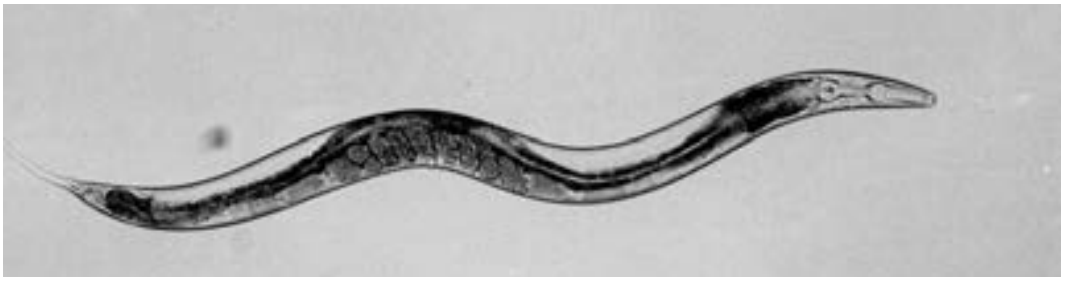
Bohemian Rhapsody Parody (Worm Show)

http://www.youtube.com/watch?v=g_Agq0r63CQ&feature=related



Caenorhabditis elegans: a roundworm (nematode)

Biology 322 Fall 2012 : *Course Business*

Dr. Carol Trent trent@biol.wwu.edu
Office Hours: Tues & Thurs 10:30-11:30am or by appointment

Course Web Site:
http://fire.biol.wwu.edu/trent/trent/Biol322index.html
See Required Reading Assignment entitled ***Inspired Choices***

Course content: In this course, we will examine various topics in genetics using four different model organisms:

- the small, free-living nematode ***Caenorhabditis elegans***,
- the diminutive mustard ***Arabidopsis thaliana,***
- the charming jewel wasp ***Nasonia vitripennis*****,**
- the gutsy bacterium ***Escherichia coli.***

We will use the first three organisms to explore topics relating to eukaryotic genetics and we will use *Escherichia coli* to explore basic concepts in mutagenesis and prokaryotic gene exchange

Lab manual: In lieu of a laboratory manual, each week you will be provided with handouts describing the laboratory exercises or experiments to be performed. ***You should have a basic genetics text handy for the duration of the quarter. See links to online texts on the course web site.***

More on Course Objectives

Content goals:

(i.)You should understand and be able to apply classical genetic and molecular genetic principles in a laboratory setting. Specifically, you should obtain a reasonably sophisticated understanding of several major aspects of genetics, including Mendelian genetics, prokaryotic genetics, and molecular genetics.

(ii.) You should acquire skills in handling model organisms, keeping detailed research records, analyzing data and writing scientific reports.

Process goals:

(i.) You should improve your critical thinking skills through the analysis of experimental data using statistics and probability.

(ii.) You should improve your quantitative reasoning skills.

(iii.) You should improve your written communication skills.

Lab periods:

Prior to each lab period, you are required to write, in your own words, an a summary of what we will be doing in that that day. You will submit your summary via a Google.doc form no later than noon on the day of the lab period. ***Your first google submission will be due on Tuesday Oct 2 by noon.***

Most of the work involved in the assignments will be performed during the scheduled lab periods. Occasionally you may be required to come to the lab at other times to set up crosses and score progeny. At the beginning of each lab period we will have a short discussion over what will be done that day and whether any work outside the scheduled lab period will be necessary.

Lab and lecture attendance is mandatory. Unexcused absences are unacceptable.

Assignment Type	Name		
			Due Date
Homework 1	Mendel Revisited	15	2-Oct
Homework 2	Mendel ChiSquare	15	
Lab Report	Online Databases MLH1	15	
Lab Report	aha genotyping	30	
Lab Data Workup	Mutation rates	15	
Homework 3	Forward Mutagenesis	20	
Lab Data Workup	Nasonia Genotypes	15	
Lab Report	RifR Sequence analysis	35	
In Class Presentat	Forward Mutagenesis	20	
	Total Points	180	
Class Participation		25	
Lab Notebookd & Google Forms		100	
Quiz	Quiz 1		
Quiz	Quiz 2		
Exam	Final Quiz		
	Total	125	
	GRAND TOTAL	430	

The quizzes will be designed to test your understanding of the laboratory exercises and lecture material and ***will be announced ahead of time.***

The number of points you receive for "***class participation***" will depend on your interest and participation in the laboratory exercises and class discussions. In other words, just showing up for every lab will not guarantee a 25-point score. Allocation of points will be influenced by your

- punctuality (are you always on time?)
- engagement (are you focused upon the lab or more interested in socializing?)
- organization, safe behavior, and consideration of other students.

DG-Women-Closed-toe-slip-
284 × 321 - D&G **Closed-toe Shoes**
mycolorfashion.com

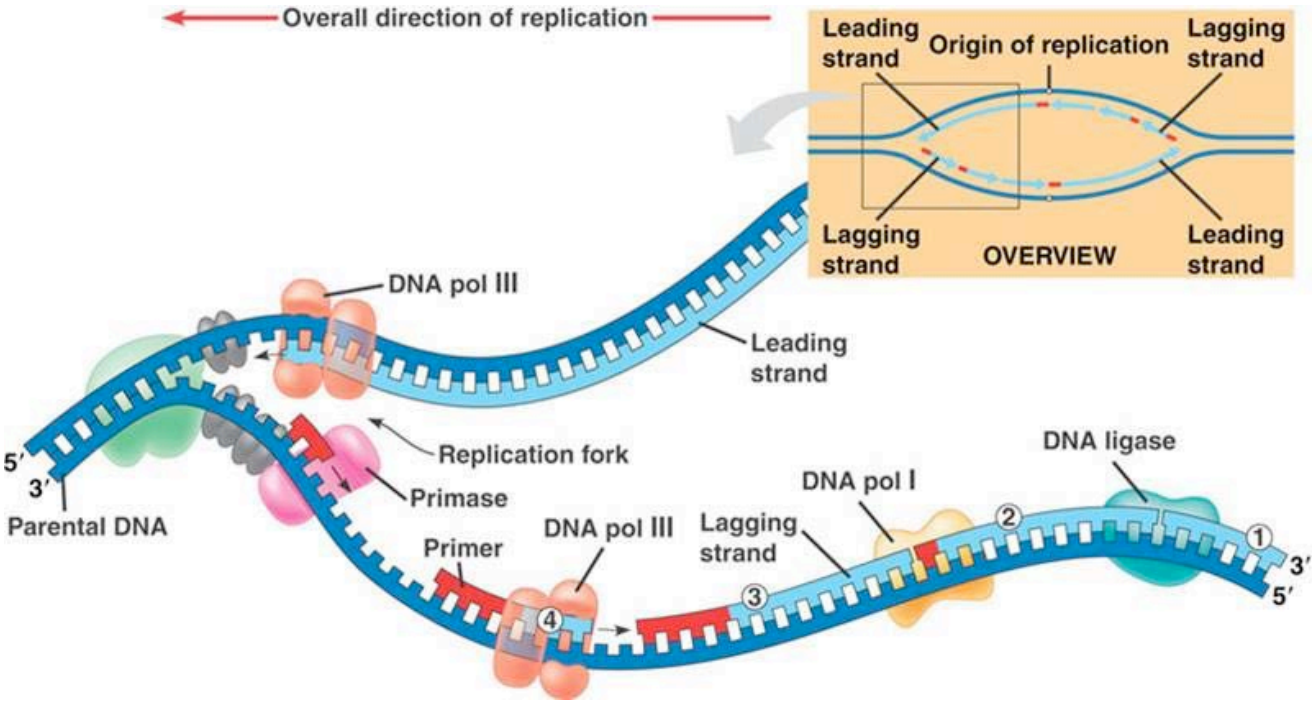
Lab Dress Code: You are absolutely required to wear ***closed-toed shoes*** while working in the laboratory. For labs where we are running gels laced with ethidium bromide you should wear clothing that protects your legs (no short or skirts) and your arms.

