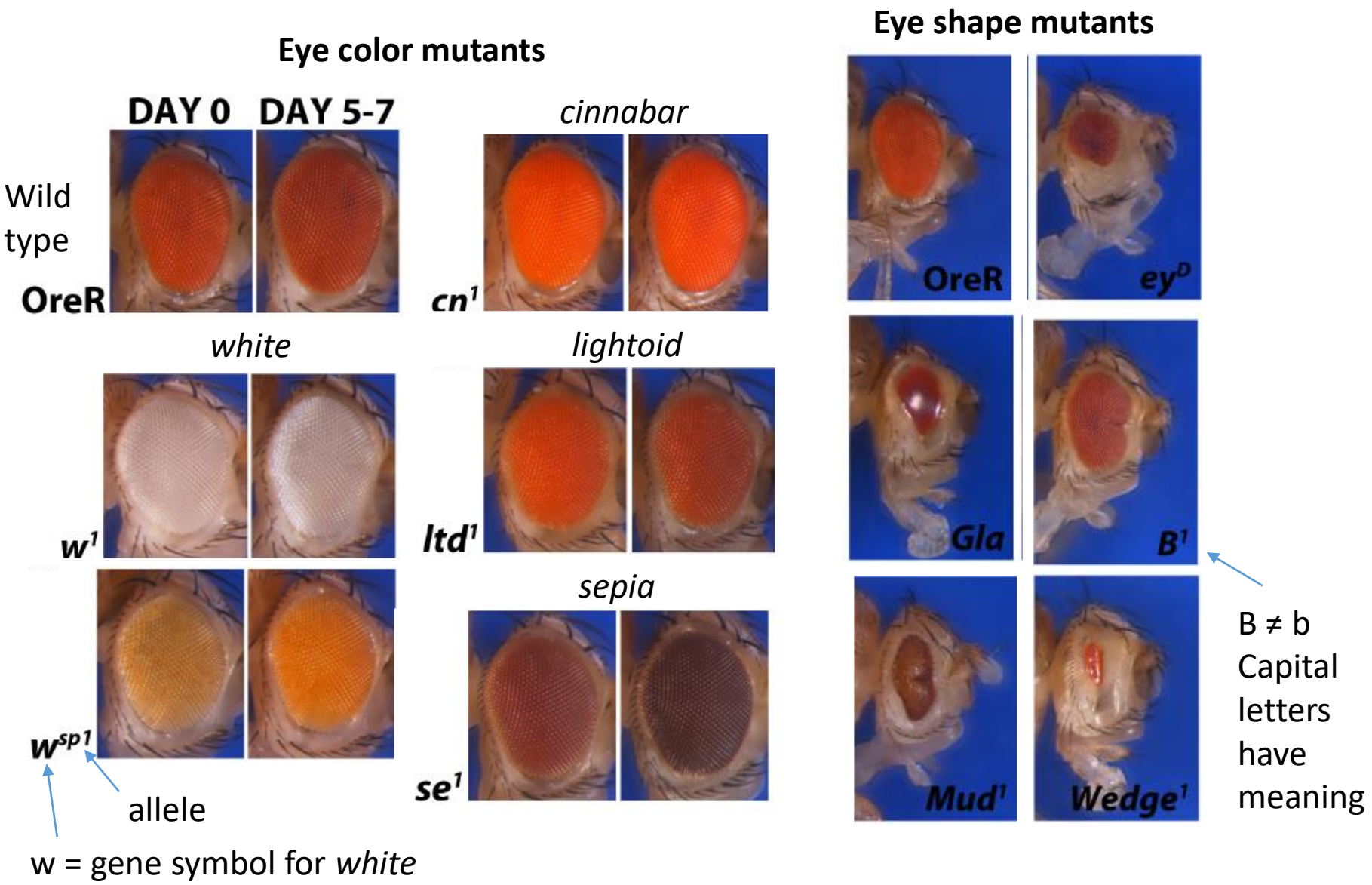
3. Collect the lucky ones and set-up new crosses



4. Discard the rest



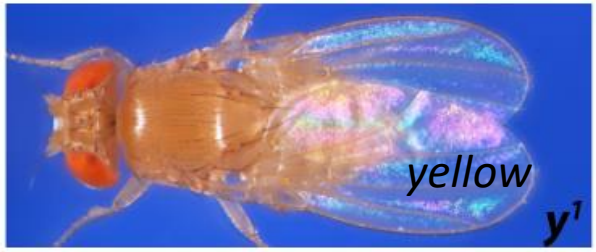
Reason 4: Mutant characteristics are easy to see



Images from Holtzman and Kaufman

Reason 4: Mutant characteristics are easy to see

Body color mutants



Wing shape mutants

Bristle mutants

Wild type

snail

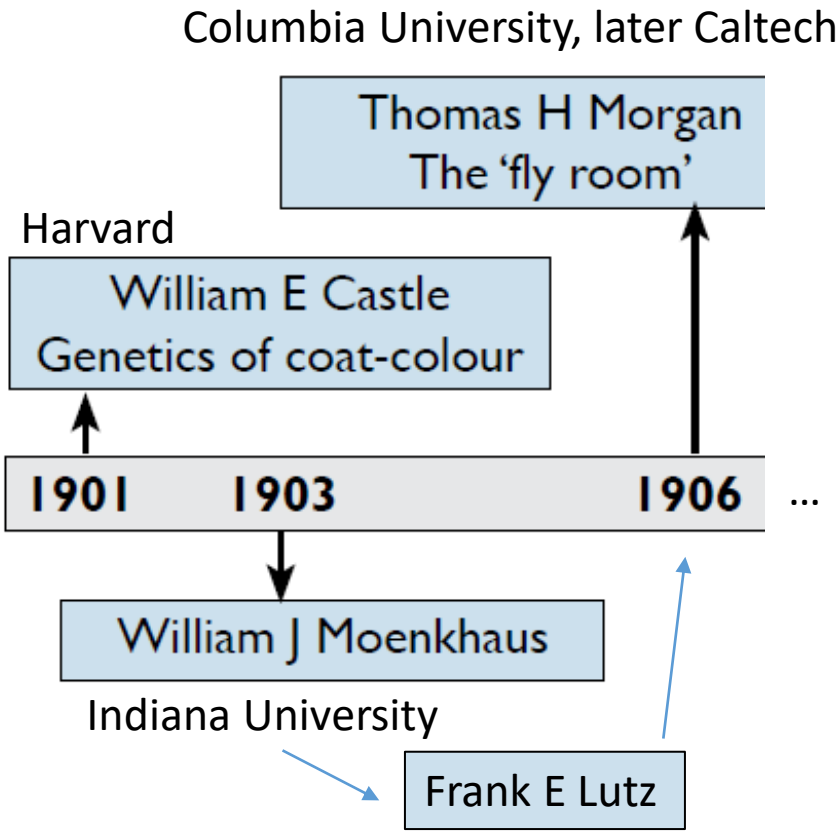
Stubble

Reasons 5 - 9: Genetics!

But before getting into the details lets take a quick look at history…

A little bit of history…

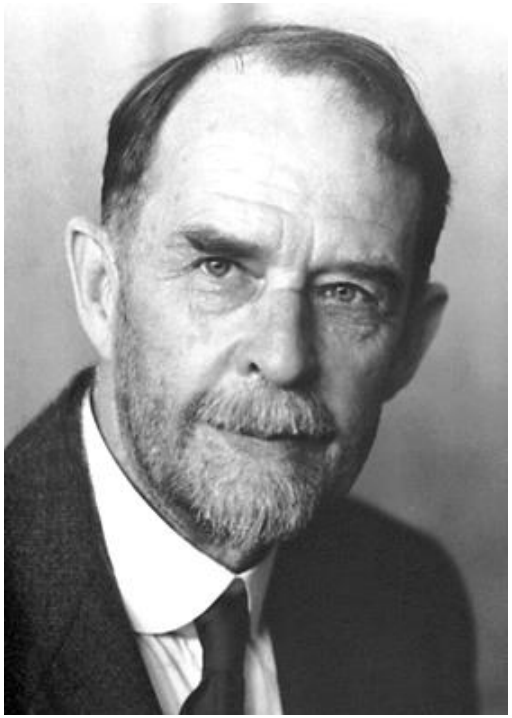
- 1900s
  - Movement to introduce new experimental model organisms into laboratories



Thomas Hunt Morgan with fly drawings.

Stephenson and Metcalfe (2013)
J R Physicians Edinb 43: 70-75

The beginnings of *Drosophila* genetics



The Nobel Prize in Physiology or Medicine 1933
Thomas H. Morgan

JULY 22, 1910] **SCIENCE**

SPECIAL ARTICLES

SEX LIMITED INHERITANCE IN DROSOPHILA

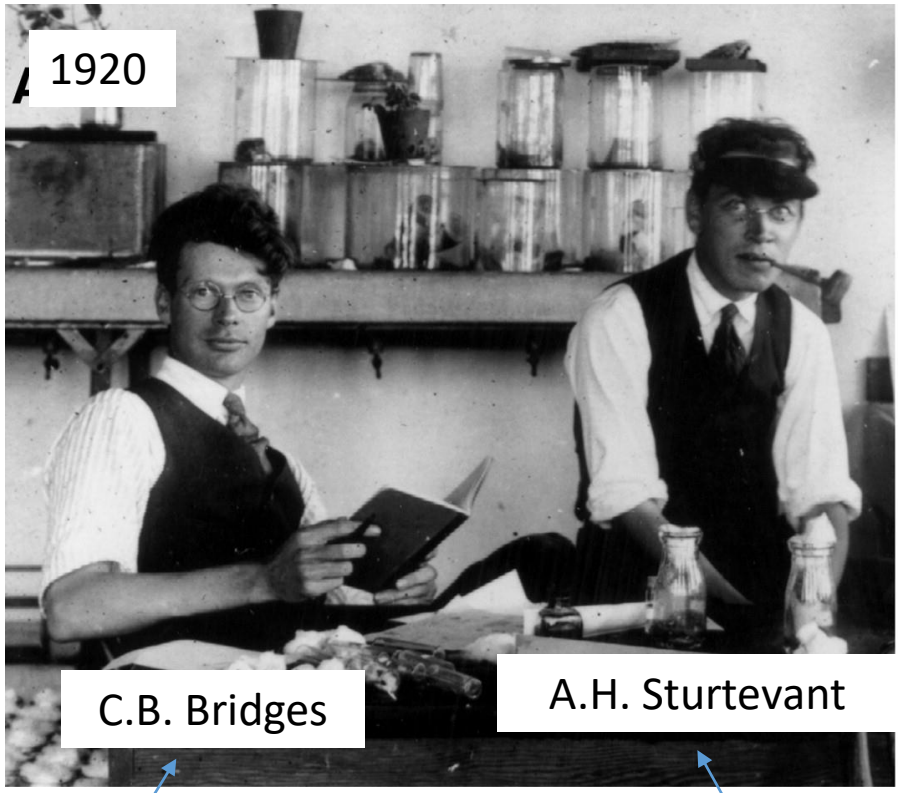
IN a pedigree culture of *Drosophila* which had been running for nearly a year through a considerable number of generations, a male appeared with white eyes. The normal flies have brilliant red eyes. ...

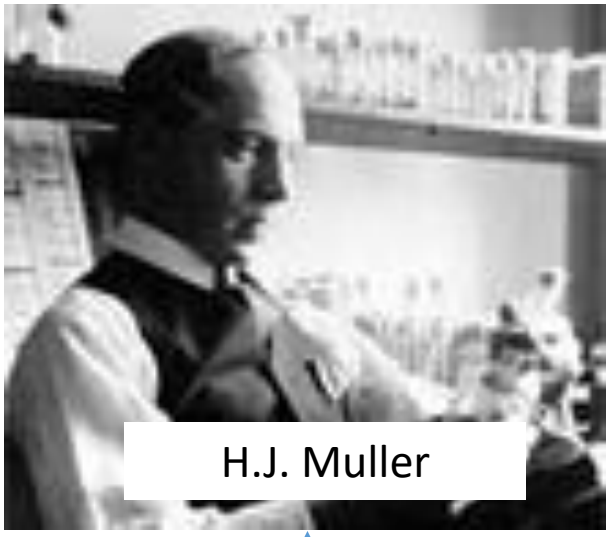
T. H. MORGAN

WOODS HOLE, MASS.,
July 7, 1910

Images from nobelprize.org

Morgan's famous students





Nobel Prize winner, 1946
Found that X-ray caused mutations (1927)

Drew the definitive maps of the salivary glands polytene chromosomes (1935)
- Later discovered first deletion

Produced genetic linkage map of Drosophila X chromosome (1911)
- Received National Medal of Science (1967)

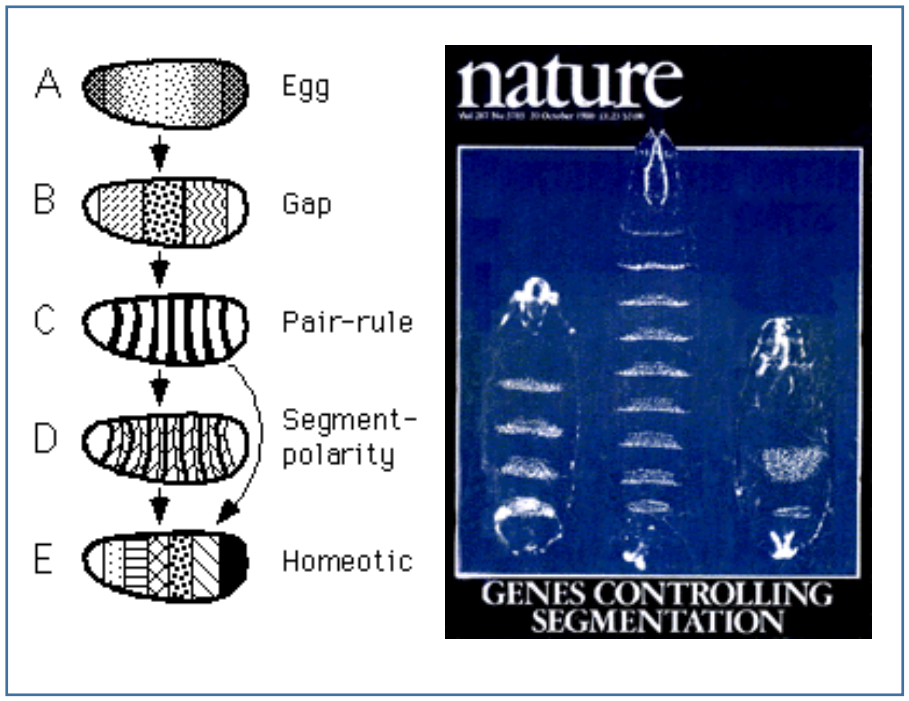
- Generated the first **balancer chromosome** (1918)
  - Sturtevant continued the rest

1995 Nobel Prize winners: for their discoveries concerning "the genetic control of early embryonic development"

Christiane Nusslein-Vollhard and Eric Wieschaus

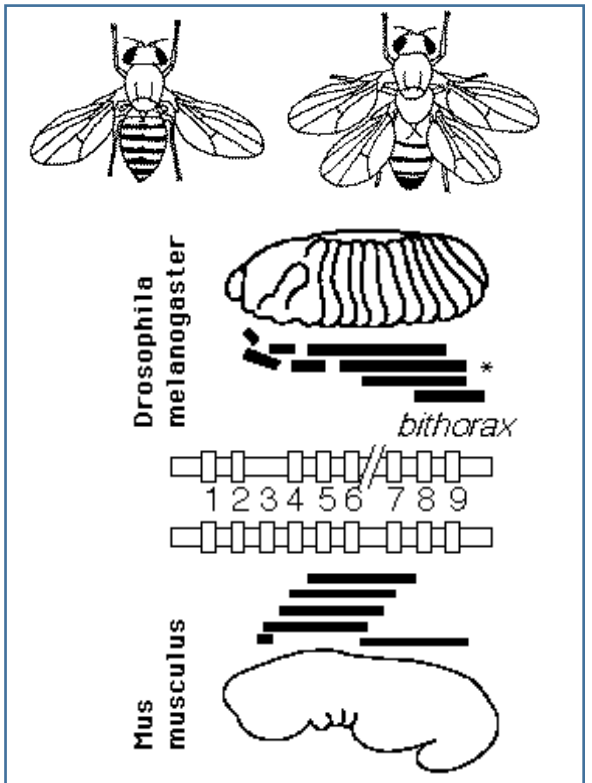
European Molecular Biology Laboratory (EMBL), Heidelberg

Performed mutagenesis screens to identify genes that control embryonic development (known as homeotic genes)



Edward Lewis (Caltech)

