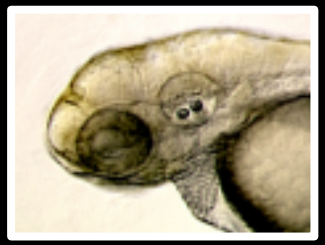
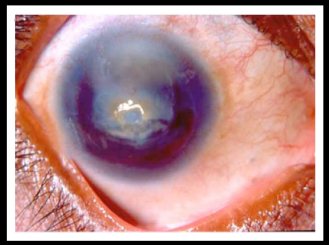
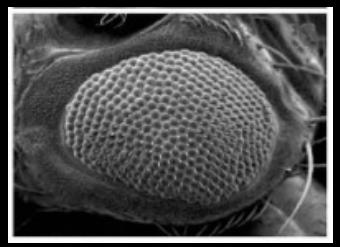
NATIONAL CENTER FOR BIOMEDICAL ONTOLOGY

ZFIN The Zebrafish Information Network

PHENOSCAPE

FlyBase

Linking Animal Models and Human Diseases

Supported by NIH P41 HG002659 and U54 HG004028

Cambridge University & the University of Oregon

Yvonne Bradford
Melissa Haendel
Kevin Schaper
Erik Segerdell
Amy Singer
Sierra Taylor

FlyBase

Michael Ashburner
Rachel Drysdale
George Gkoutos
David Sutherland

BBOP

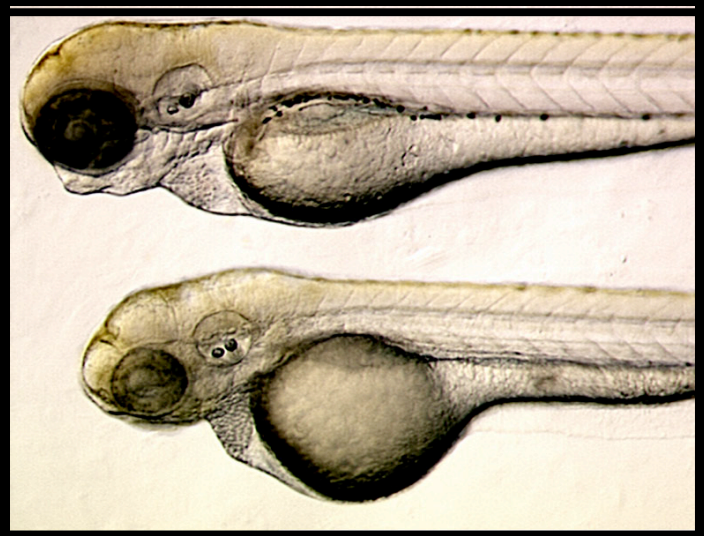
Mark Gibson
Suzi Lewis
Chris Mungall
Nicole Washington

Linking Animal Models and Human Diseases

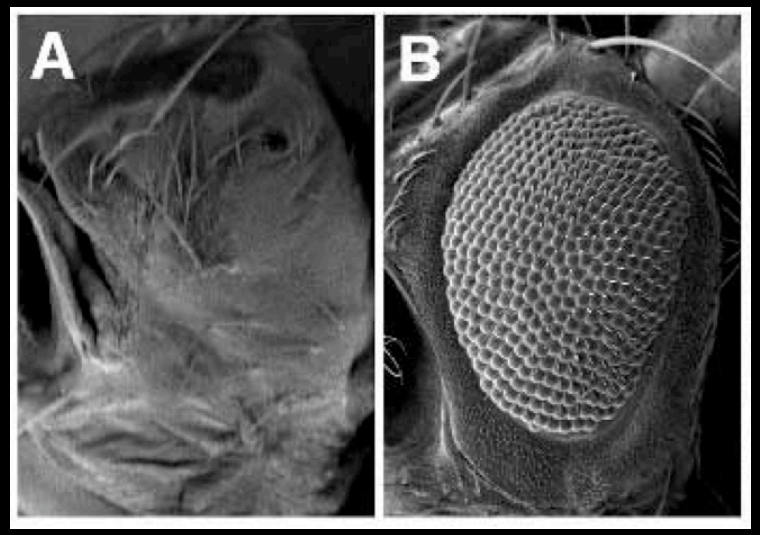
Develop methods to:

- Describe phenotypes
- Compare descriptions (annotations)
- Search phenotypes within and across species

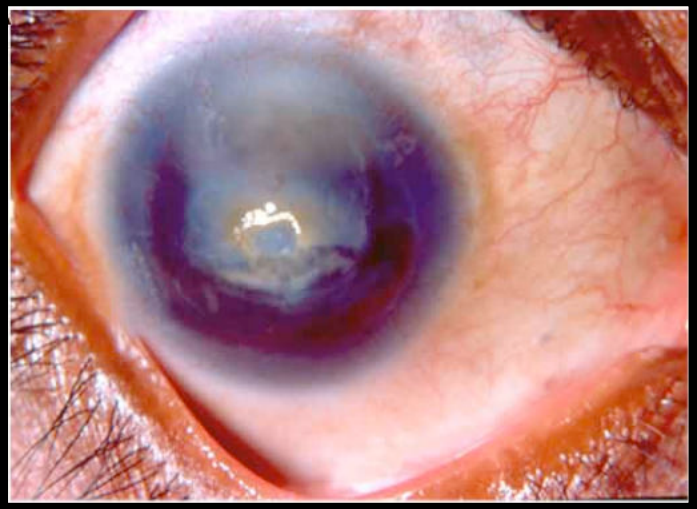
EYA gene mutants



zebrafish



fly

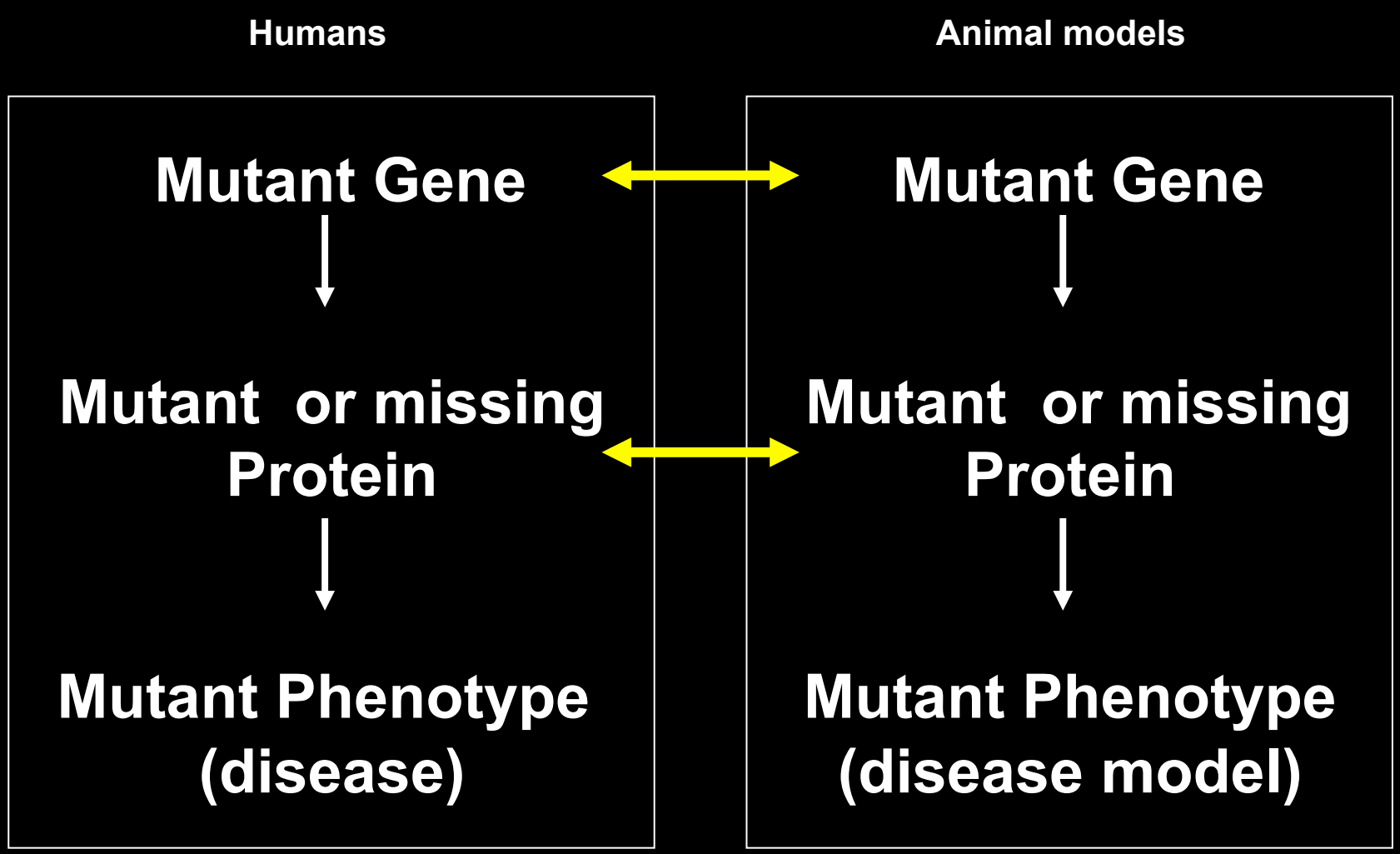


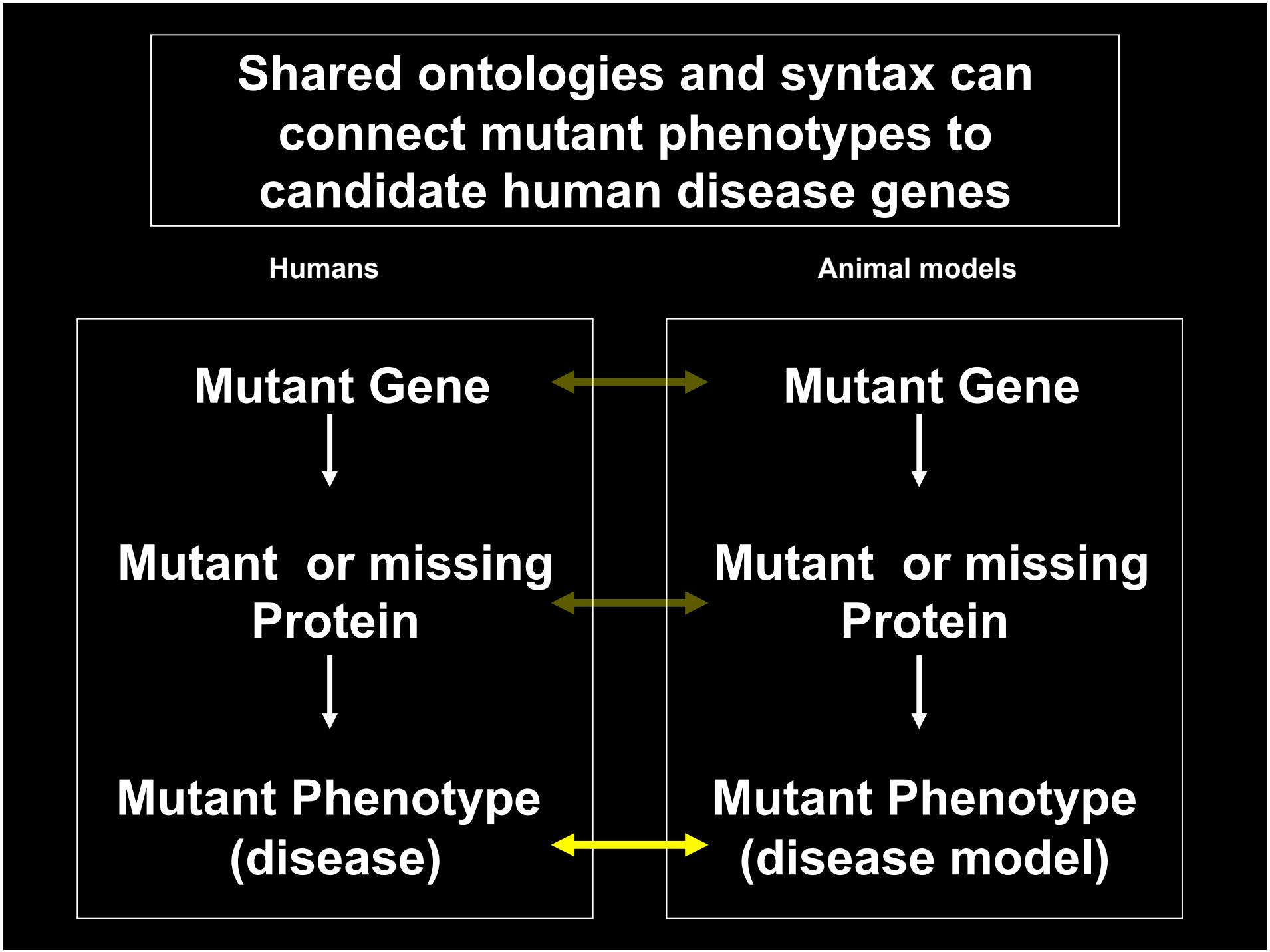
human

Animal disease models

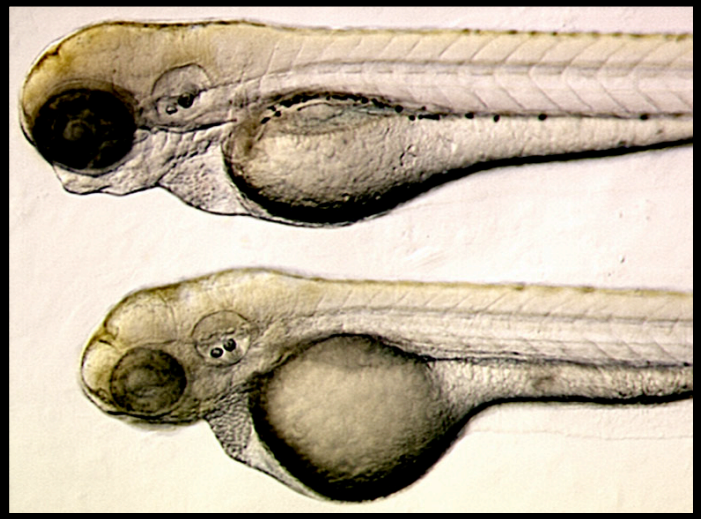
Humans	Animal models
Mutant Gene	Mutant Gene
↓	↓
Mutant or missing Protein	Mutant or missing Protein
↓	↓
Mutant Phenotype (disease)	Mutant Phenotype (disease model)

Sequence analysis (BLAST) can connect animal genes to human genes




Shared ontologies and syntax can connect mutant phenotypes to candidate human disease genes
Humans
Animal models
Mutant Gene
Mutant or missing Protein
Mutant Phenotype (disease)
Mutant Gene
Mutant or missing Protein
Mutant Phenotype (disease model)

Annotation of *eya* mutant phenotype



Phenotype	=	Entity	+	Quality
EQ_1	=	eye	+	small
EQ_2	=	kidney	+	hypoplastic

Ontologies for Phenotype Annotation

Phenotype (clinical sign) = Entity + Quality

Anatomical ontology
Cell & tissue ontology
Developmental ontology
Gene ontology
biological process
molecular function
cellular component