Closed-toed Shoes - Shoes - Product Reviews, Compare Prices, and ...
Shop for **Closed-toed Shoes** Shoes and read product reviews. Find cheap prices on Shoes from a selection of Timberland, Keen, Nomad Footwear, Bordello, ...
www.shopping.com/-**Closed–toed+Shoes** - Cached

Course Timetable

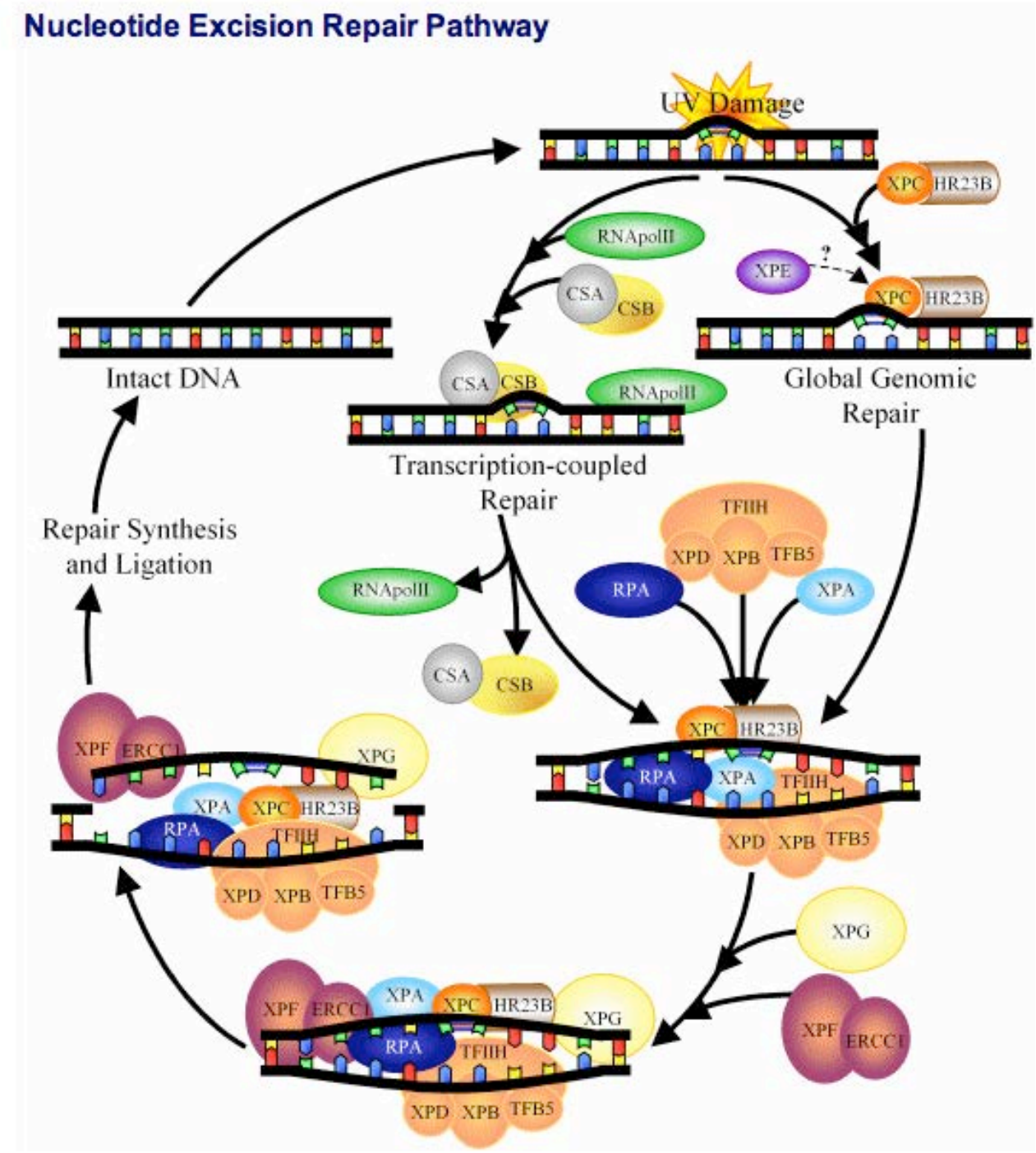
http://fire.biol.wwu.edu/trent/trent/322timetable.pdf

What process is shown here? And how do we know that this is what happens?