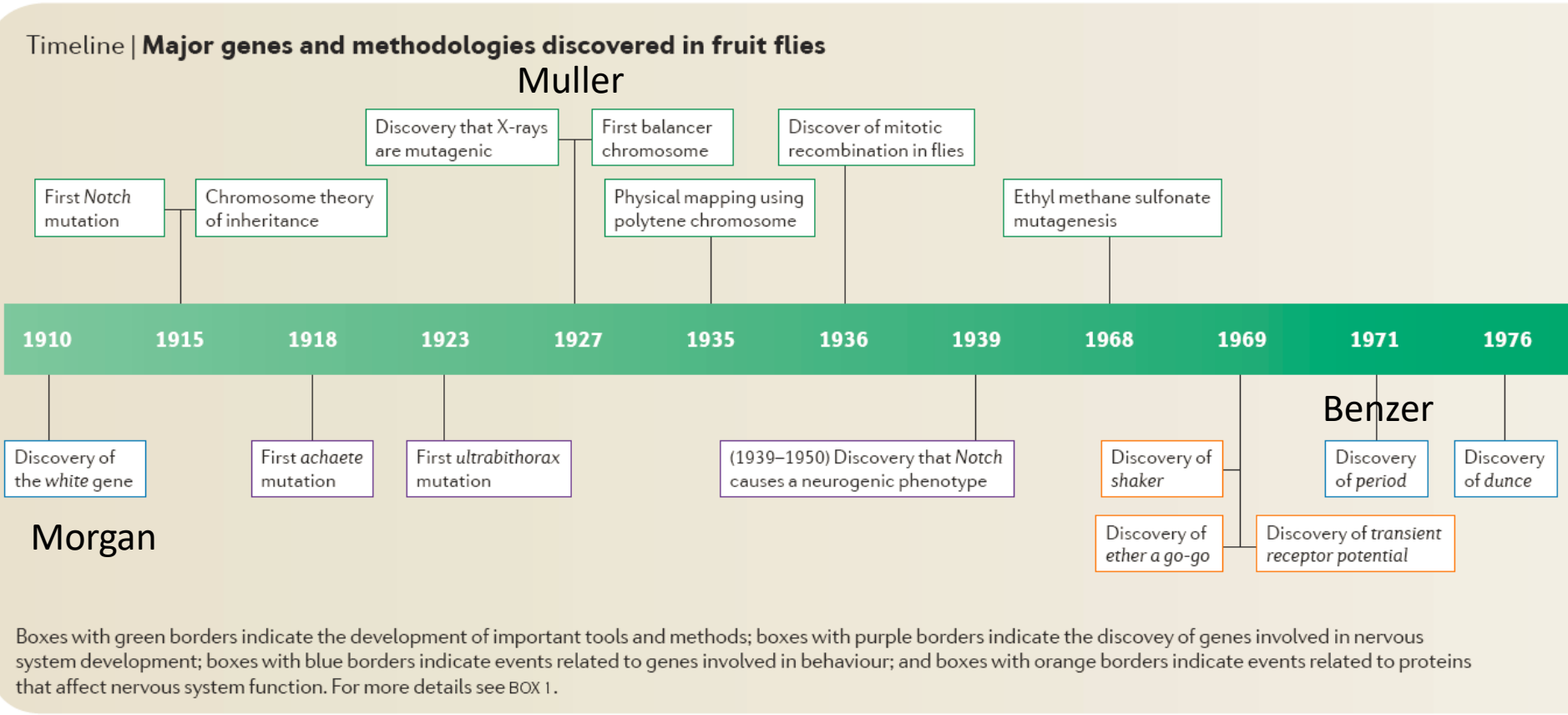
Discovered Hox genes (subset of homeotic genes) by first studying a fly with 2 pairs of wings (bithorax mutation)



Lewis, E.B. (1978) A Gene Complex Controlling Segmentation in Drosophila. *Nature* 276, 565-570

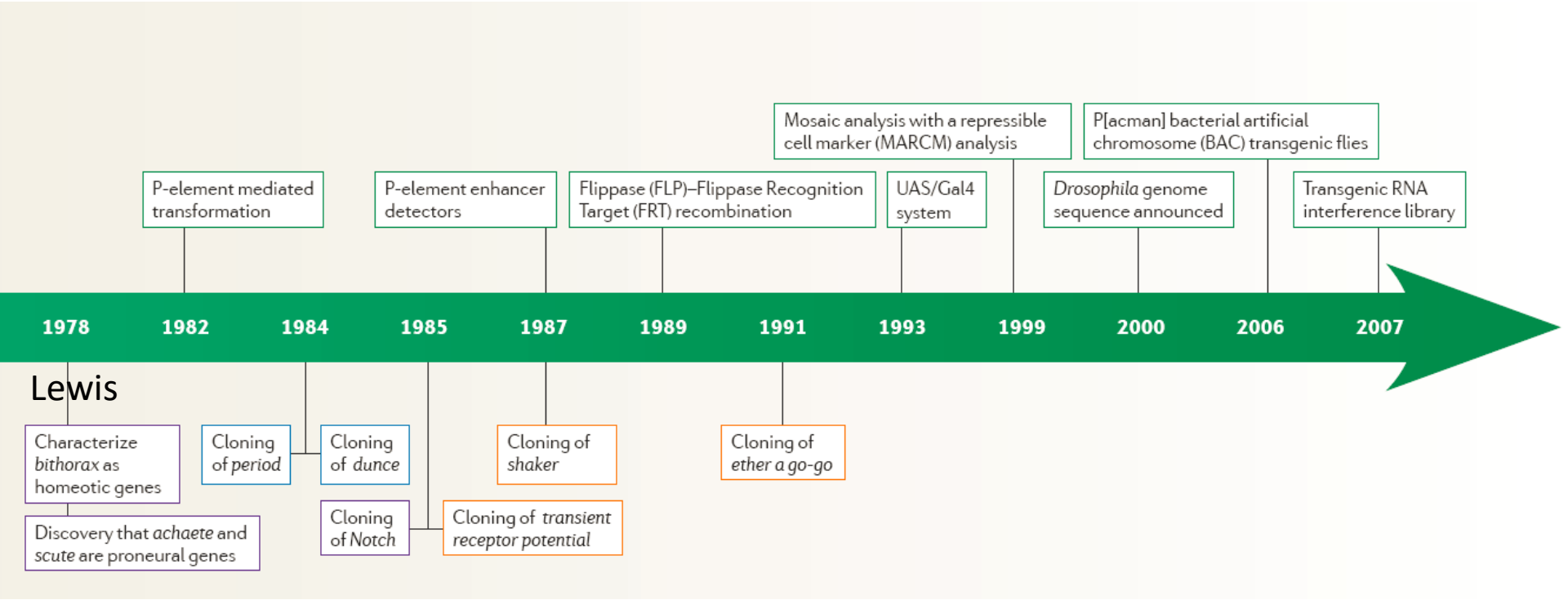
https://www.nobelprize.org/nobel_prizes/medicine/laureates/1995/press.html

Major genes and methodologies discovered in flies (1910 – 1976)



Bellen et al (2010) Nature Reviews Neuroscience 11: 514-522

Major genes and methodologies discovered in flies (1978 - 2007)

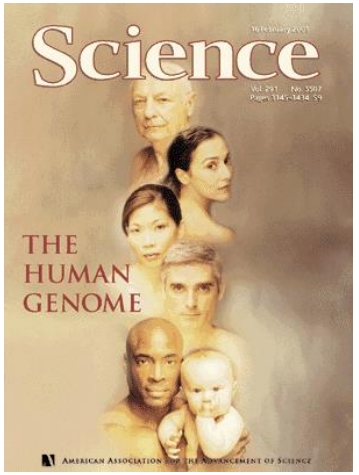


Bellen et al (2010) Nature Reviews Neuroscience 11: 514-522

Reason 5: Genome information available

Drosophila Genome sequenced in 2000

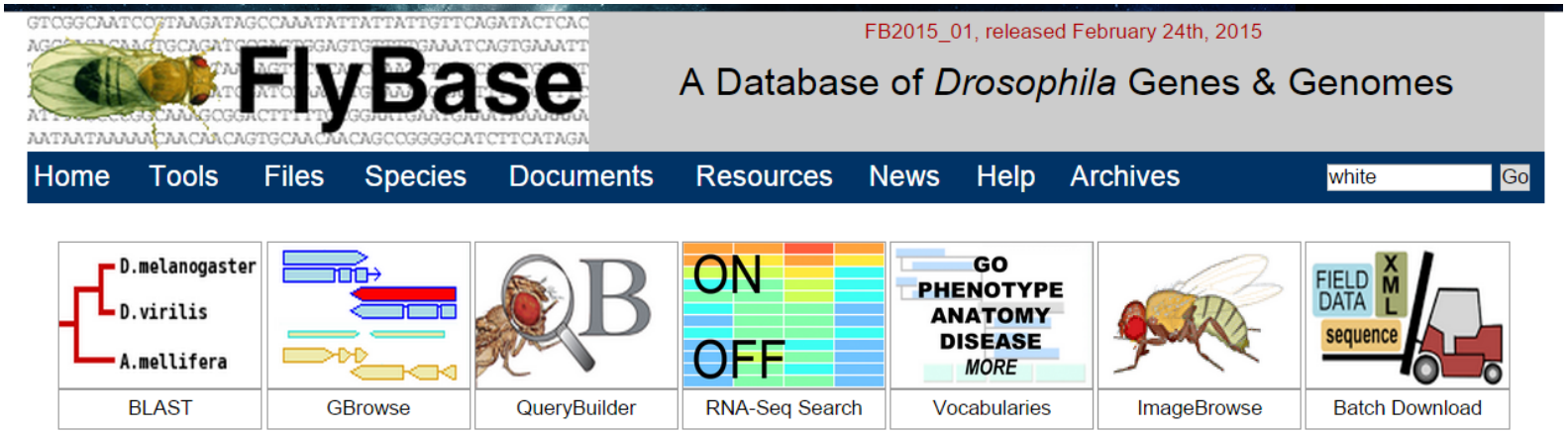
2001 the Human Genome was published



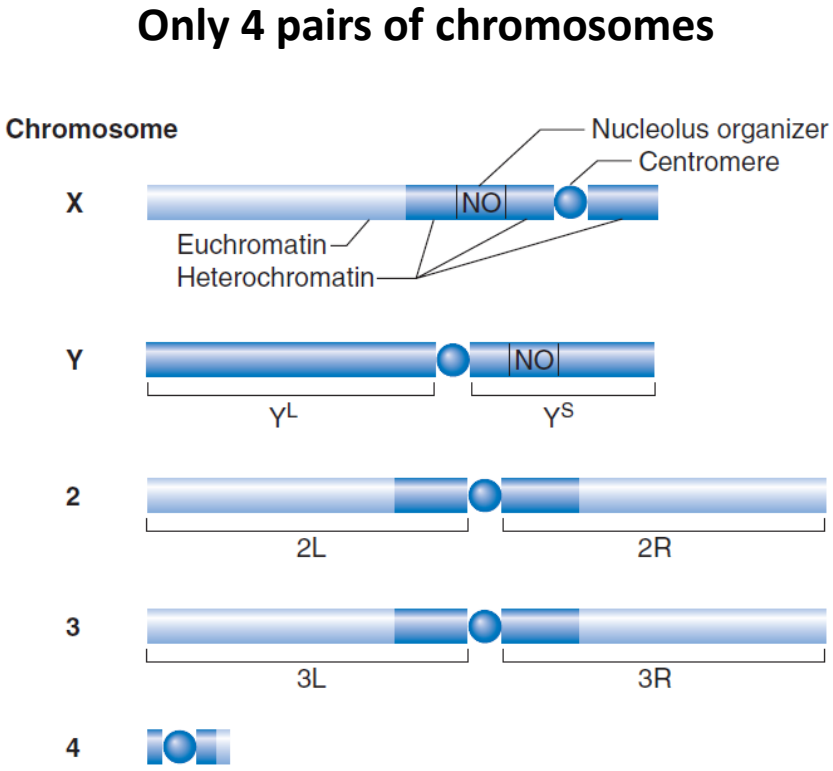
Craig Venter's Celera group

NIH group lead by Francis Collins

All genome information found in one webpage!



Reason 6: Only 4 pairs of chromosomes



- Encoding ~14,000 genes
- ~40% nucleotide or protein sequence similarity between flies and humans
- ~75% of disease-related genes in humans have functional orthologs in the fly

Image from Reference D Genetics 4th Ed. Hartwell et al. (2004)

Nomenclature for wild type flies

Genotype for wild type flies (i.e. OreR, Canton-S)

♀

Chr. #	X	2	3	4
	+	+	+	+
	+	+	+	+

← + indicates wild type chromosome

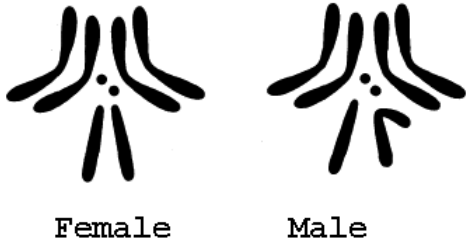
The way to write it: **+/+ ; +/+ ; +/+ ; +/+** = **+; + ; +; +** = **OreR or WT**

Semicolon separates Chr. X from Chr.2

Brackets separates chromosomes

♂

Chr. #	X Y	2	3	4
	+	+	+	+
	7	+	+	+



The way to write it: **+/7 ; +/+ ; +/+ ; +/+** = **+/7; + ; +; +** = **OreR or WT**

Nomenclature for mutant flies

Genotype

♀

Chr. #	X	2	3	4
	w^{1118}	Cy^1	Sb^1, e^1	+
	w^{1118}	+	e^1	+

Lowercase = recessive phenotype
Uppercase = dominant phenotype
Alleles = superscript

The way to write it: ***w^{1118} ; Cy^1 /+ ; Sb^1, e^1/e^1***

Homozygous mutation, written once

Mutation in heterozygous form, written over '+' sign

Alleles within same chromosome

No need to write chr. 4

Phenotype

white eyed fly with curly wings and stubble hair

Easier to see differences when compared to WT

Reason 7: Many genetic tools available

Balancer Chromosomes (first one generated by Muller)

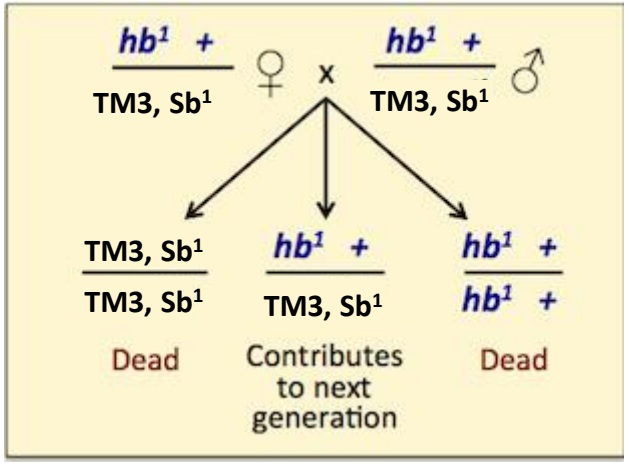
- Modified chromosomes carrying multiple inversions and other mutations
- Used as genetic tools
- Available for chromosome X, 2 and 3 (not 4)

- Three main properties of a Balancer chromosome:
  1. **Lethal** in homozygous form (carry recessive mutations, except for chromosome X)
  2. Carry **visible markers**
     - Example mutations encoding curly wings, stubble bristles, etc
  3. Do **not** undergo recombination

Why they are so great?

- allow investigators to maintain mutations in heterozygous stocks, without having to genotype
- Mutations in essential genes can easily be studied
  - more than 95% of the mutations in essential genes can be maintained easily and effectively

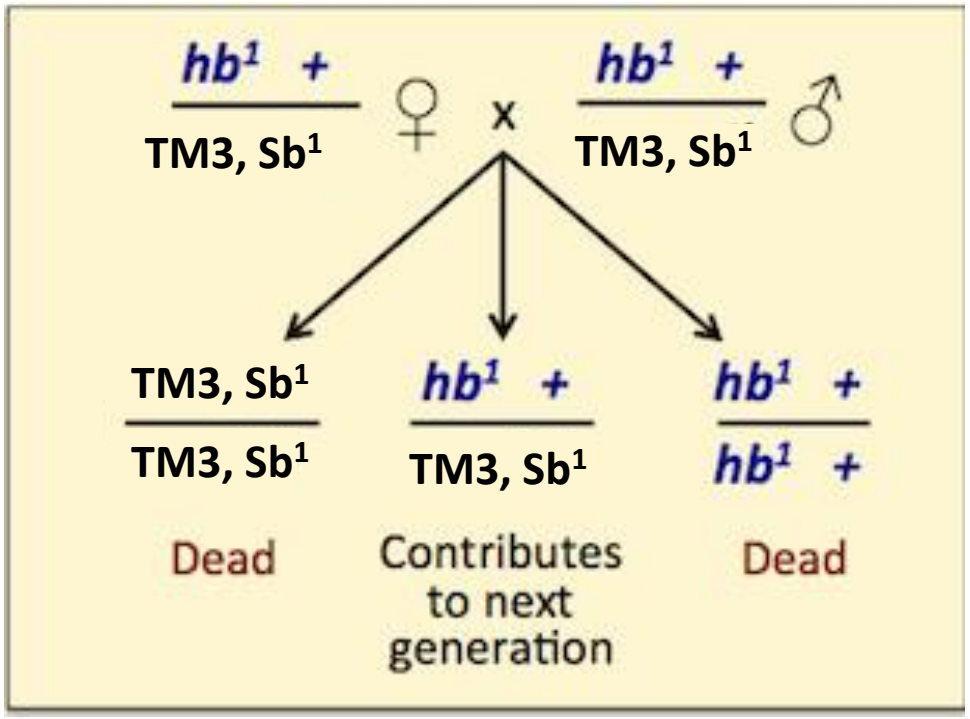
Maintenance of a recessive deleterious mutation