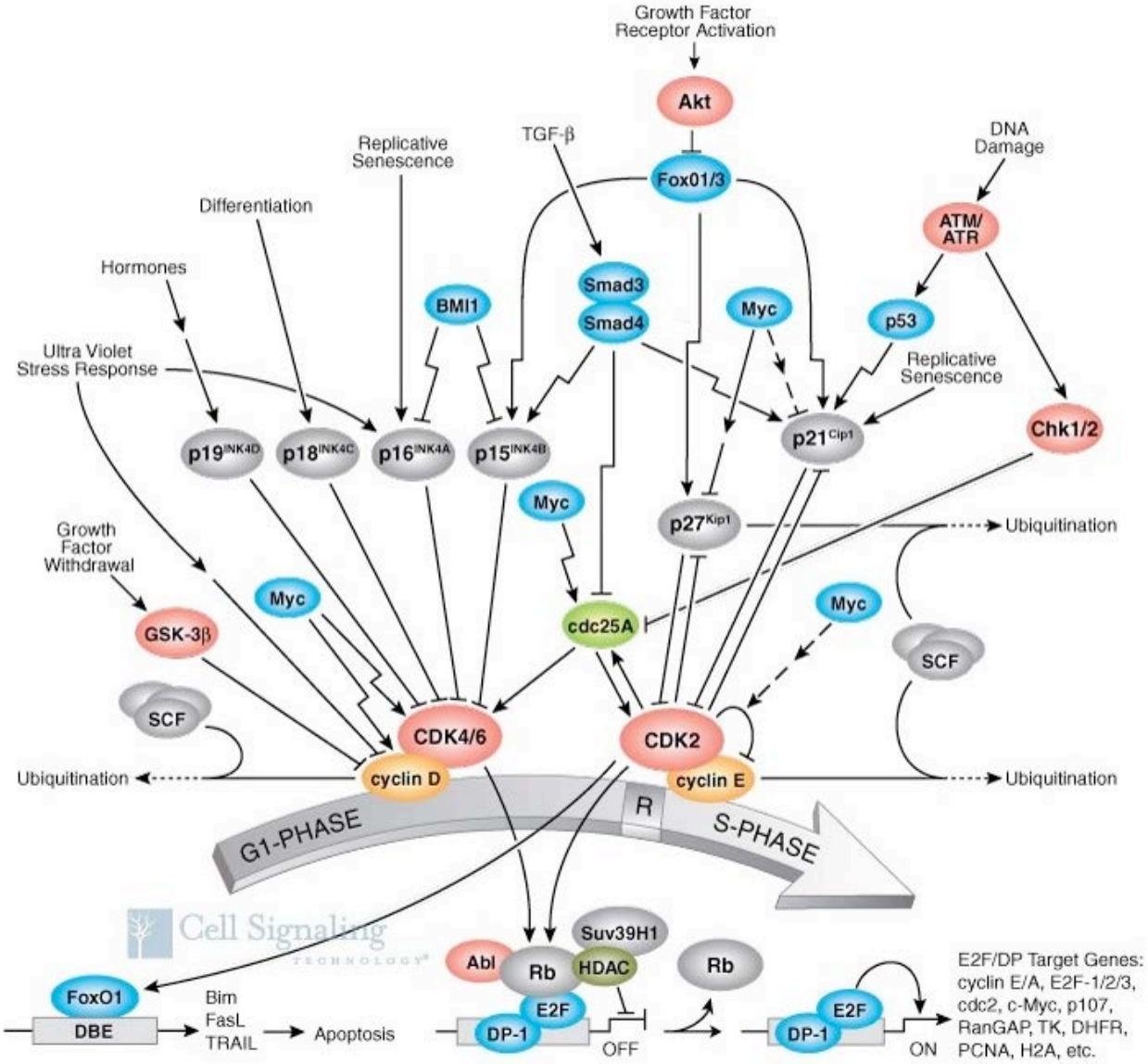


and this?

http://ccr.coriell.org/sections/collections/nigms/ner_pathway.aspx?PgI



What is going on here?
and how do we know it?



http://www.cellsignal.com/reference/pathway/Cell_Cycle_G1S.html

If we start out knowing nuthing about how the cell copies its DNA or controls its progression through the cell cycle

How would you even get a foothold if you were starting at the beginning with no knowledge of any of the genes involved in the process?

We can't study all organisms, so we single out a collection of "model" organisms to study

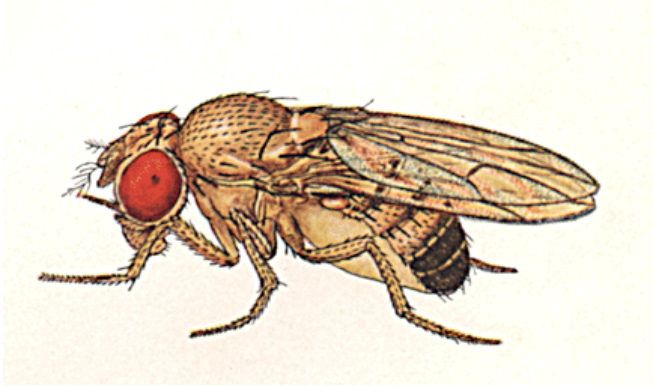
What do we mean by the term model organism?

What does this term imply about the research done on this organism or about the knowledge gained from studying this organism?

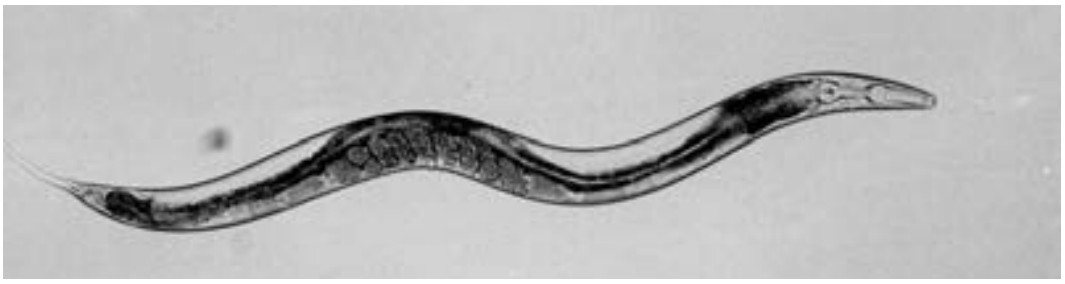
***model system*:**
a label we apply to species that we
http://www.dnalc.org/ddnalc/resources/model_organisms.html

(i) study in detail
(ii) use as a basis for constructing a general understanding of how biological processes work

What organisms are favored by geneticists?



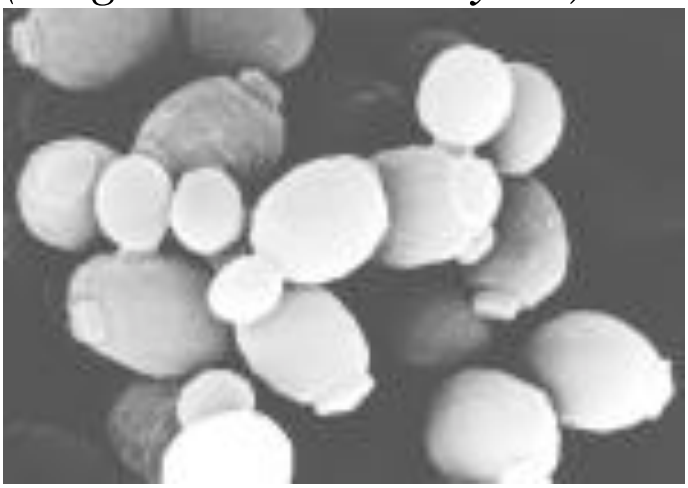
Drosophila melanogaster: a fruit fly



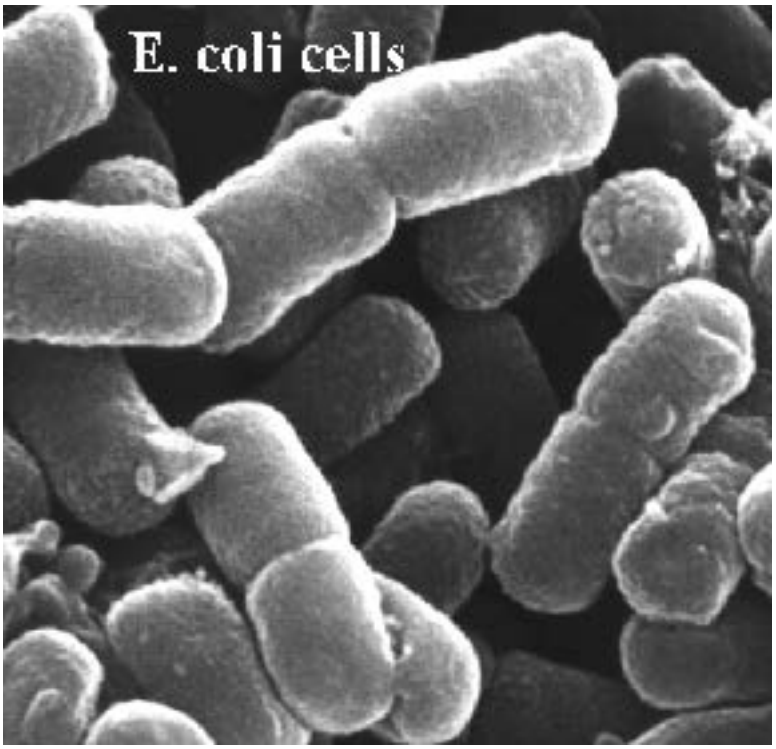
Caenorhabditis elegans: a roundworm (nematode)

small flowering plant in the mustard family
Arabidopsis thaliana

Saccharomyces cerevisiae
(single-celled eukaryote)



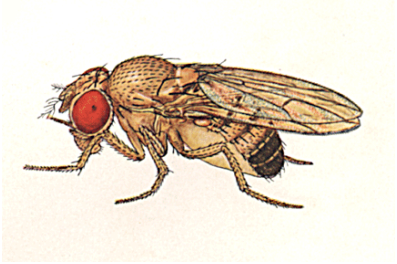
this organism is dear to us because???



Escherichia coli: a gut bacteria (prokaryote)

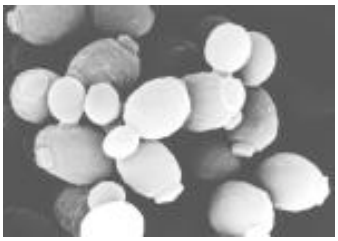
Some Organisms with sequenced genomes

Drosophila melanogaster



Caenorhabditis elegans: free-living roundworm

Saccharomyces cerevisiae: yeast



Arabidopsis thaliana: a weed

What do we mean by a "Sequenced genome?

What question comes to mind when you view these organisms?

Establishing the credibility of using less complex model organisms to learn about more complex organisms or the converse…

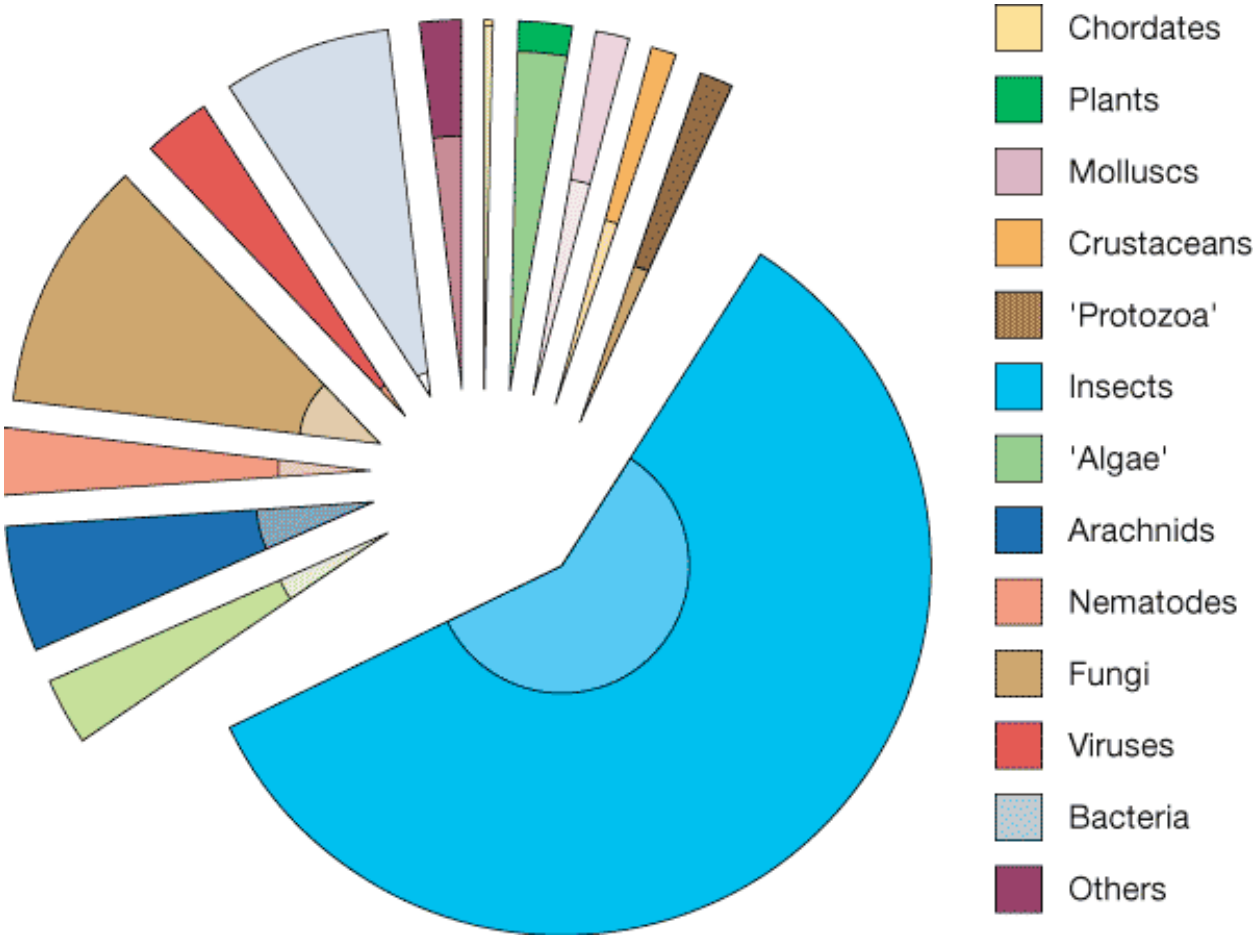
Let's start by considering biodiversity and species numbers:

How many different species are there on earth?

Nature 418: 362 July 25, 2002

" there is currently no concensus on the total number of species: estimates range from 4 million to 100 million….. roughly 1.7 million organisms have been named and formally described"

Figure 4 Species richness in major groups of organisms. The main 'pie' shows the species estimated to exist in each group; the hatched area within each slice shows the proportion that have been formally described. Data from ref.



Nature 405: 212 May 11, 2000

Sarah Palin on the fruit fly

http://www.youtube.com/watch?v=Eg1vIeuQT1s

neurexin 1 & autism

http://www.ncbi.nlm.nih.gov/pubmed/18179900

Okay so convince Sarah: HOW or WHY can what we learn about worms or flies or a plant tell us about how a human functions or what kinds of genes we have?
(see also pgs 27-29 of this lecture)

Justification for the use of these organisms takes the form of two lines of argument:

Practical line of argument

Theoretical line of argument

Reasons for choosing these particular organisms :

- some practical –
- some serendipitous
- some carefully considered
- some related to the importance of the organism to human health and welfare (or commercial value)

What do we mean by practical reasons?