TM3, Sb¹ = example of a balancer

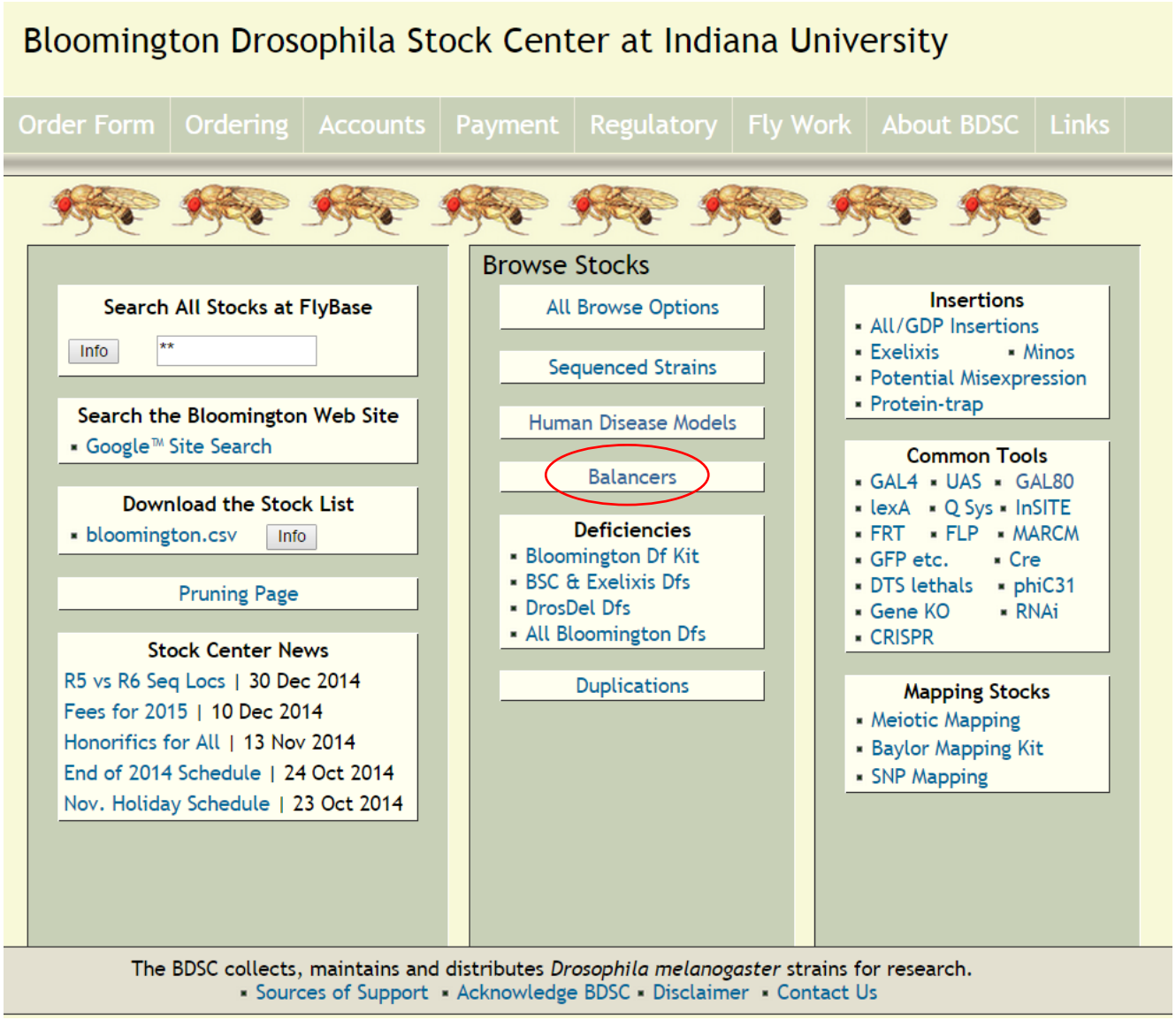
Reference: Bellen et al (2010) Nature Reviews Neuroscience 11: 514-522
Image: http://flystocks.bio.indiana.edu/Browse/balancers/balancer_intro.htm#how

Maintenance of a recessive deleterious mutation



TM3, Sb^1 = example of a balancer

http://flystocks.bio.indiana.edu/



http://flystocks.bio.indiana.edu/

Home | Browse | Search | Order | Fees | Accounts | Fly Food | Supplies | Import Permits

Chromosome 2 balancers at Bloomington

Bloomington Drosophila Stock Center INDIANA UNIVERSITY

All useful balancers for the second chromosome found in Bloomington stocks are included here (at least that is the intention), but only one or a few stocks that we consider to be generally useful as a source of each balancer are shown. Use the Search option to find all possible stocks that carry a given balancer.

With a few exceptions to support searches, only markers that vary from those defined by the core balancer symbol (FM7, CyO, TM3, etc.) are shown in the genotype. See Balancer Definitions for a description of the aberrations and markers defined by each balancer symbol used in the Bloomington stock list.

Not all balancers are equal! See An Introduction to Balancers for an explanation of how to choose a good balancer.

More information and pictures:
CyO, P{ActGFP}JMR1

Go back to the Main balancer page.

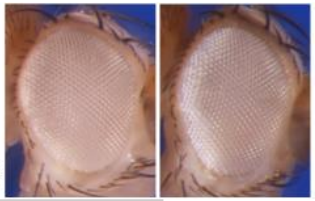
	Stk #	Balancer chr	Genotype
Balancers without fluors or lacZ (see below for "Green" and "Blue" balancers)			
1	2555	CyO	CyO/sna[Sco]
2	1571	CyO	nw[D] Pin[Yt]/CyO; ry[506] e[1]
3	3628	CyO	y[1] w[*]; nub[2] b[1] sna[Sco] pr[1] cn[1]/CyO
4	1702	CyO, Adh[nB]	Df(2R)X1, Mef2[X1]/CyO, Adh[nB]
5	25	CyO, amos[Roi-1]	Df(2L)cl-h1/CyO, amos[Roi-1]
6	6813	CyO, amos[Roi-1] bw[1]	Cam[4c1] L[2] bw[1]/CyO, P{ry[+t7.2]=sevRas1.V12}FK1
7	4105	CyO, amos[Roi-1] cn[*] pr[+]	l(2)N7-6[1] pr[1] cn[1] PPO1[Bc]/CyO, amos[Roi-1] cn[*] pr[+]
8	3995	CyO, amos[Roi-1] cn[2P] bw[1]	pi[[2]]/CyO, amos[Roi-1] cn[2P] bw[1]
9	6243	CyO, b[*]	w[1]; Df(2L)TE35BC-31, b[1] pr[1] pk[1] cn[1] sp[1]/CyO, b[*]
10	2626	CyO, b[81f2] rk[81f2]	Dp(2;2)Cam11, b[1] pr[1] pwn[1]/CyO, b[81f2] rk[81f2]
11	4902	CyO, cl[4]	Gpo-1[n322]/CyO, cl[4]
12	4520	CyO, Df(2L)noc20	Dp(2;2)Cam10, dp[ov1] b[1] noc[TE35B] pr[1] cn[1] bw[1]/CyO, Df(2L)noc20
13	6109	CyO, Df(2R)cn-S3	dac[9] pk[sple-3]/CyO, Df(2R)cn-S3
14	3919	CyO, Df(2R)cn-S6	cos[5] cn[1] bw[1] sp[1]/CyO, Df(2R)cn-S6
15	6071	CyO, Dp(2;2)b[81f1], b[81f1] stan[81f1]	In(2L)b82a1, Adh[UF] pr[1] cn[1]/CyO, Dp(2;2)b[81f1], b[81f1] stan[81f1]
16	3186	CyO, Dp(2;2)M(2)m[+]	Df(2L)M36F-S5/CyO, Dp(2;2)M(2)m[+]

Reason 7: Many genetic tools available

Need a mutant?

- Check what's available on stock collections
  - Spontaneous mutations
  - X-ray or EMS (Ethyl methane sulfonate) generated
    - Point mutations, deletion, inversions, etc.
  - Transgenes
    - Including those encoding RNAi
- Ask the *Drosophila* community!

1st stop at: http://flybase.org/



FB2015_01, released February 24th, 2015

FlyBase

A Database of *Drosophila* Genes & Genomes

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2015 Release Schedule | 12 Dec 14
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3rd APDRC | 11 May 15
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Species: include non-Dmel species Search

Enter text:

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

Commentary See all commentaries

***Dmel* R6 assembly**

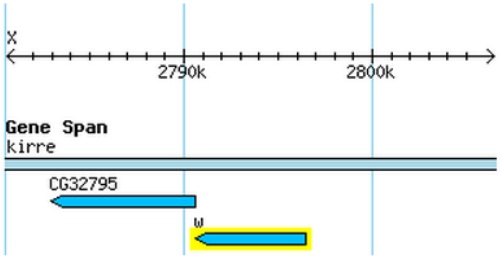
D. melanogaster Release 6

Jul 16, 2014. With the FB2014_04 web site update of FlyBase, we have incorporated the BDGP's new *D. melanogaster* Release_6 assembly. While much of the euchromatic sequence has remain unchanged, each of the major arm scaffolds 2L, 2R, 3L, 3R and X has had more centric heterochromatic sequences added to the assembly. The sequences of the Release_5 heterochromatic scaffolds 2LHet, 2RHet, 3LHet, 3RHet and XHet have either been incorporated into the major arm scaffolds or are provided as small individual scaffolds with the other remaining unassembled scaffolds. In FlyBase, we are not presenting pseudo arms consisting of concatenation of mapped but unordered and unoriented scaffolds within Release_6 (comparable to arm U). Rather, the assembly contains 1870 total scaffolds

General Information			
Symbol	Dmel\w	**Species**	*D. melanogaster*
Name	white	**Annotation symbol**	CG2759
Feature type	protein_coding_gene	**FlyBase ID**	FBgn0003996
Gene Model Status	Current	**Stock availability**	80266 publicly available
Also Known As	EG:BACN33B1.1, DMWHITE		
Genomic Location			
Cytogenetic map	3B6-3B6	**Sequence location**	X:2,790,599..2,796,466 [-]

Genomic Maps

GBrowse



Decorated FASTA

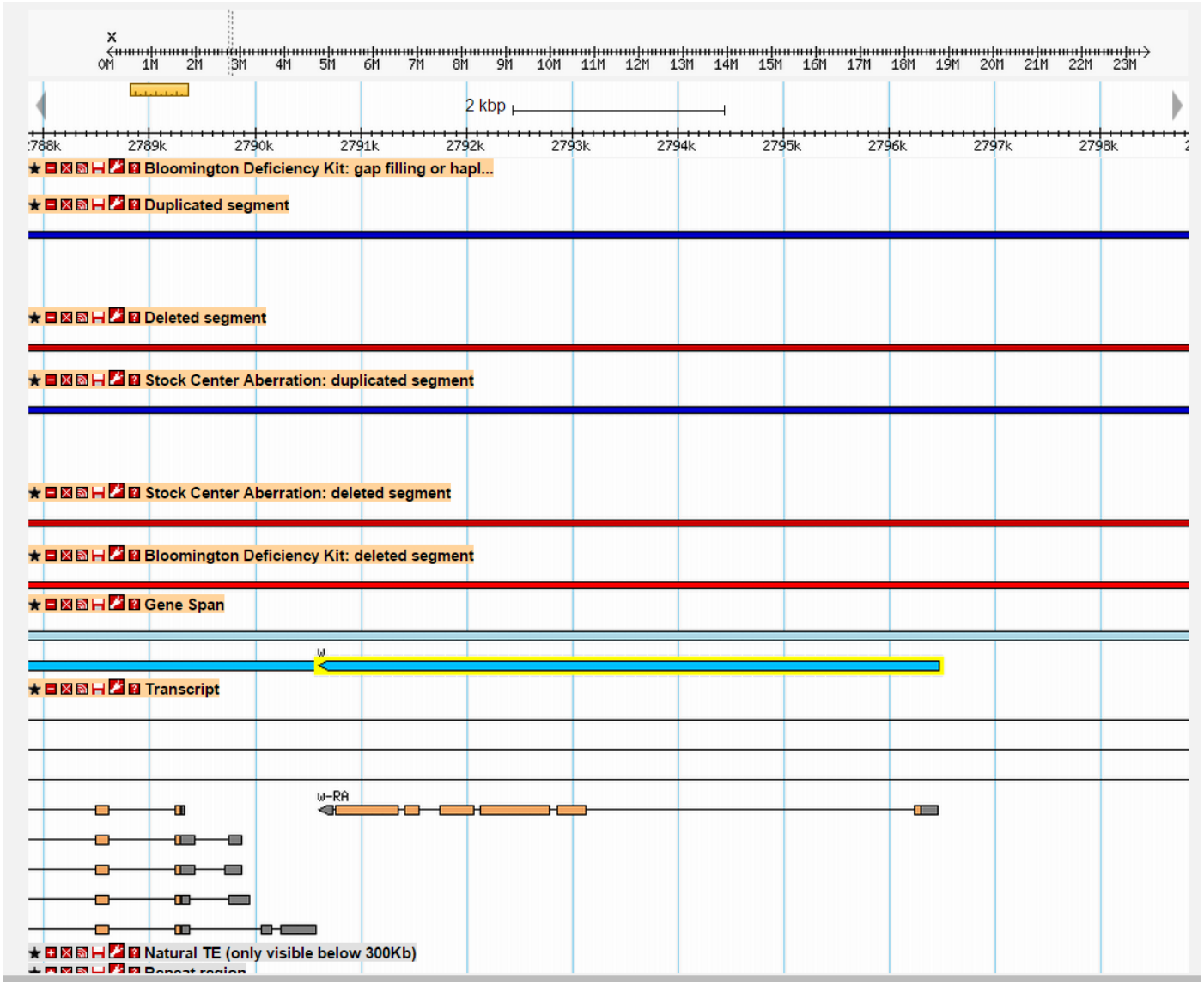
Get genome region

Gene region

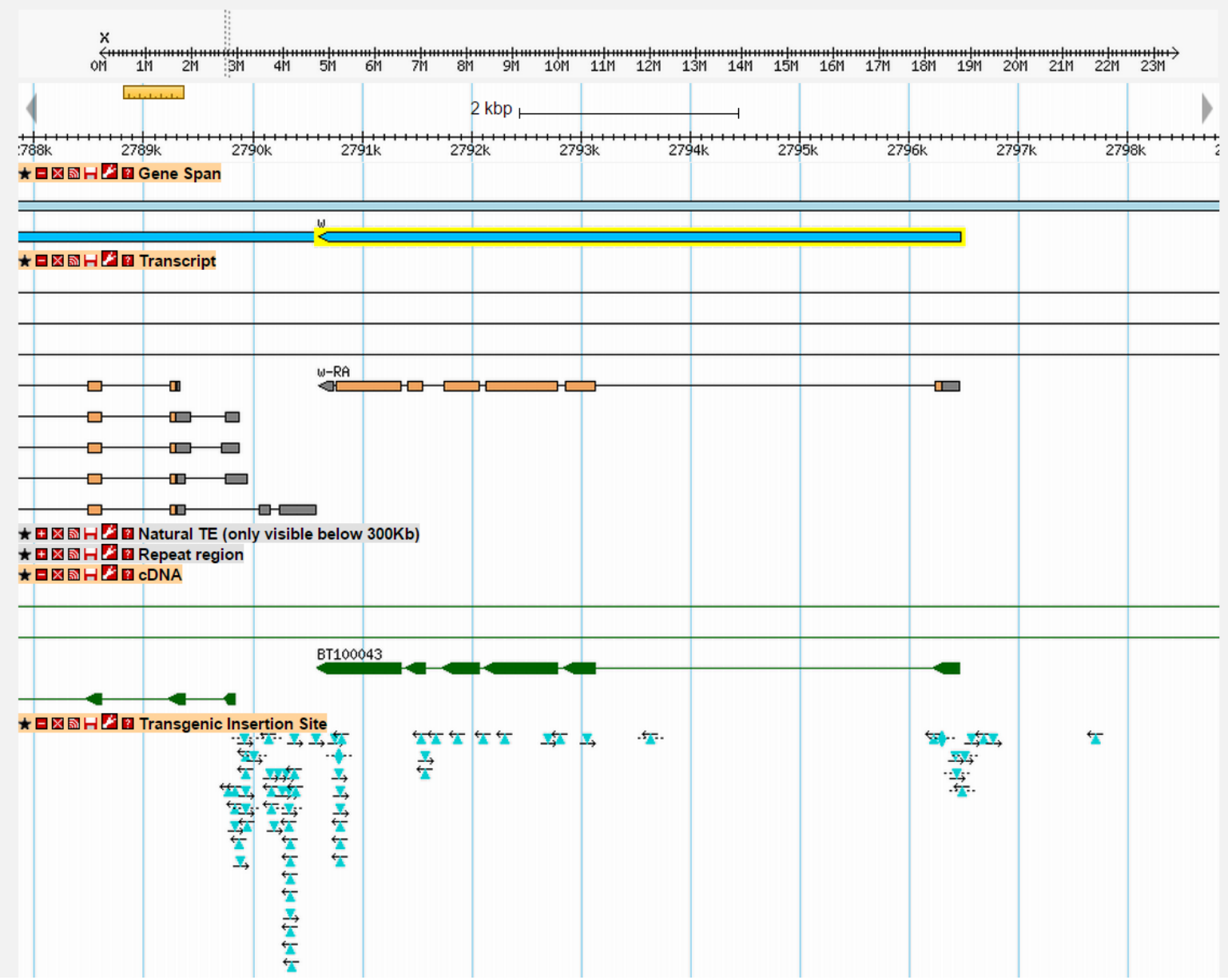
Get FastA

Families, Domains and Molecular Function	
Protein Family (UniProt, Sequence Similarities)	Belongs to the ABC transporter superfamily. ABCG family. Eye pigment precursor importer (TC 3.A.1.204) subfamily. {ECO:0000305}. (P10090)
Protein Domains/Motifs	**UniProt (Sequence Similarities)** Contains 1 ABC transporter domain. {ECO:0000255|PROSITE-ProRule:PRU00434}. (P10090) **InterPro** ABC transporter-like; AAA+ ATPase domain; Pigment precursor permease; ABC-2 type transporter; ABC

Deletions available covering the *white* gene



Also available are P-element insertions (blue triangles) at the *white* gene



Reason 7: Many genetic tools available

Need a mutant?

Someone else generated mutant flies I need…

Buy it from a fly Stock center

- **Bloomington**
- DrosDel
- Exelixis (Harvard)
- FlyORF
- GDP (Baylor)
- Kyoto
- NIG-Fly
- VDRC

80,266 fly stocks you can buy for *w* gene!

FlyBase

FB2015_01, released February 24th, 2015

Gene Dmel\w

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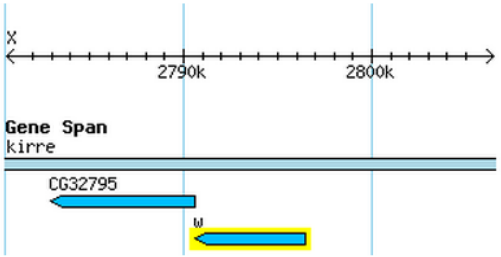
General Information			
Symbol	Dmel\w	**Species**	*D. melanogaster*
Name	white	**Annotation symbol**	CG2759
Feature type	protein_coding_gene	**FlyBase ID**	FBgn0003996
Gene Model Status	Current	**Stock availability**	80266 publicly available
Also Known As	EG:BACN33B1.1, DMWHITE		
Genomic Location			
Cytogenetic map	3B6-3B6	**Sequence location**	X:2,790,599..2,796,466 [-]

Genomic Maps

GBrowse



Decorated FASTA

Get genome region

Gene region

Get FastA

Families, Domains and Molecular Function	
Protein Family (UniProt, Sequence Similarities)	Belongs to the ABC transporter superfamily. ABCG family. Eye pigment precursor importer (TC 3.A.1.204) subfamily. {ECO:0000305}. (P10090)
Protein Domains/Motifs	**UniProt (Sequence Similarities)** Contains 1 ABC transporter domain. {ECO:0000255|PROSITE-ProRule:PRU00434}. (P10090) **InterPro** ABC transporter-like; AAA+ ATPase domain; Pigment precursor permease; ABC-2 type transporter; ABC

22 fly stocks you can buy for *Rab32* gene!