Features of a good genetic model system

✔ = applies to *Caenorhabditis elegans*

- **✔ Small size**
- **✔ Ease of culture (low maintenance)**
- **✔ Short generation time**
- **✔ Large brood size**
- **✔ Easily assayed phenotypes (but what about microorganisms?)**
- **✔ Self-fertilization**
- **✔ Small genome size -- helps with genome scale analyses**
- **✔ Some aspect of the organism (life-cycle, anatomy, etc.) lends itself to scientific inquiry**
- **✔ Has been the subject of prior studies that provide relevant background information: produces significant pool of literature and lab protocols**
- **✔ "Common" organism with may locations and habits (ecological and evolutionary studies)**

Why is a fly or a worm or a plant a credible model system for other organisms?

We can justify the use of these organism based on practical arguments (limited time, space, money, etc.)

But how do we establish the biological (theoretical) credibility for using studying these organisms

In other words, why are less complex organisms credible models for humans and vice-versa?

This argument is based on knowledge of history of life on earth

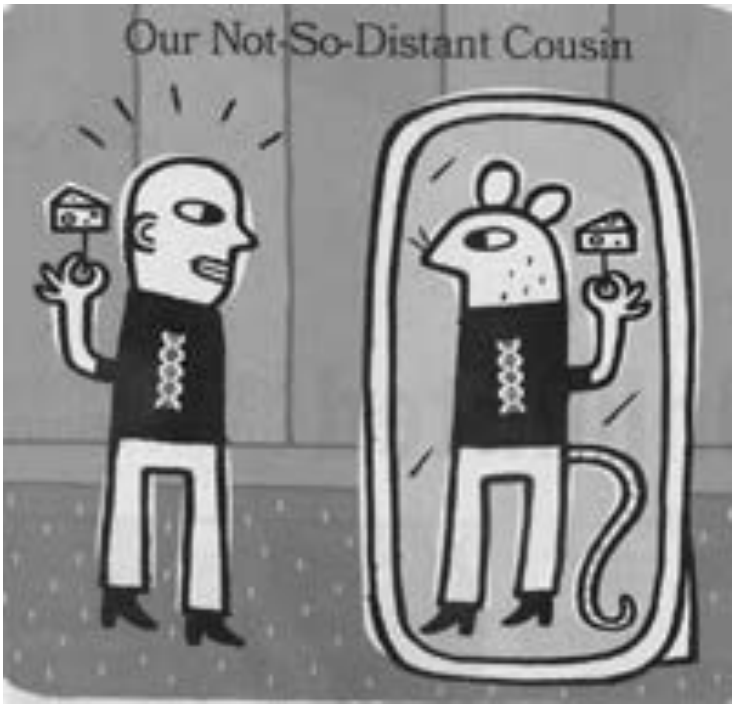
- These model systems are credible because of our common evolutionary history
- This common evolutionary origin has insured that all genomes share the same chemical composition and critical features of replication and information management.
- And many different genomes share many of the same genes -- as a result of the common origin of all species on earth

So studying the function of a gene in one organism may lead to an understanding of what the gene does in another organism, such as humans

How similar is the human genome to the genome of other organisms?

Some remarkable data from the mouse genome project:

- The last common ancestor of mice and humans lived alongside the dinosaurs
- Despite 75 million years of separate evolution, of the 30,000 genes found in the mouse genome, 99% have direct counterpoints in the human genome



Let's go further a field to more distantly related organisms

Our common evolutionary origin has insured that all genomes share the same chemical composition and critical features of replication and information management

A Our evolutionary lineage and the heritage we share with our model organism relatives.

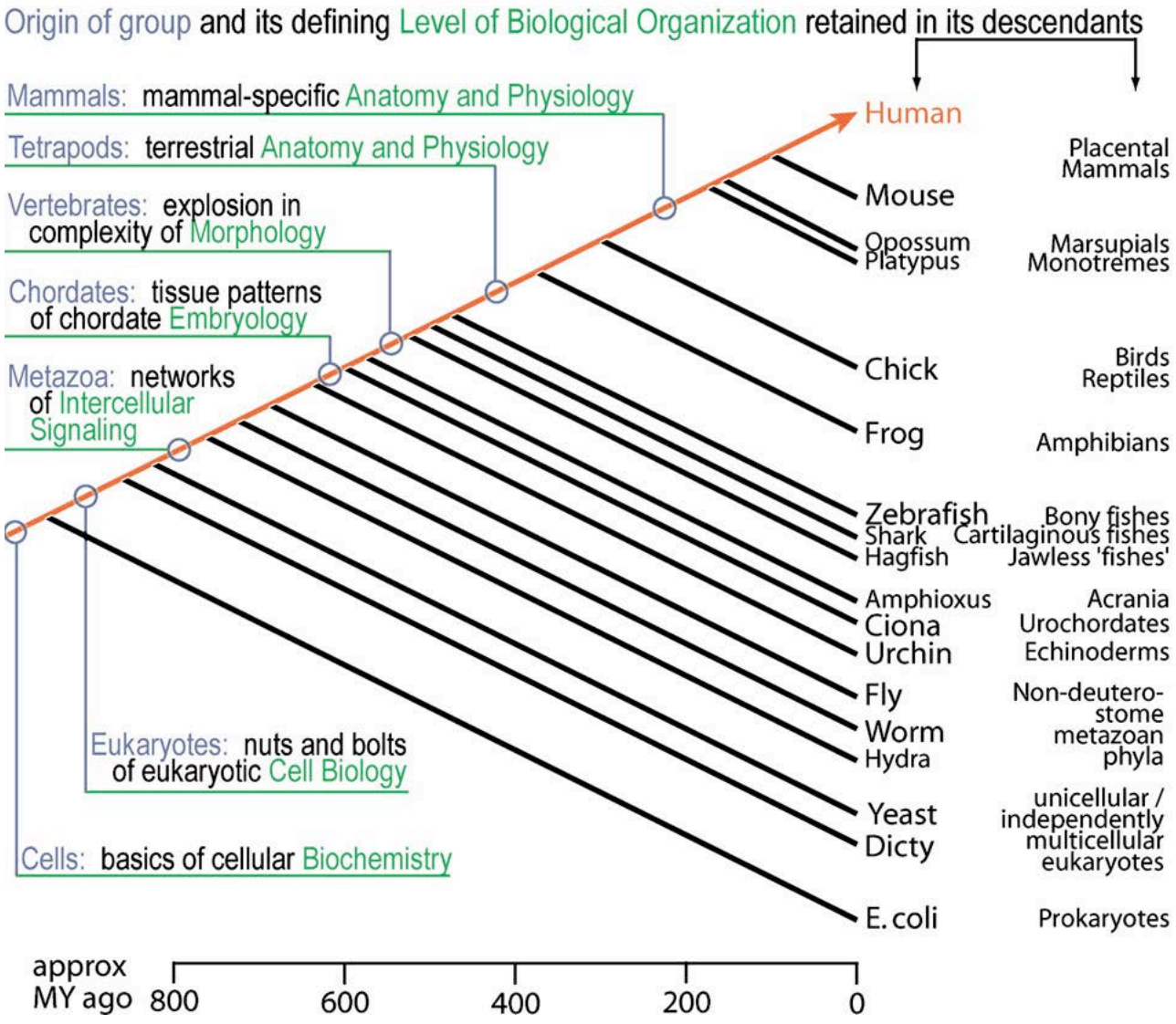


Figure 19-22 (9th edition of IGA) The distribution of human proteins according to the identification of significantly related proteins in other species. Note that about 1/5 of human proteins have been identified only within the vertebrate lineage whereas, at the other extreme, 1/5 have been identified in all of the major branches of the evolutionary tree.

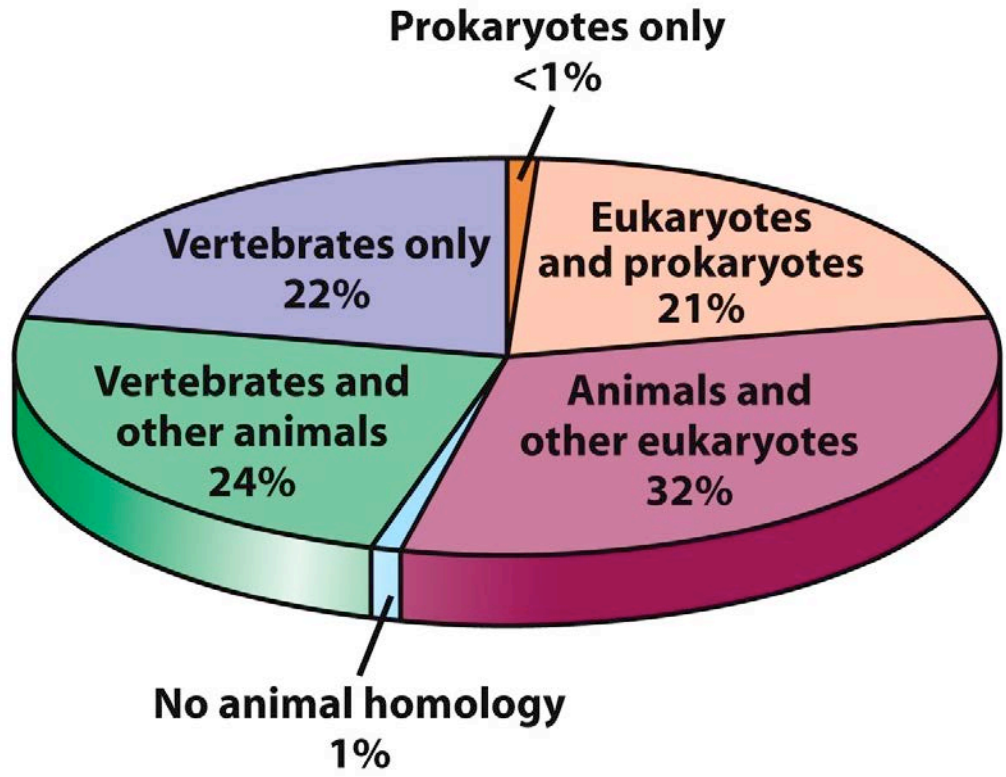


Figure 19-22
Introduction to Genetic Analysis, Ninth Edition

Vertebrate only: *22% of human genes are vertebrate specific (interestingly, the Nature paper did not parse out mammalian specific genes for this figure)*
Vertebrates and other animals: *24% are found in invertebrates as well as vertebrates*
No animal homology: *1% not found in other organisms*
Animals and other eukaryotes: *32% are also found in "non-animal" eukaryotes which would include -----?*
Euks and proks*: 21% of human genes are shared with eukaryotic and prokaryotic organisms: When the genome of the domains Archea, Bacteria and Eukarya are compared, we find a core of* ***500 ancient genes*** *that are*

present in all organisms. These genes were present in the last common ancestor before the divergence of these three lineages ~ 2 billion years ago. The functions of these core genes are central to fundamental, universal cellular processes.

***Prokaryotic only**: <1% of human are also found in prokaryotes and other vertebrates but not in other eukaryotes (huh?)*

Figure 38 from Nature 409: 902 Feb 15, 2001 ***Initial Sequencing and Analysis of the Human Genome***

Distribution of homologs of predicted human proteins. For each protein, a homolog to phylogenetic lineage was considered present if a search of the NCBI nonredundant protein sequence database, using the gapped BLASTP program, gave a random expectation E value of < 0.001. Additional searches for probable homologs with lower sequence conservation were also performed and used the same E value cutoff.