Try out the beta release of "FlyBase 2.0" at beta.flybase.org

FlyBase

FB2017_02, released April 18, 2017

Gene Dmel\Rab32

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

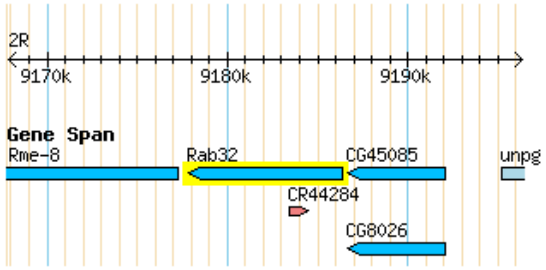
FlyGene Wiki Help Open All Close All

General Information			
Symbol	Dmel\Rab32	**Species**	*D. melanogaster*
Name	Rab32	**Annotation symbol**	CG8024
Feature type	protein_coding_gene	**FlyBase ID**	FBgn0002567
Gene Model Status	Current	**Stock availability**	22 publicly available
Also Known As	ltd, Rab-RP1		
Gene Snapshot	In progress. Contributions welcome.		
Genomic Location			
Cytogenetic map	45B2-45B3	**Sequence location**	2R:9,177,864..9,186,342 [-]
Recombination map	2-60		

Genomic Maps

GBrowse

JBrowse



Decorated FASTA

Get genome region

Gene region

Get FastA

Other Genome Views

The following external sites may use different assemblies or annotations than FlyBase.

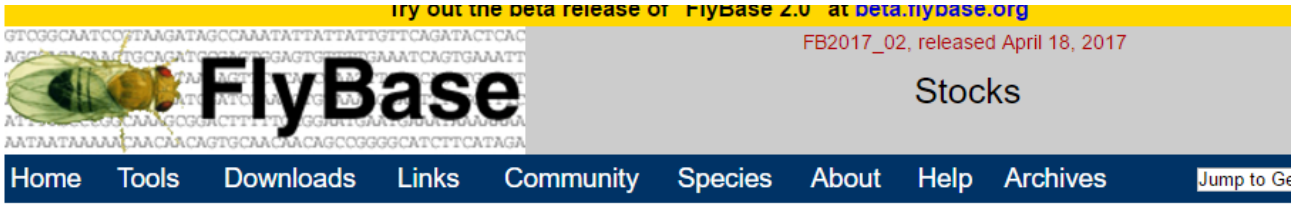
NCBI Genome Data Viewer

UCSC Genome Browser

Families, Domains and Molecular Function

22 fly stocks you can buy for *Rab32* gene!

Mutants, RNAi lines, YFP-Tagged proteins, etc.



22 matches Convert to Stocks Results Analysis/R

#	Collection	Stock No.	Genotype
1	Exelixis at Harvard Medical School	-	PBac{RB}Rab32[e00716]
2	Exelixis at Harvard Medical School	-	PBac{RB}Rab32[e02183]
3	Vienna Drosophila Resource Center	v104348	P{KK107695}VIE-260B
4	Vienna Drosophila Resource Center	v330262	P{VSH330262}attP40
5	Exelixis at Harvard Medical School	-	P{XP}Rab32[d06912]
6	Bloomington Drosophila Stock Center	338	Rab32[1]
7	Kyoto Stock Center	105856	Rab32[1]
8	Bloomington Drosophila Stock Center	429	ptc[tuf-1] Rab32[1]
9	Kyoto Stock Center	105908	ptc[tuf-1] Rab32[1]
10	Bloomington Drosophila Stock Center	24448	w[1118]; Mi{ET1}Rab32[MB03690]
11	Kyoto Stock Center	125815	w[1118]; P{RS5}Rab32[5-HA-5064]
12	Bloomington Drosophila Stock Center	62558	w[1118]; TI{TI}Rab32[EYFP]
13	Kyoto Stock Center	103684	w[*]; P{GawB}Rab32[NP0628] / CyO
14	Bloomington Drosophila Stock Center	23280	y[1] w[*]; P{w[+mC]=UASp-YFP.Rab32.Q79L}mRpL19[03]
15	Bloomington Drosophila Stock Center	9816	y[1] w[*]; P{w[+mC]=UASp-YFP.Rab32.Q79L}sprt[08]
16	Bloomington Drosophila Stock Center	23281	y[1] w[*]; P{w[+mC]=UASp-YFP.Rab32.T33N}Eb1[04]
17	Bloomington Drosophila Stock Center	9815	y[1] w[*]; P{w[+mC]=UASp-YFP.Rab32}RhoGDI[11]
18	Bloomington Drosophila Stock Center	28002	y[1] v[1]; P{y[+t7.7] v[+t1.8]=TRiP.JF02836}attP2
19	Bloomington Drosophila Stock Center	20166	y[1] w[67c23]; P{w[+mC] y[+mDint2]=EPgy2}Rab32[EY07166]
20	Bloomington Drosophila Stock Center	389	S[1] wg[Sp-1] ab[2] Rab32[1]/SM5
21	Kyoto Stock Center	112535	y[*] w[*]; P{GawB}Rab32[NP1146] / CyO, P{UAS-lacZ.UW14}UW14
22	Bloomington Drosophila Stock Center	38956	y[1] v[1]; P{y[+t7.7] v[+t1.8]=TRiP.HMS01870}attP40/CyO

Reason 8: Many genetic tools available

Didn't find a mutant for your gene of interest?

Then Do-It-Yourself!

- Transposon (P-element) transformations
  - Discovered in the 1970's
    - disrupt endogenous genes by insertion
  - Scientists then used P-elements not only for transgenesis, but also to induce deletions and to stimulate homologous recombination

Discovery of P-elements to cause sterility

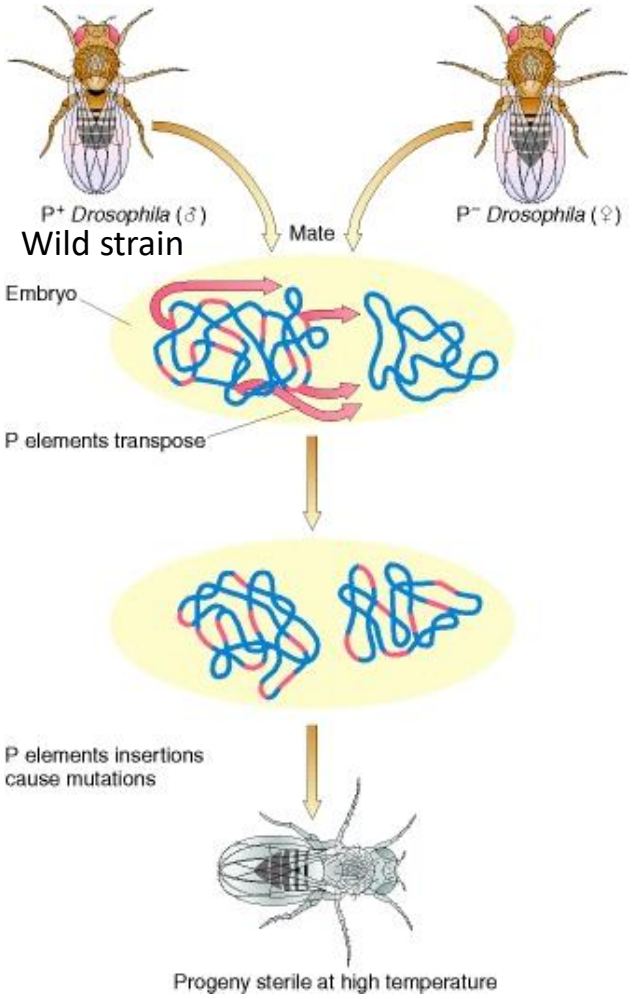
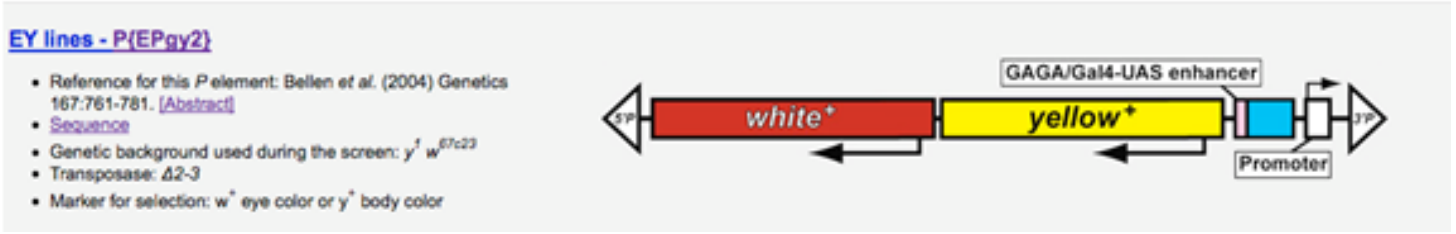


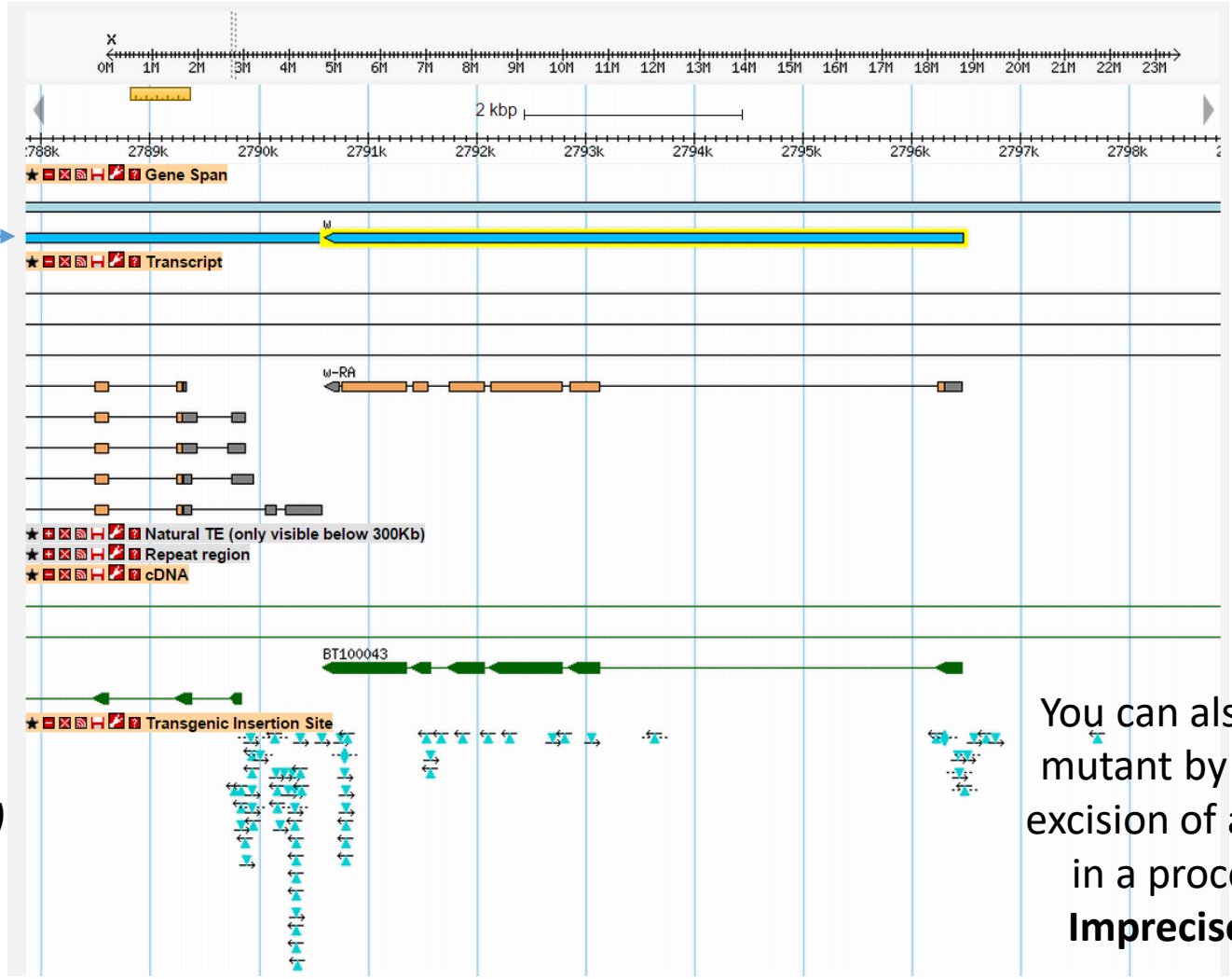
Image from Griffiths AJF, Gelbart WM, Miller JH, et al. (1999) Modern Genetic Analysis Chapter 13

Many P-elements available

Example of the structure of a P-element



white gene



P-elements available (blue triangles)

You can also generate mutant by forcing the excision of a P-element in a process called **Imprecise excision**