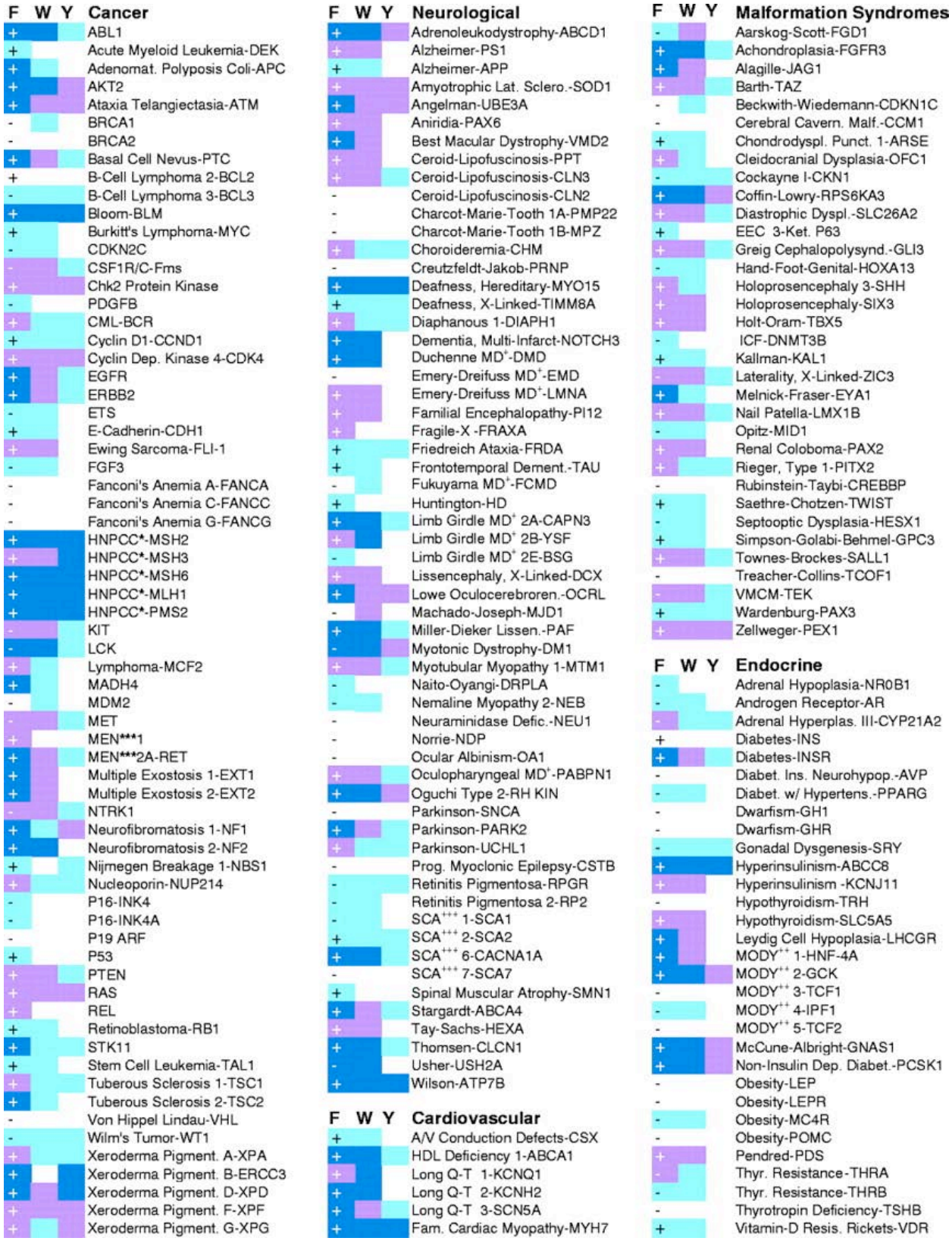

F W Y Cancer
ABL1
Acute Myeloid Leukemia-DEK
Adenomat. Polyposis Coli-APC
AKT2
Ataxia Telangiectasia-ATM
BRCA1
BRCA2
Basal Cell Nevus-PTC
B-Cell Lymphoma 2-BCL2
B-Cell Lymphoma 3-BCL3
Bloom-BLM
Burkitt's Lymphoma-MYC
CDKN2C
CSF1R/C-Fms
Chk2 Protein Kinase
PDGFB
CML-BCR
Cyclin D1-CCND1
Cyclin Dep. Kinase 4-CDK4
EGFR
ERBB2
ETS
E-Cadherin-CDH1
Ewing Sarcoma-FLI-1
FGF3
Fanconi's Anemia A-FANCA
Fanconi's Anemia C-FANCC
Fanconi's Anemia G-FANCG
HNPCC*-MSH2
HNPCC*-MSH3
HNPCC*-MSH6
HNPCC*-MLH1
HNPCC*-PMS2
KIT
LCK
Lymphoma-MCF2
MADH4
MDM2
MET
MEN***1
MEN***2A-RET
Multiple Exostosis 1-EXT1
Multiple Exostosis 2-EXT2
NTRK1
Neurofibromatosis 1-NF1
Neurofibromatosis 2-NF2
Nijmegen Breakage 1-NBS1
Nucleoporin-NUP214
P16-INK4
P16-INK4A
P19 ARF
P53
PTEN
RAS
REL
Retinoblastoma-RB1
STK11
Stem Cell Leukemia-TAL1
Tuberous Sclerosis 1-TSC1
Tuberous Sclerosis 2-TSC2
Von Hippel Lindau-VHL
Wilm's Tumor-WT1
Xeroderma Pigment. A-XPA
Xeroderma Pigment. B-ERCC3
Xeroderma Pigment. D-XPD
Xeroderma Pigment. F-XPF
Xeroderma Pigment. G-XPG
F W Y Neurological
Adrenoleukodystrophy-ABCD1
Alzheimer-PS1
Alzheimer-APP
Amyotrophic Lat. Sclero.-SOD1
Angelman-UBE3A
Aniridia-PAX6
Best Macular Dystrophy-VMD2
Ceroid-Lipofuscinosis-PPT
Ceroid-Lipofuscinosis-CLN3
Ceroid-Lipofuscinosis-CLN2
Charcot-Marie-Tooth 1A-PMP22
Charcot-Marie-Tooth 1B-MPZ
Choroideremia-CHM
Creutzfeldt-Jakob-PRNP
Deafness, Hereditary-MYO15
Deafness, X-Linked-TIMM8A
Diaphanous 1-DIAPH1
Dementia, Multi-Infarct-NOTCH3
Duchenne MD+-DMD
Emery-Dreifuss MD+-EMD
Emery-Dreifuss MD+-LMNA
Familial Encephalopathy-PI12
Fragile-X -FRAXA
Friedreich Ataxia-FRDA
Frontotemporal Dement.-TAU
Fukuyama MD+-FCMD
Huntington-HD
Limb Girdle MD+ 2A-CAPN3
Limb Girdle MD+ 2B-YSF
Limb Girdle MD+ 2E-BSG
Lissencephaly, X-Linked-DCX
Lowe Oculocerebroren.-OCRL
Machado-Joseph-MJD1
Miller-Dieker Lissen.-PAF
Myotonic Dystrophy-DM1
Myotubular Myopathy 1-MTM1
Naito-Oyangi-DRPLA
Nemaline Myopathy 2-NEB
Neuraminidase Defic.-NEU1
Norrie-NDP
Ocular Albinism-OA1
Oculopharyngeal MD+-PABPN1
Oguchi Type 2-RH KIN
Parkinson-SNCA
Parkinson-PARK2
Parkinson-UCHL1
Prog. Myoclonic Epilepsy-CSTB
Retinitis Pigmentosa-RPGR
Retinitis Pigmentosa 2-RP2
SCA+++ 1-SCA1
SCA+++ 2-SCA2
SCA+++ 6-CACNA1A
SCA+++ 7-SCA7
Spinal Muscular Atrophy-SMN1
Stargardt-ABCA4
Tay-Sachs-HEXA
Thomsen-CLCN1
Usher-USH2A
Wilson-ATP7B
F W Y Cardiovascular
A/V Conduction Defects-CSX
HDL Deficiency 1-ABCA1
Long Q-T 1-KCNQ1
Long Q-T 2-KCNH2
Long Q-T 3-SCN5A
Fam. Cardiac Myopathy-MYH7
F W Y Malformation Syndromes
Aarskog-Scott-FGD1
Achondroplasia-FGFR3
Alagille-JAG1
Barth-TAZ
Beckwith-Wiedemann-CDKN1C
Cerebral Cavern. Malf.-CCM1
Chondrodyspl. Punct. 1-ARSE
Cleidocranial Dysplasia-OFC1
Cockayne I-CKN1
Coffin-Lowry-RPS6KA3
Diastrophic Dyspl.-SLC26A2
EEC 3-Ket. P63
Greig Cephalopolysynd.-GLI3
Hand-Foot-Genital-HOXA13
Holoprosencephaly 3-SHH
Holoprosencephaly-SIX3
Holt-Oram-TBX5
ICF-DNMT3B
Kallman-KAL1
Laterality, X-Linked-ZIC3
Melnick-Fraser-EYA1
Nail Patella-LMX1B
Opitz-MID1
Renal Coloboma-PAX2
Rieger, Type 1-PITX2
Rubinstein-Taybi-CREBBP
Saethre-Chotzen-TWIST
Septooptic Dysplasia-HESX1
Simpson-Golabi-Behmel-GPC3
Townes-Brockes-SALL1
Treacher-Collins-TCOF1
VMCM-TEK
Wardenburg-PAX3
Zellweger-PEX1
F W Y Endocrine
Adrenal Hypoplasia-NR0B1
Androgen Receptor-AR
Adrenal Hyperplas. III-CYP21A2
Diabetes-INS
Diabetes-INSR
Diabet. Ins. Neurohypop.-AVP
Diabet. w/ Hypertens.-PPARG
Dwarfism-GH1
Dwarfism-GHR
Gonadal Dysgenesis-SRY
Hyperinsulinism-ABCC8
Hyperinsulinism -KCNJ11
Hypothyroidism-TRH
Hypothyroidism-SLC5A5
Leydig Cell Hypoplasia-LHCGR
MODY++ 1-HNF-4A
MODY++ 2-GCK
MODY++ 3-TCF1
MODY++ 4-IPF1
MODY++ 5-TCF2
McCune-Albright-GNAS1
Non-Insulin Dep. Diabet.-PCSK1
Obesity-LEP
Obesity-LEPR
Obesity-MC4R
Obesity-POMC
Pendred-PDS
Thyr. Resistance-THRA
Thyr. Resistance-THRB
Thyrotropin Deficiency-TSHB
Vitamin-D Resis. Rickets-VDR