Mutagenesis using P-elements

1. Imprecise excision – Old school but still useful

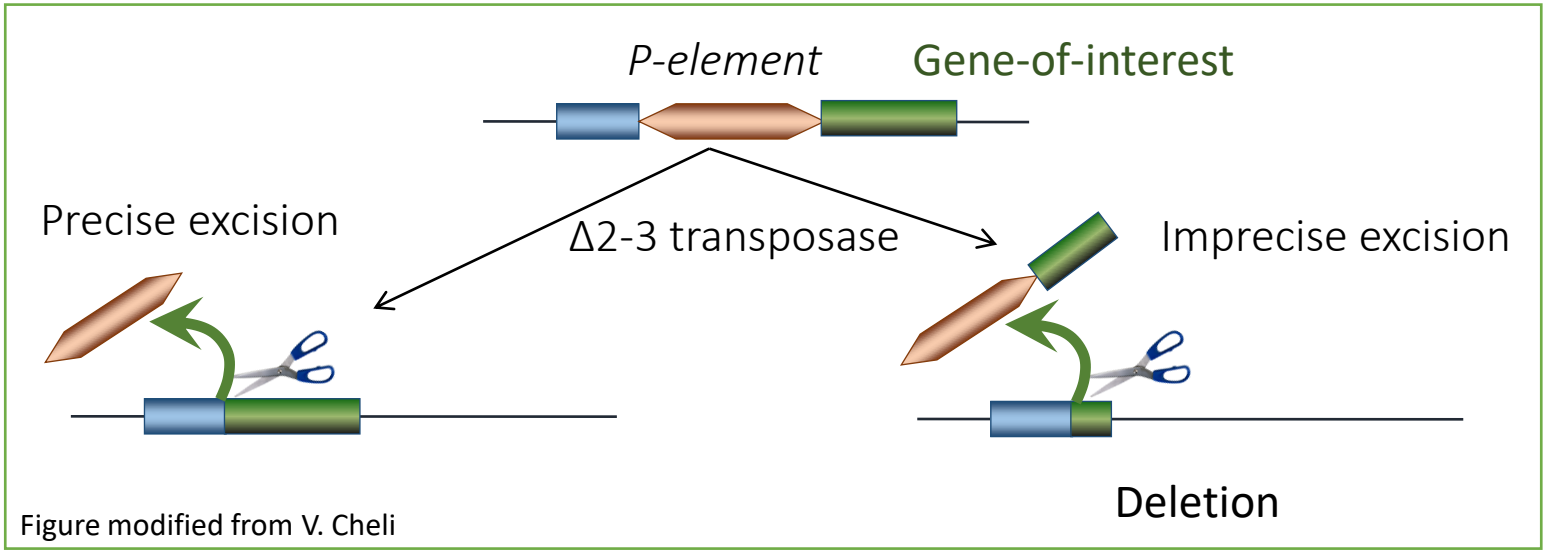


Figure modified from V. Cheli

2. Homologous recombination by incorporating FRT sites on P-elements

- expression of the enzyme Flipase (Flp) will induce recombination at FRT sites

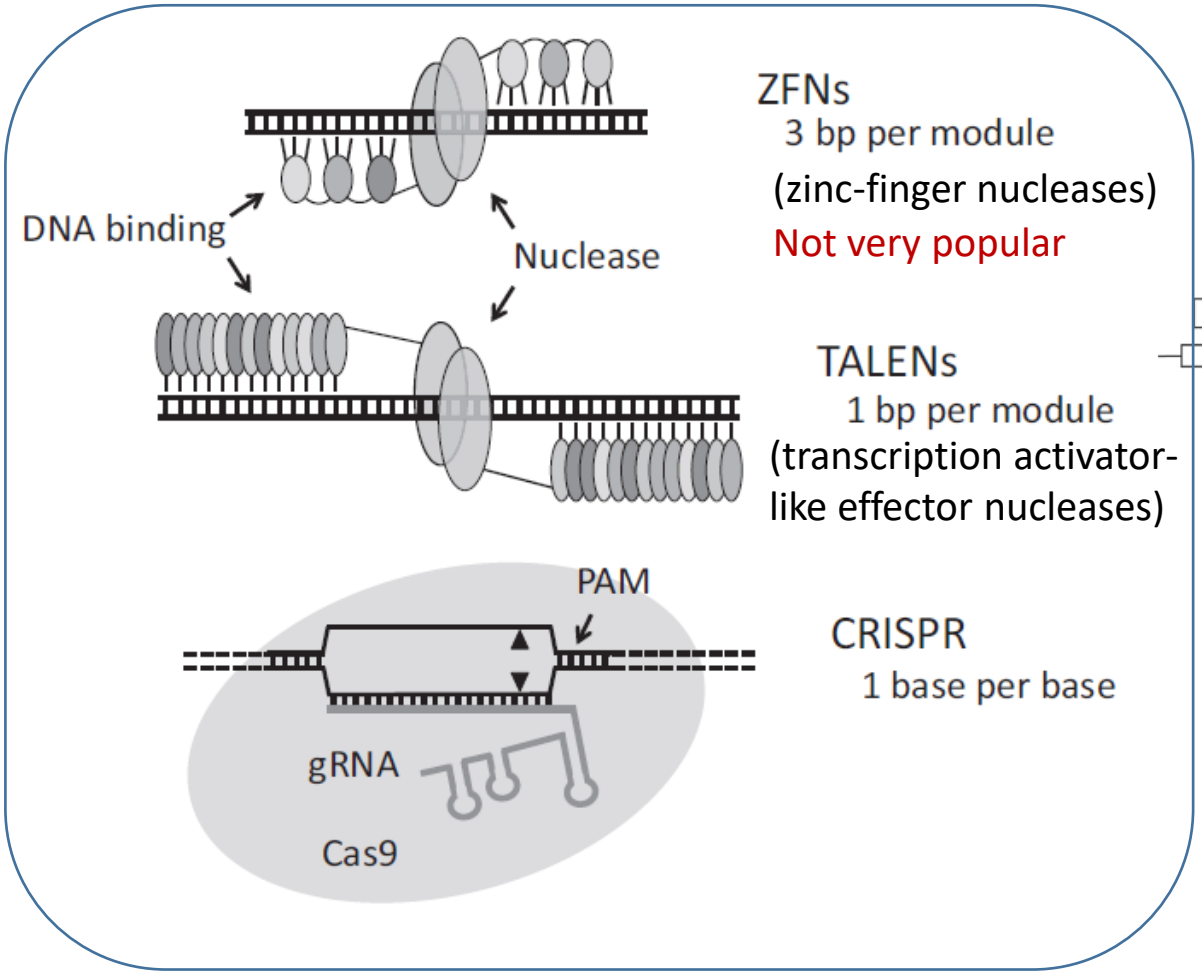
PBac{WH}

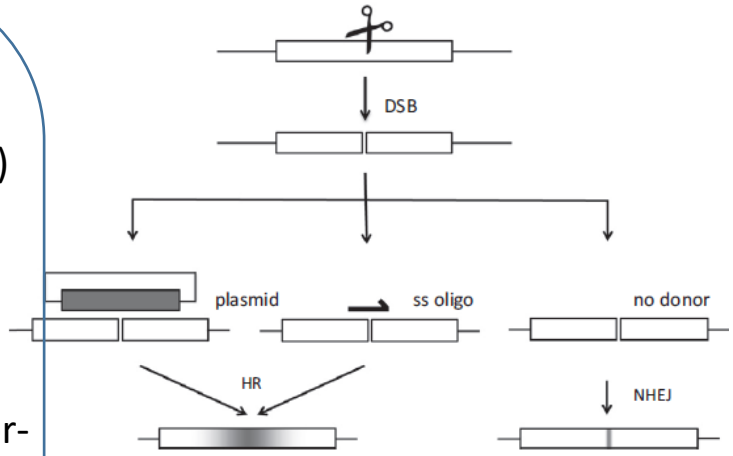
- Exelixis collection - line names start with "f"
- Reference Thibault *et al.* (2004) Nature Genetics 36:283-287. [Abstract]

Limitations of using P-elements: availability and genomic location

Reason 8: Many genetic tools available

- Latest techniques for mutagenesis using chimeric nucleases





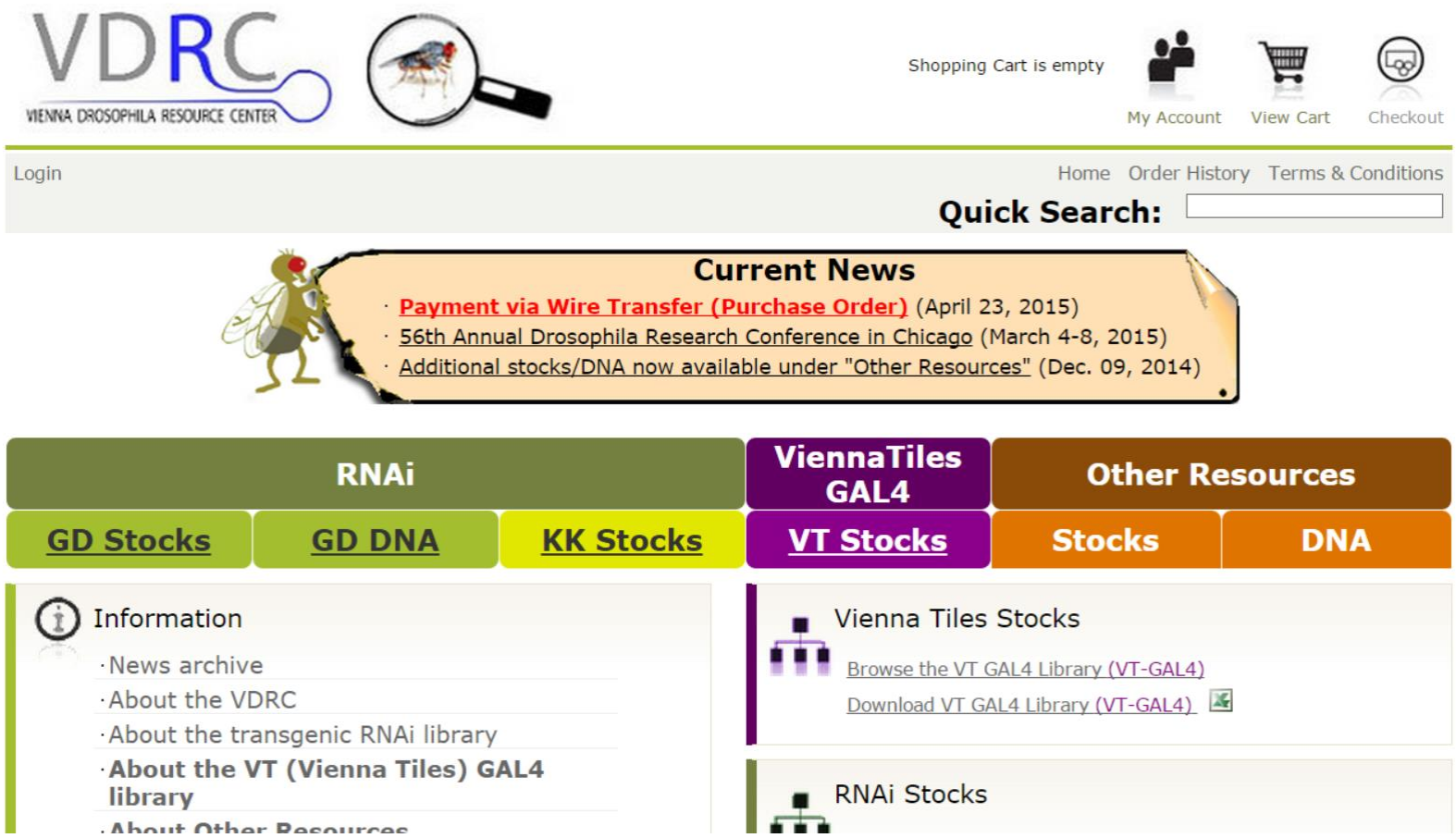
Beumer and Carroll (2014) Methods 68: 29-37

Reason 8: Many genetic tools available

Try to knockdown your gene of interest

RNAi collections available

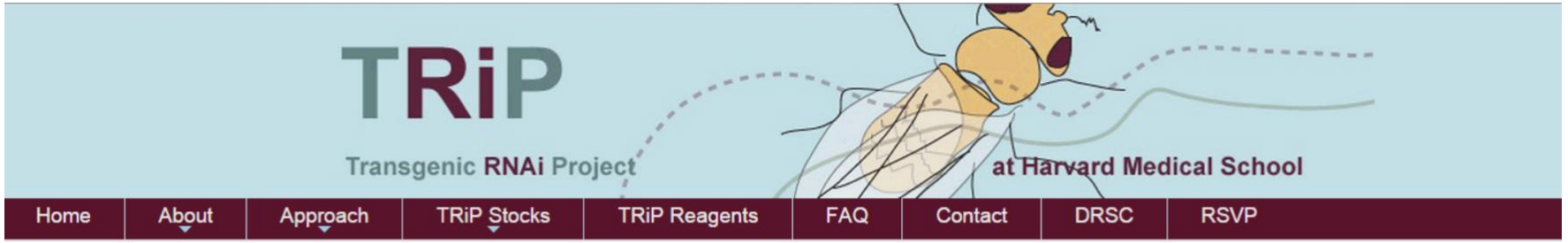
Vienna Drosophila resource center (VDRC)



Reason 8: Many genetic tools available

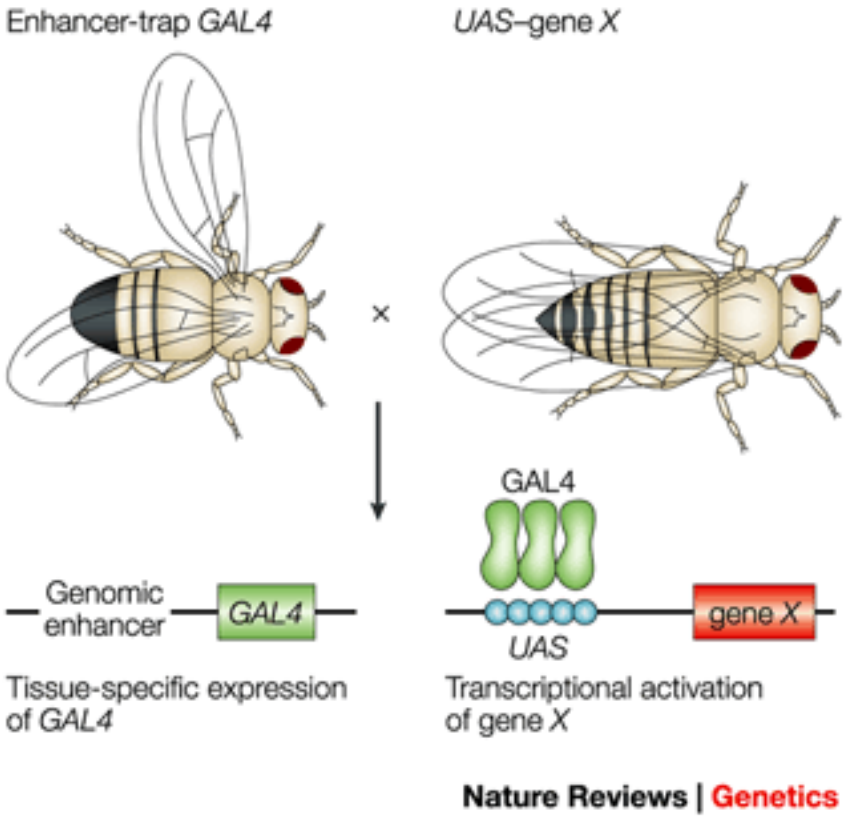
RNAi collections available

Transgenic RNAi Project (TRiP) at Harvard



Reason 9: The UAS/GAL4 system

Developed by the lab of Norbert Perrimon at Harvard
Published in 1994
GAL4 is a yeast transcription factor



UAS = upstream activation sequence

Figure from Johnston (2002) *Nature Reviews Genetics* **3**, 176-188

Reason 9: The UAS/GAL4 system

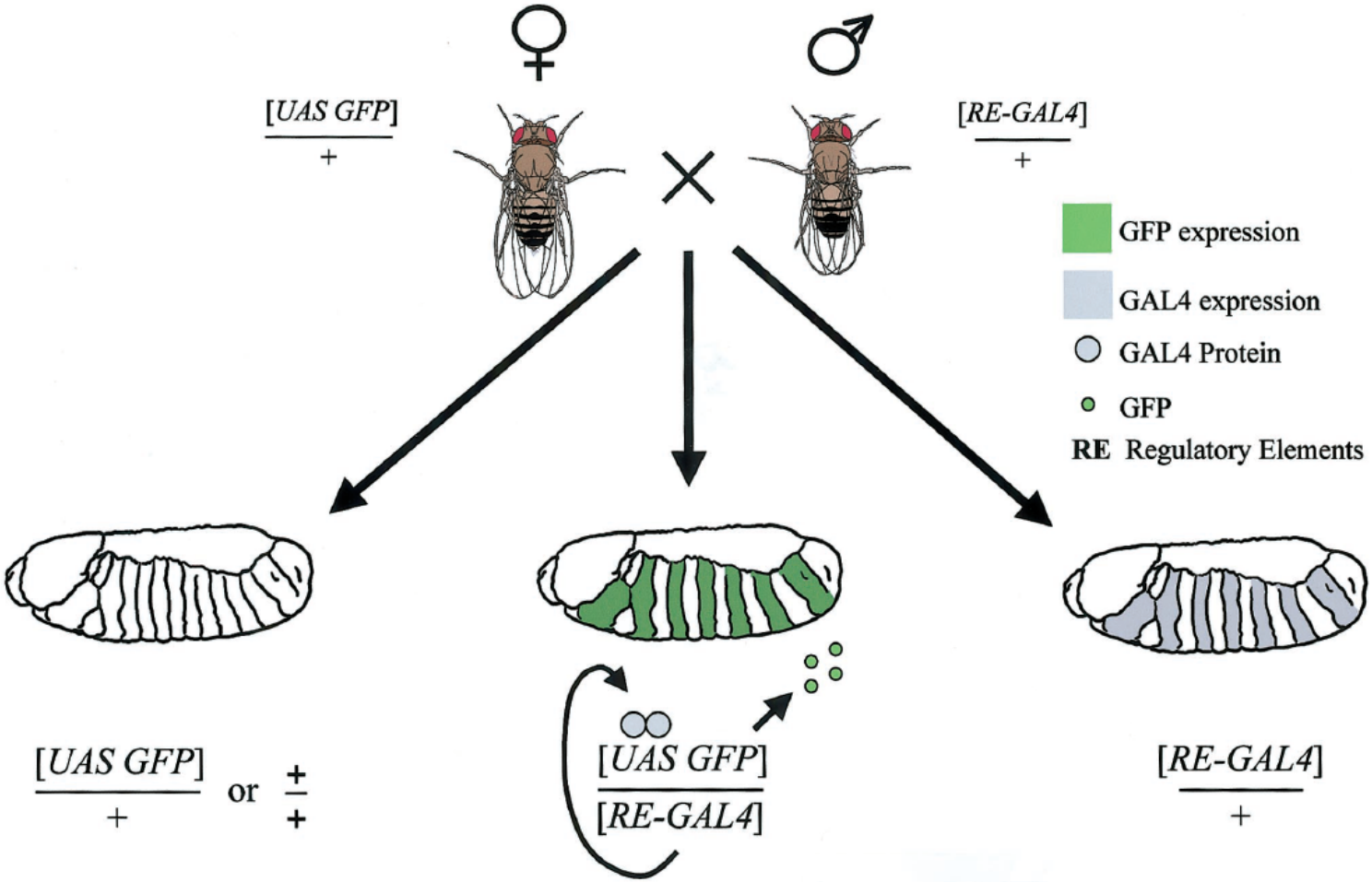
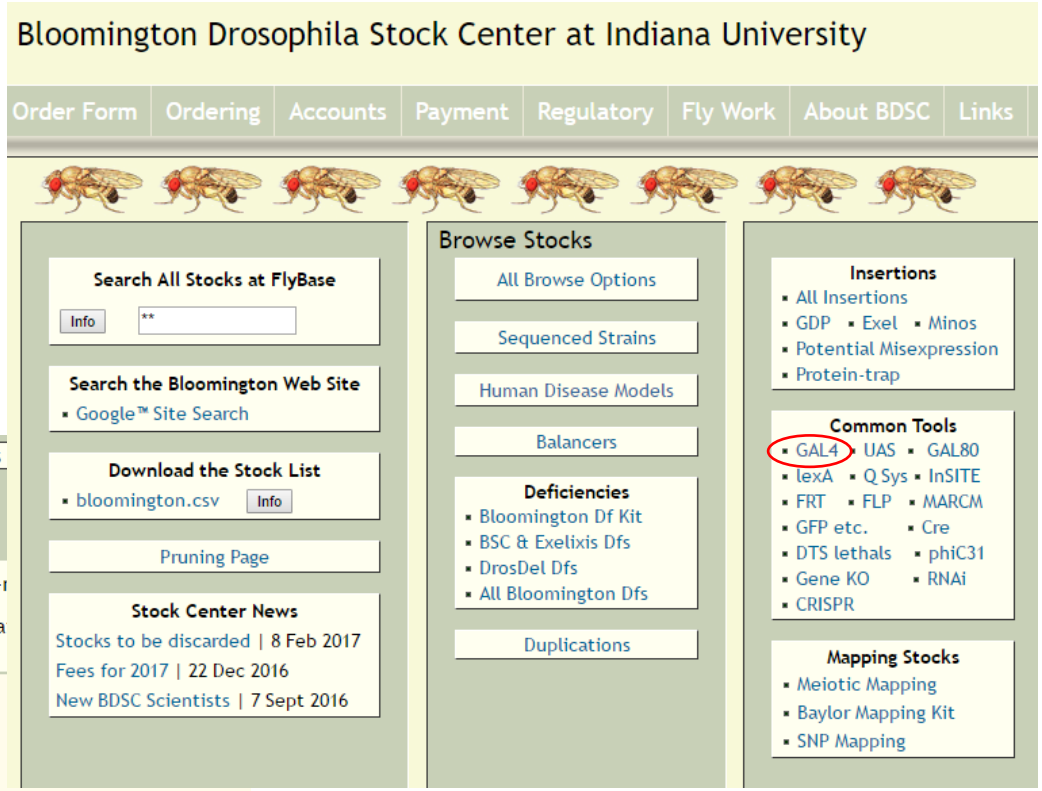
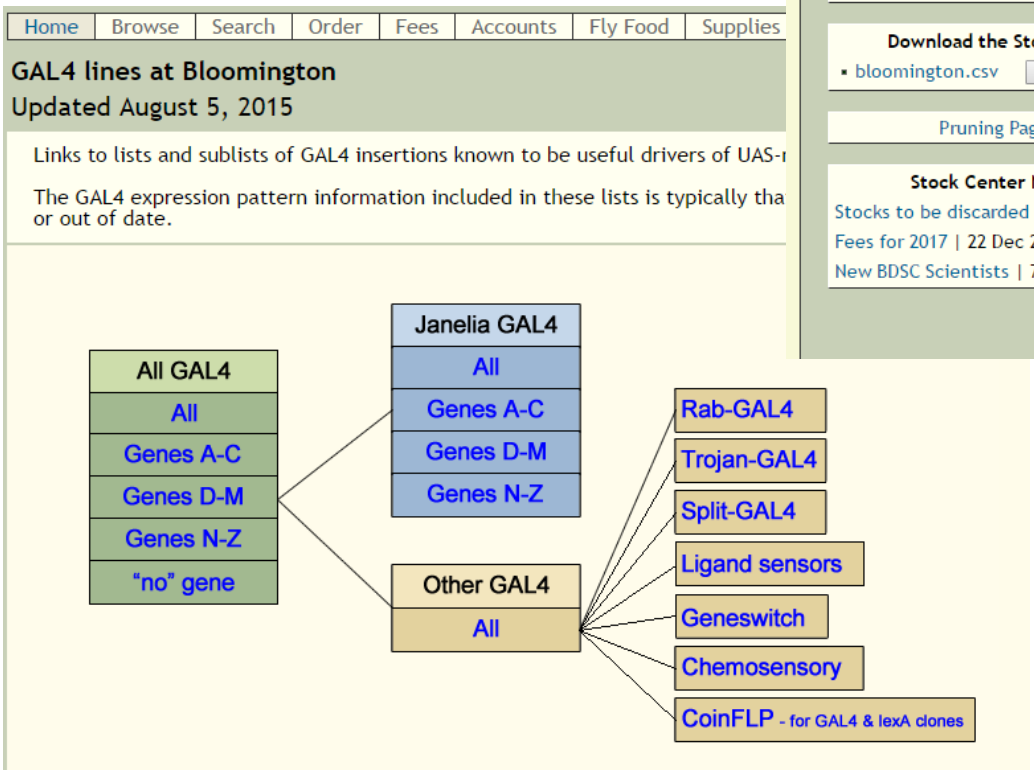


Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

You can buy a fly line carrying a GAL4 under the control of the promoter of your favorite gene



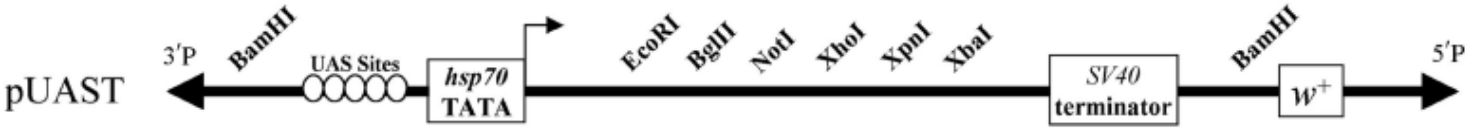


Reason 9: The UAS/GAL4 system

Generating your gene-of-interest downstream of a UAS sequence

Steps:

1. Cloning of your gene-of-interest into a vector
   -Various vectors available



2. Injection of vector into fly egg
   -Many companies do that for you
   Random insertion or site-specific insertion using integrase ϕC31
3. Select transgenic flies using marker
   -Red eye color, body color etc.

Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

Hormone-responsive GAL4 induction known as *GeneSwitch*

Gal4-hormone chimeras

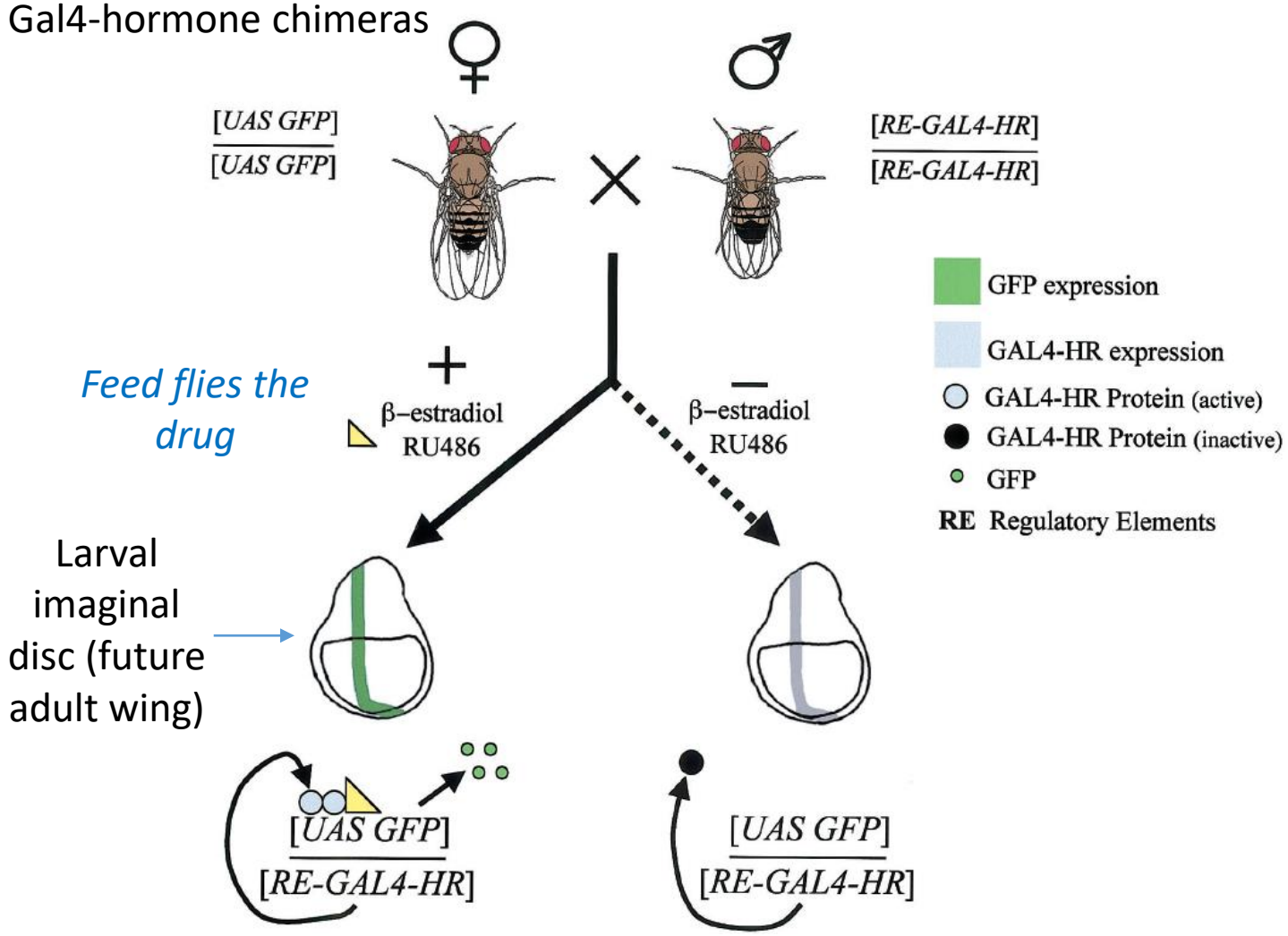


Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

GAL4 induction with the FLP/FRT system using a *Flp-out* cassette

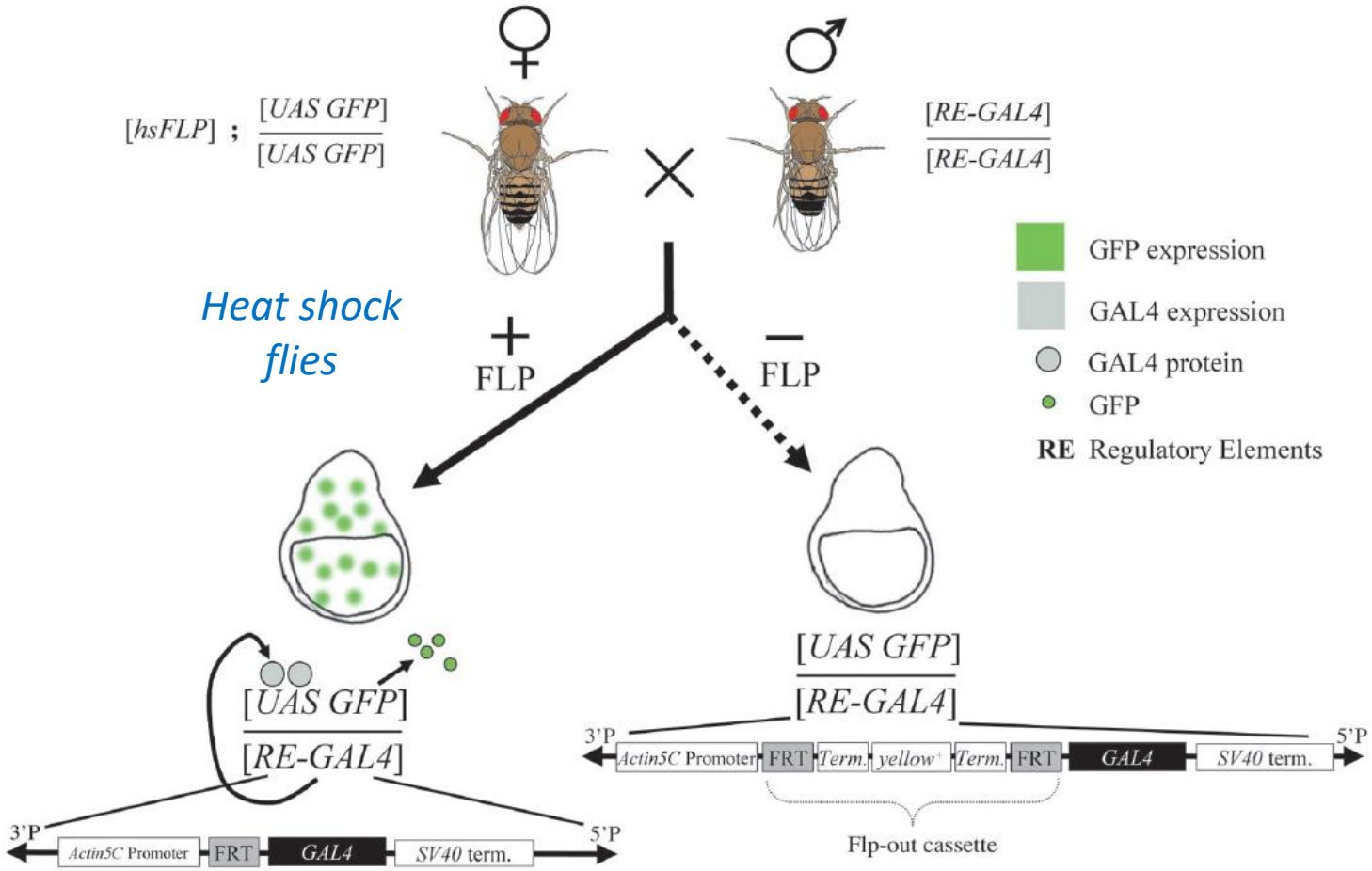


Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

UAS responder induction with the FLP/FRT system using a *Flp-out* cassette

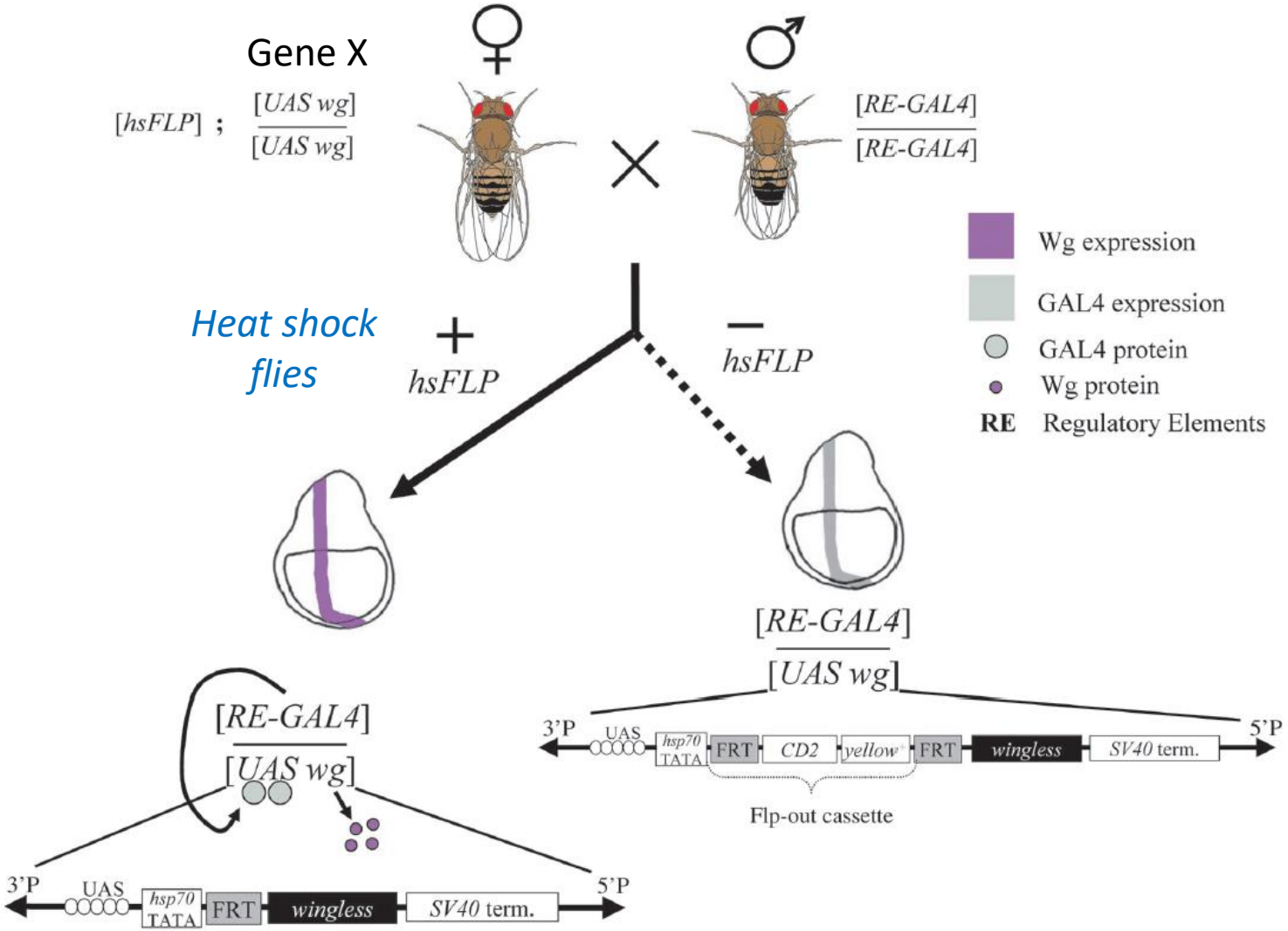
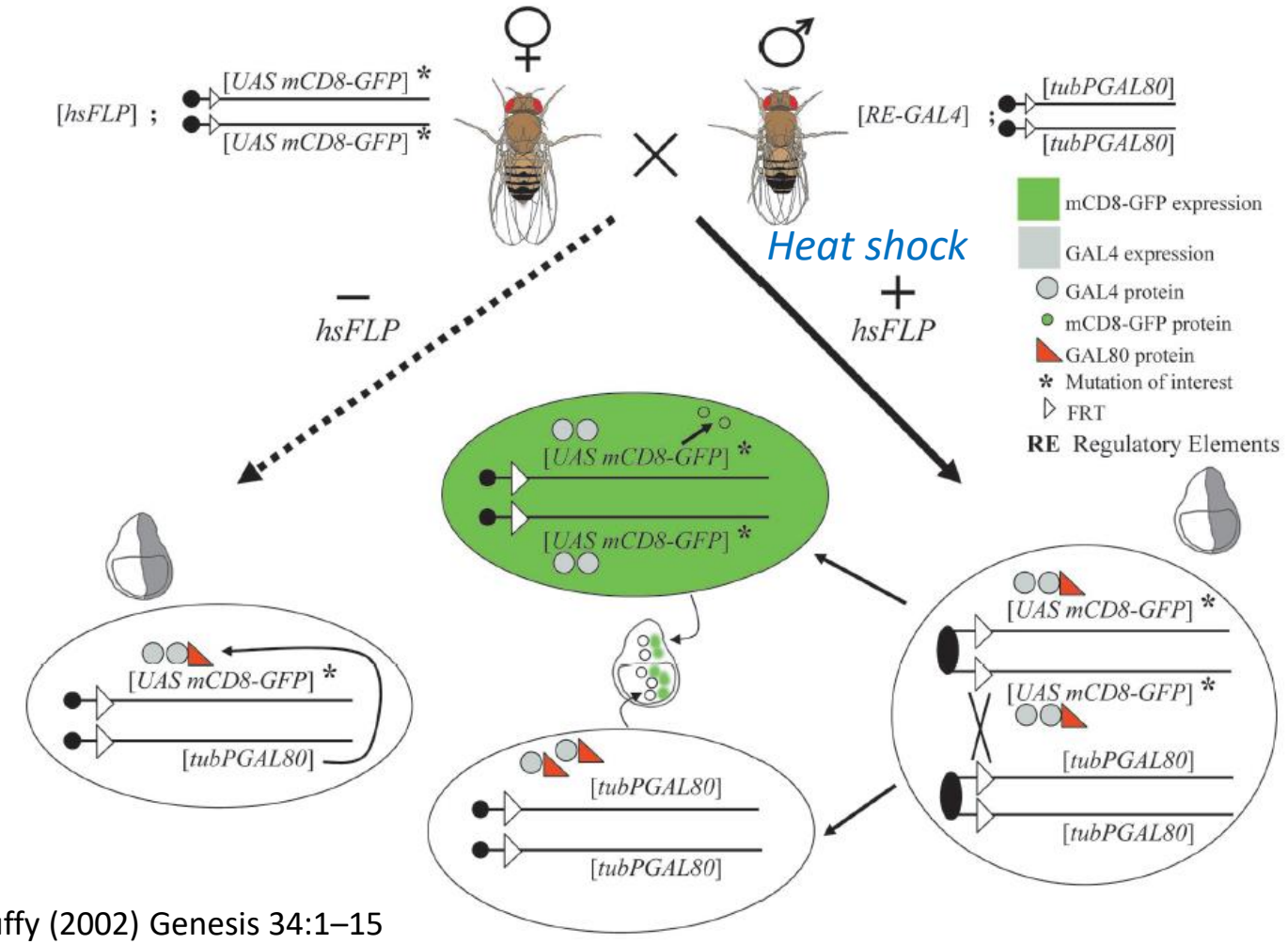


Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

Clonal analysis using MARCM
(Mosaic Analysis with a Repressible Cell Marker, Lee and Luo 1999)
- combines the GAL4/UAS, GAL80, and FLP/FRT systems to label the mutant cells



Gal80 = Gal4 inhibitor

Figure from Duffy (2002) Genesis 34:1–15

Reason 9: The UAS/GAL4 system

Scheme of the TARGET system used to control expression of UAS-mRFPHtt^{Q138} in *escargot*+ cells (ISC/EBs)

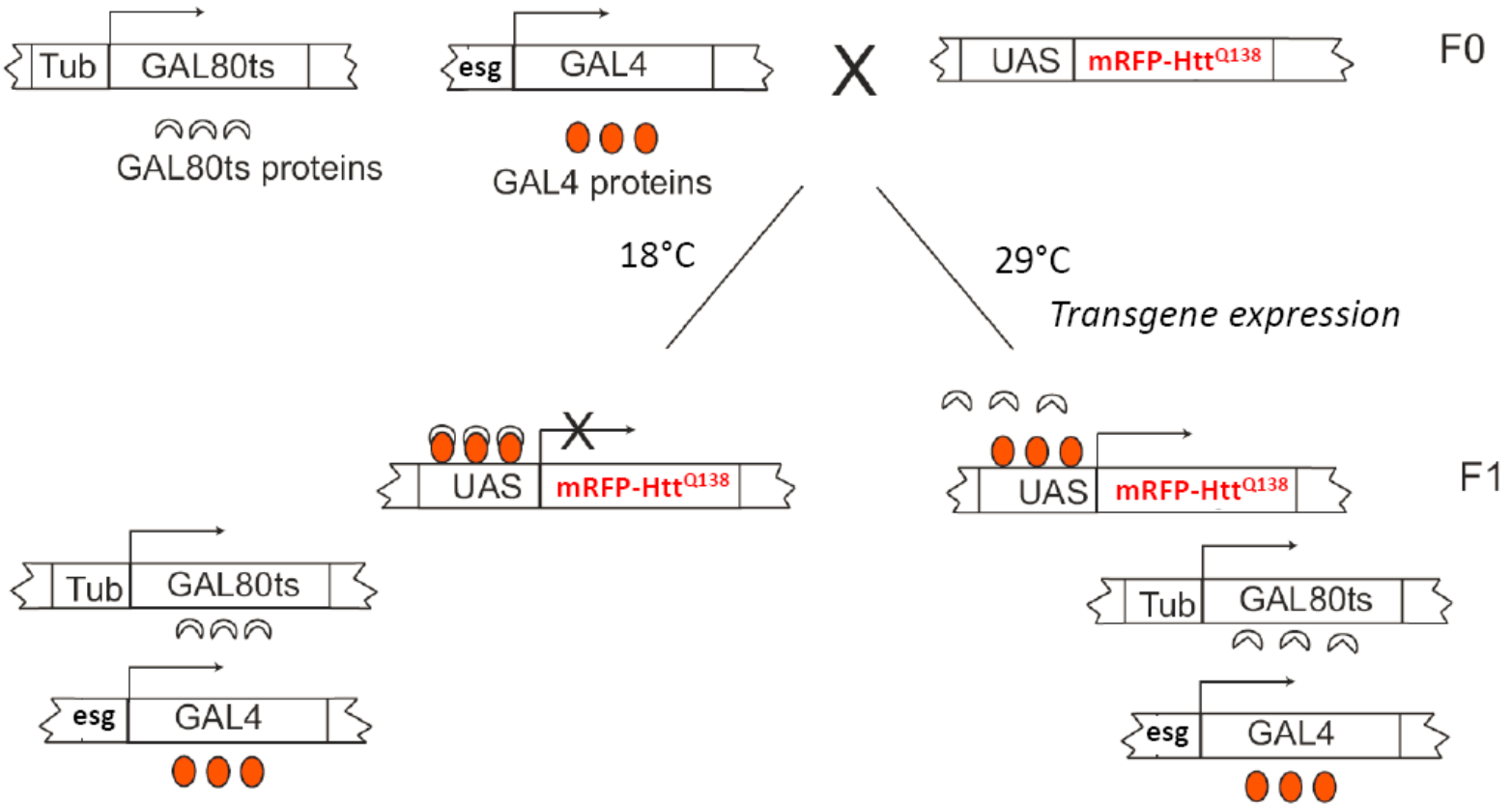


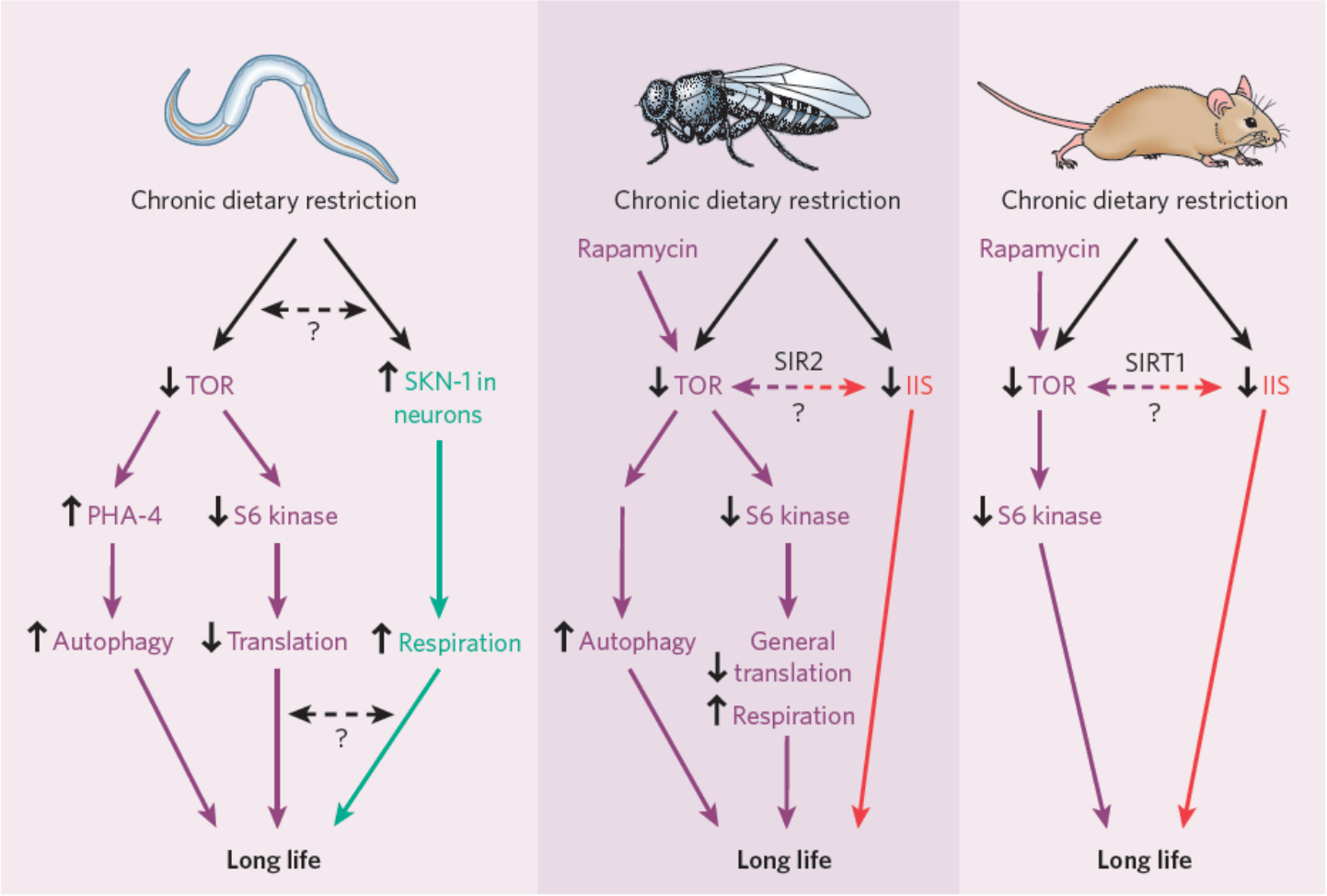
Figure modified from Wang and Zhong (2004) *Science Signaling* (220), p 5.
TARGET - temporal and regional gene expression targeting

Reason 9: The UAS/GAL4 system

- **Tissue-specific** expression
  - Using tissue-specific Gal4 driver
- **Temporal-controlled** expression
  - Drug-inducible system
  - Temperature-sensitive Gal80
- Generation of **Mosaics**
  - MARCM
    - To study cell autonomous function
- Combine with transgene encoding RNAi's
- Allows large-scale screenings
  - When looking for modifiers of your gene-of-interest or for a particular phenotype

Reason 10: You can study aging

Pathways that influence lifespan extension in response to chronic dietary restriction



Kenyon (2010) Nature 464: 504-512

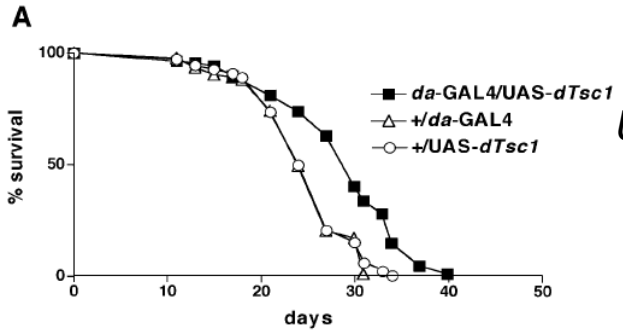
Reason 10: You can study aging

Current Biology, Vol. 14, 885–890, May 25, 2004, ©2004 Elsevier Ltd. All rights reserved. DOI 10.1016/j.cub.2004.03.059

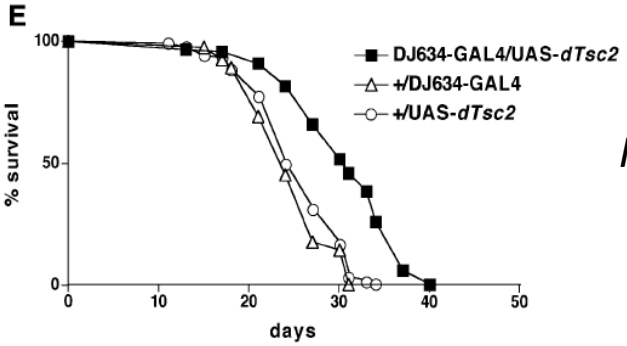
Regulation of Lifespan in *Drosophila* by Modulation of Genes in the TOR Signaling Pathway

Pankaj Kapahi, Brian M. Zid, Tony Harper, Daniel Koslover, Viveca Sapin, and Seymour Benzer*
Division of Biology 156-29
California Institute of Technology
Pasadena, California 91125

Overexpression of TOR inhibitor extends lifespan

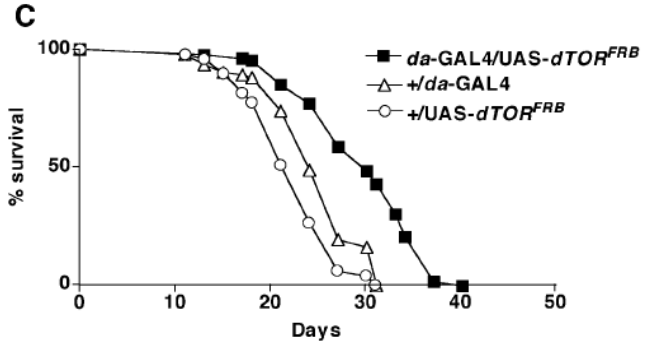


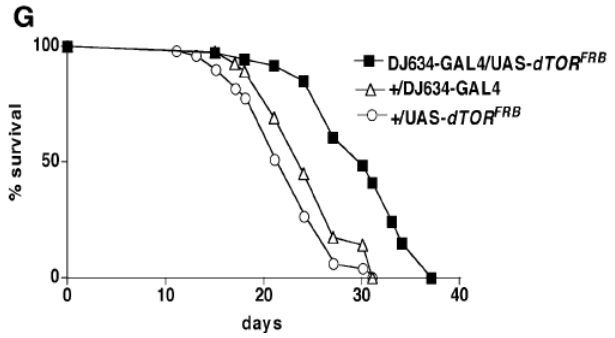
Ubiquitous expression



Fat body only expression

TOR DN inhibitor extends lifespan





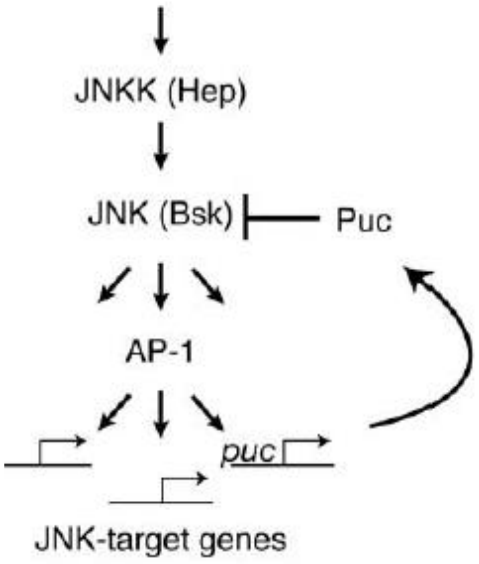
Reason 10: You can study aging

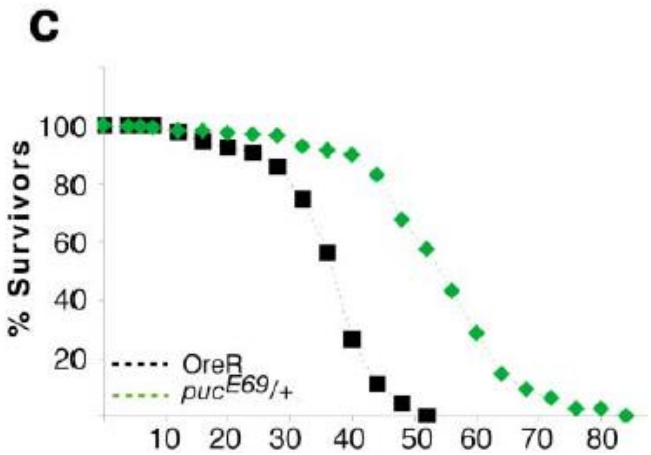
Developmental Cell, Vol. 5, 811–816, November, 2003, Copyright ©2003 by Cell Press

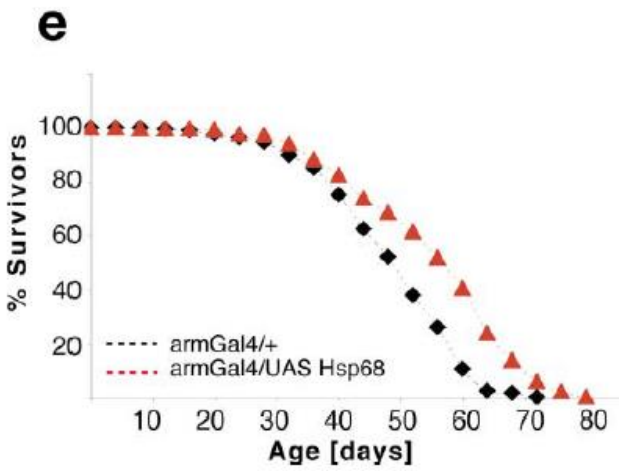
JNK Signaling Confers Tolerance to Oxidative Stress and Extends Lifespan in *Drosophila*

Meng C. Wang, Dirk Bohmann,* and Heinrich Jasper*
Department of Biomedical Genetics
University of Rochester Medical Center
601 Elmwood Avenue, Box 633
Rochester, New York 14642

Increased JNK Signaling Extends Lifespan







Reason 10: You can study aging

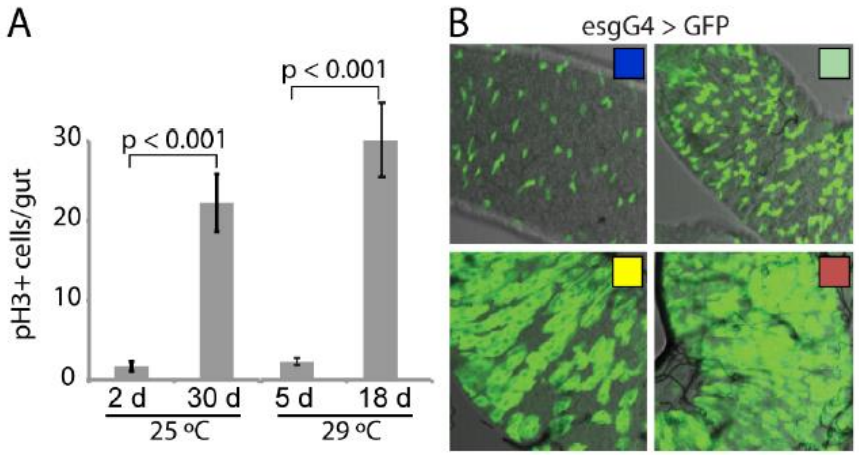
OPEN ACCESS Freely available online

PLoS GENETICS

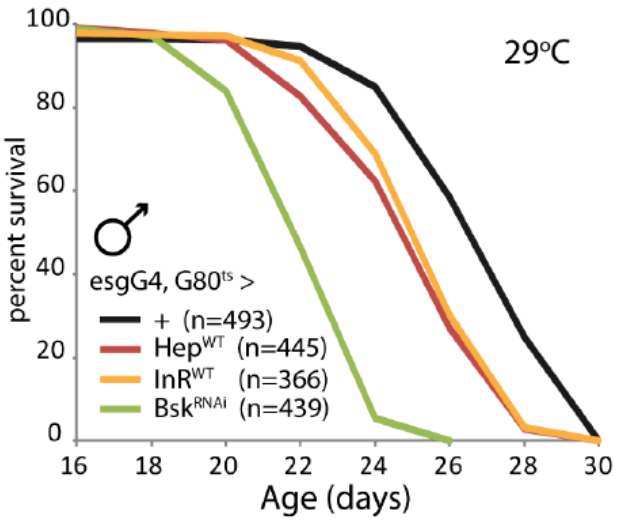
Lifespan Extension by Preserving Proliferative Homeostasis in *Drosophila*