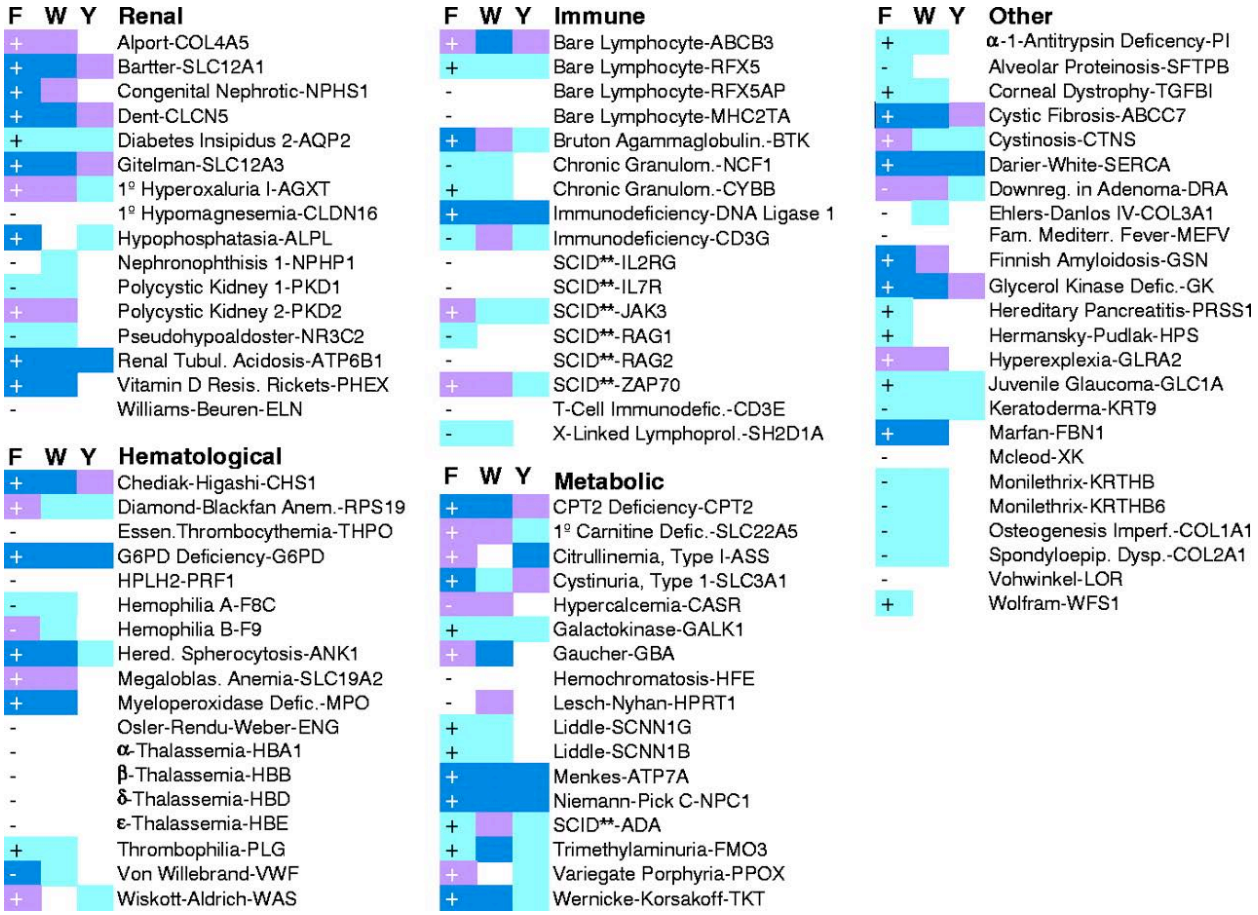
Figure 1. (continued). Fly (F), worm (W), and yeast (Y) genes showing similarity to human disease genes. This collection of human disease genes was selected to represent a cross section of human pathophysiology and is not comprehensive. The selection criteria require that the gene is actually mutated, altered, amplified, or deleted in a human disease, as opposed to having a function deduced from experiments on model organisms or in cell culture.

*Results are scaled according to various levels of statistical significance***, reflecting a level of confidence in either evolutionary homology or functional similarity:*

- **White boxes:** indicating no or weak similarity; no equivalent sequence
- **Light blue and purple boxes:** equivalent sequence with different levels of confidence; quantitative assessment based on BLAST E value
- **Dark blue boxes:** indicate the highest degree of sequence conservation.

A plus sign *indicates confidence that the corresponding Drosophila gene product is the functional equivalent of the human protein, based on non-computational evidence*
A minus sign *indicates that the researchers were unable to identify a likely functional equivalent of the human protein.*

***Results are scaled according to various levels of statistical significance, reflecting a level of confidence in either evolutionary homology or functional similarity. White boxes represent BLAST E values $>1 \times 10^{-6}$, indicating no or weak similarity; light blue boxes represent E values in the range of 1×10^{-6} to 1×10^{-40}; purple boxes represent E values in the range of 1×10^{-40} to 1×10^{-100}; and dark blue boxes represent E values $<1 \times 10^{-100}$, indicating the highest degree of sequence conservation.



See also nice example of using models to identify ancient genes and their roles in conserved processes:

Self destructive Behavior in Cells May Hold Key to a Longer Life
http://fire.biol.wwu.edu/trent/trent/cellrecycling.pdf

Other reasons why biologists care so much about the genome projects of non-human animals:

Despite the commonalities unifying plants, animals, and microbes, ***genomic information is also key to the incredible biodiversity that exists on this planet***

It is the differences in our genomes that make you and me different from a sunflower or a spider