Benoît Biteau[1☯], Jason Karpac[1☯], Stephen Supoyo[1], Matthew DeGennaro[2], Ruth Lehmann[2], Heinrich Jasper[1*]

Age-related increase in the frequency of mitotic cell in the aging intestine of wild-type flies

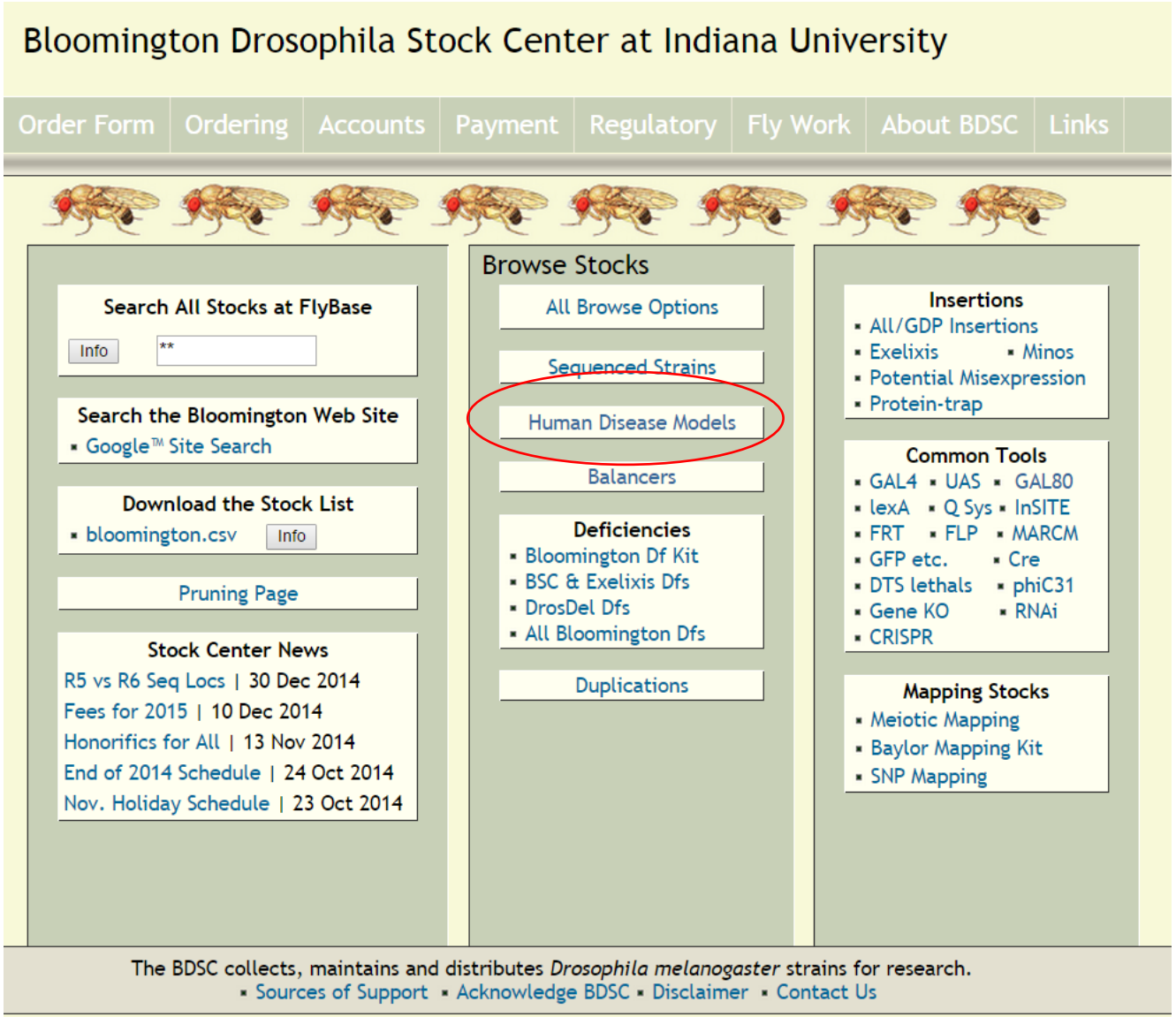


Flies with impaired intestinal homeostasis and regeneration are short lived



Reason 10: You can study many human diseases

http://flystocks.bio.indiana.edu/



Reason 10: You can study many human diseases

Home | Browse | Search | Order | Fees | Accounts | Fly Food | Supplies | Import Permits

Drosophila and Human Disease
Updated January 16, 2015

Bloomington Drosophila Stock Center INDIANA UNIVERSITY

An increasing number of fly lines are being developed which faithfully model various aspects of human disease and human health-related processes. Listed on these pages (see links below) are fly stocks available at Bloomington which can be used to study a variety of human diseases as well as human health-related subjects such as metabolism.

In addition to characterized fly models of human disease, we may also list putative orthologues for disease-associated genes not yet studied in flies, as well as stocks for studying associated genes and pathways. We identify orthologues using a variety of tools, including Homologene and DIOPT, the literature and our own BLAST searches. You should confirm orthology using your own favorite method. Be advised that inferring function from sequence/phylogeny-based orthology is often, but not always, a valid assumption.

....

Disease	Representative OMIM ID (Online Mendelian Inheritance in Man)
Alzheimer disease	MIM# 104300
Angelman syndrome	MIM# 105830
Amyotrophic lateral sclerosis	MIM# 105400
Cardiovascular diseases	
Coffin-Lowry Syndrome	MIM# 303600
Cornelia de Lange Syndrome	MIM# 122470
Fragile X Syndrome	MIM# 300624
Frontotemporal dementia and/or Amyotrophic lateral sclerosis	MIM# 105550
Galactosemia	MIM# 230400
Glycerol kinase deficiency	MIM# 307030
Hereditary spastic paraplegia	MIM# 182600
Huntington disease	MIM# 143100
Hypoparathyroidism-retardation-dysmorphism syndrome (HRD)	MIM# 241410
Machado-Joseph Disease (aka MJD; Spinocerebellar Ataxia 3; SCA3)	MIM# 109150
Metabolism/Diabetes/Obesity	
Microcephaly, primary	MIM# 251200
Mitochondrial-related disorders	
Muscular dystrophies	
Neurofibromatosis, type I	MIM# 162200
Neuronal ceroid lipofuscinosis	MIM# 256730
Niemann-Pick disease	MIM# 257220
P-type ATPase disorders	
Parkinson disease	MIM# 168600

Drosophila and Human Disease
Updated December 15, 2016

An increasing number of fly lines are being developed which faithfully model various aspects of human disease and human health-related proce
a variety of human diseases as well as human health-related subjects such as metabolism.

In addition to characterized fly models of human disease, we may also list putative orthologues for disease-associated genes not yet studied in
tools, including Homologene and DIOPT, the literature and our own BLAST searches. You should confirm orthology using your own favorite meth
valid assumption.

IMPORTANT - In some instances, not every available stock for a particular gene is listed. See here for a list of our inclusion/exclusion criteria. F
the full list of available lines on the relevant FlyBase gene page.

These pages are a work in progress and we welcome any and all input. If you see any errors, notice missing genes or stocks, have suggestions or
BDSC, please contact us.

Download a csv or Excel (xlsx) file containing all the disease gene stocks found on these pages with a column that includes the full genotype of

Outside resources:
DRSC Disease Gene Query (DIOPT-DIST) - a query tool for associating human disease and related human genes with orthologues in fly, mouse, C.
a table that includes disease, associated human gene and the fly orthologue
Drosophila Models of Human Disease - a blog for fly models of human disease with a focus on reporting new key papers, new resources (e.g. fly
Homophila - a database of OMIM-derived human disease genes and their fly homologs
LAMHDI - a database of animal strains and stocks (including Drosophila) associated with human disease
Bonini neurodegeneration list - a list of fly mutants with neurodegenerative phenotypes from Lessing and Bonini (2009).
Tennessen metabolism gene list - a list of genes predicted to function in metabolic pathways from Jason Tennessen.

Disease	Representative OMIM ID (Online Mendelian Inheritance in Man)
Alzheimer disease	MIM# 104300
Angelman syndrome	MIM# 105830
Amyotrophic lateral sclerosis	MIM# 105400
Cardiovascular diseases	
Coffin-Lowry Syndrome	MIM# 303600
Cornelia de Lange Syndrome	MIM# 122470
Fragile X Syndrome	MIM# 300624
Frontotemporal dementia and/or Amyotrophic lateral sclerosis	MIM# 105550
Galactosemia	MIM# 230400
Glycerol kinase deficiency	MIM# 307030
Hereditary spastic paraplegia	MIM# 182600
Huntington disease	MIM# 143100
Hypoparathyroidism-retardation-dysmorphism syndrome (HRD)	MIM# 241410
Machado-Joseph Disease (aka MJD; Spinocerebellar Ataxia 3; SCA3)	MIM# 109150
Metabolism/Diabetes/Obesity	
Microcephaly, primary	MIM# 251200

Alzheimer disease

Bloomington Drosophila Stock Center INDIANA UNIVERSITY

Alzheimer disease is the most common cause of degenerative dementia in the elderly. The causes of late-onset Alzheimer disease are unclear; risk factors such as mutations in the APOE gene may be involved. Mutations in three genes have been associated with early-onset Alzheimer disease - APP, PSEN1, and PSEN2. Fly stocks in the Bloomington collection that can be used to study Alzheimer Disease are listed here.

General Information links for Alzheimer disease:
OMIM (see also links in table below)
NIH's Genetics Home Reference - includes links for GHR pages on APOE, APP, PSEN1 and PSEN2
NLM/NIH's Genetic and Rare Disease Information Center

Genes for studying Alzheimer disease			
Human gene(s)	**Human full name**	**Fly gene**	**OMIM link and/or comments**
APH1A and APH1B	Anterior pharynx defective 1A and 1B	anterior pharynx defective 1 (aph-1)	gamma-secretase complex member

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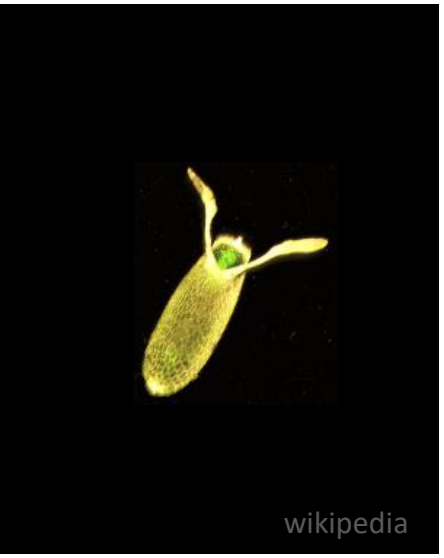
Relevant gene in stock	Fly disease model or related mutation or transgene	Stk #	Comments
Fly *aph-1* stocks			
aph-1	P{TRiP.HMS01693}attP40	38249	Expresses dsRNA for RNAi of aph-1 (FBgn0031458) under the control of UAS.
aph-1	aph-1[D35]	3917	aph-1 mutation (R99 change results in truncation of the protein between transmembrane domains 3 and 4)
Stocks carrying human *APP*			
APP	P{UAS-APP695-N-myc}TW6	6700	Expresses human amyloid precursor protein with an amino terminal myc tag under UAS control.
APP	P{UAS-APP.YFP}LG	32039	Expresses YFP-tagged human APP under the control of UAS.
APP	P{UAS-APP.695.Exel}5	33795	Expresses the 695 amino acid isoform of human APP under the control of UAS.
APP	P{UAS-APP.695.Exel}3	33796	Expresses the 695 amino acid isoform of human APP under the control of UAS.
APP - Dutch	P{UAS-APP.695.E693Q.Exel}9	33790	Expresses the 695 amino acid isoform of human APP carrying the familial Alzheimer's 'Dutch' mutation (E693Q - amino acid numbering based on APP sequence) under the control of UAS.
APP - Dutch	P{UAS-APP.695.E693Q.Exel}5	33789	Expresses the 695 amino acid isoform of human APP carrying the familial Alzheimer's 'Dutch' mutation (E693Q - amino acid numbering based on APP sequence) under the control of UAS.
APP - Dutch and French	P{UAS-APP.770.E693Q.V715M.myc.VTR}4	33791	Expresses the 770 amino acid isoform of human APP carrying the familial Alzheimer's 'Dutch' (E693Q) and 'French' (V715M) mutations (amino acid numbering based on APP sequence) under the control of UAS.
APP - Dutch and German	P{UAS-APP.770.E693Q.V715A.myc.VTR}3	33792	Expresses the 770 amino acid isoform of human APP carrying the familial Alzheimer's 'Dutch' (E693Q) and 'German' (V715A) mutations (amino acid numbering based on APP sequence) under the control of UAS.
APP - London	P{UAS-APP.V717F.LOND}LG	32036	Expresses human APP carrying the London mutation (V717F) under the control of UAS.
APP - Swedish	P{UAS-APP695-Swedish-N-myc}TS23	6701	Expresses human amyloid precursor protein with familial Alzheimer mutations and an amino terminal myc tag under UAS control.
APP - Swedish	P{UAS-APP.770.K670N.M671L.VTR}3	33793	Expresses the 770 amino acid isoform of human APP carrying the familial Alzheimer's 'Swedish' mutation (K670N and M671L - amino acid numbering based on APP sequence) under the control of UAS.
APP - Swedish	P{UAS-APP.770.K670N.M671L.E693G.VTR}7	33794	Expresses the 770 amino acid isoform of human APP carrying the familial Alzheimer's 'Swedish' (K670N, M671L) and 'Arctic' (E693G) mutations (amino acid numbering based on APP sequence) under the control of UAS.

Thanks!



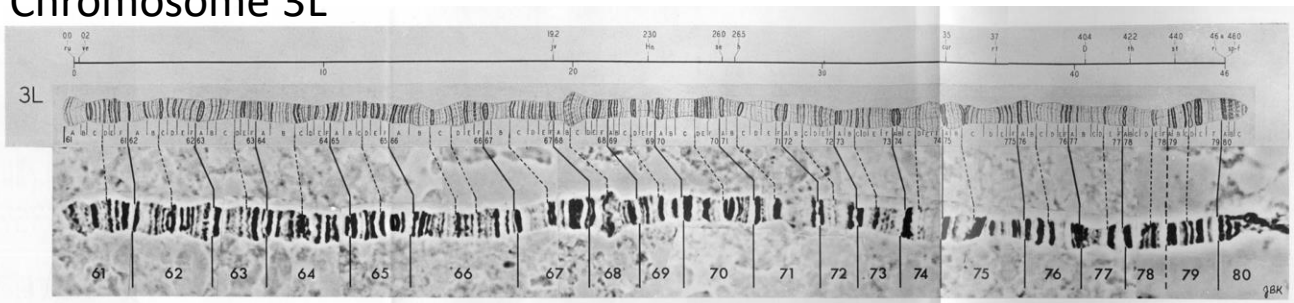
Questions?

Extra

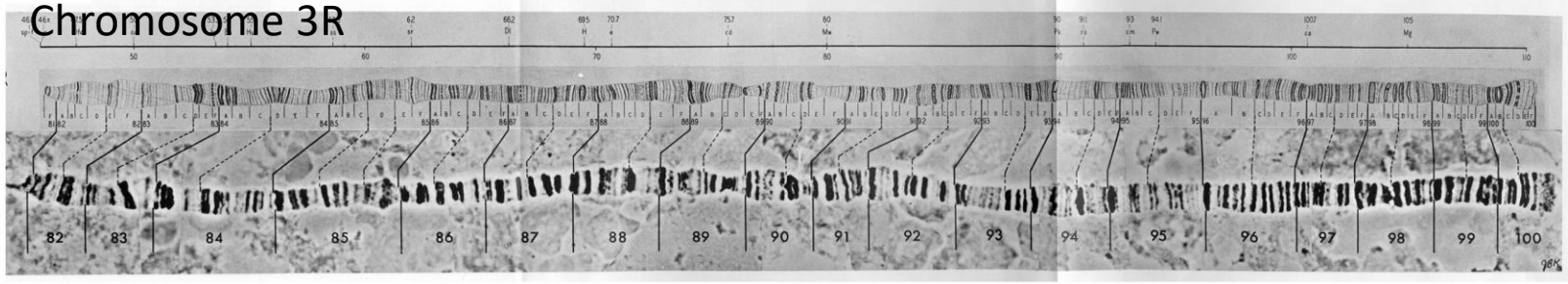
Polytene chromosomes of *Drosophila melanogaster* as sketched by Calvin B. Bridges in 1935

Calvin Blackman Bridges, 1927.
Photo courtesy of Cold Spring Harbor Laboratory Archives.

Chromosome 3L



Chromosome 3R



Images from The Interactive Fly

Bridges, C.B. (1935). *Salivary chromosome maps with a key to the banding of the chromosomes of Drosophila melanogaster*. J. Hered. 26: 60-64.

Handling

- Easily anesthetized by CO_2 or cold
- Need relatively inexpensive equipment
  - Dissecting microscope
  - Brushes
  - CO_2 tank connected to a porous plastic pad
  - Bottles or vials with food
  - Bottle with ethanol to discard unwanted flies

Fits 4 standard wide trays per shelf.

Images from Flystuff.com

A typical day in the fly room…

Images: Nana Shimosako thenode.biologists; Kathryn Orzech tolweb.org; unc.edu the wonderful fruit fly