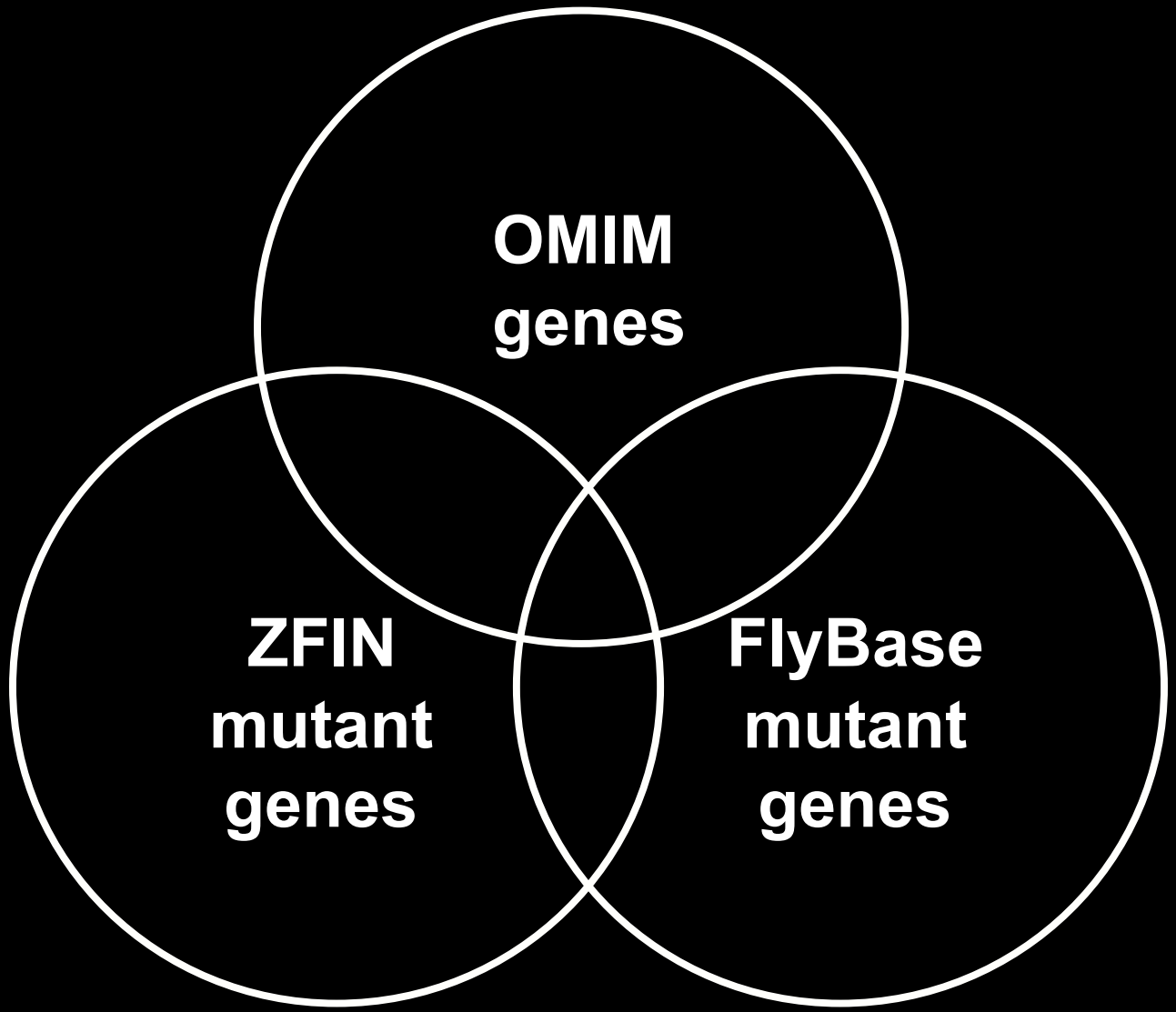
+ PATO

Linking Animal Models and Human Diseases

Develop methods to:

- Describe phenotypes
- Compare descriptions (annotations)
- Search phenotypes within and across species

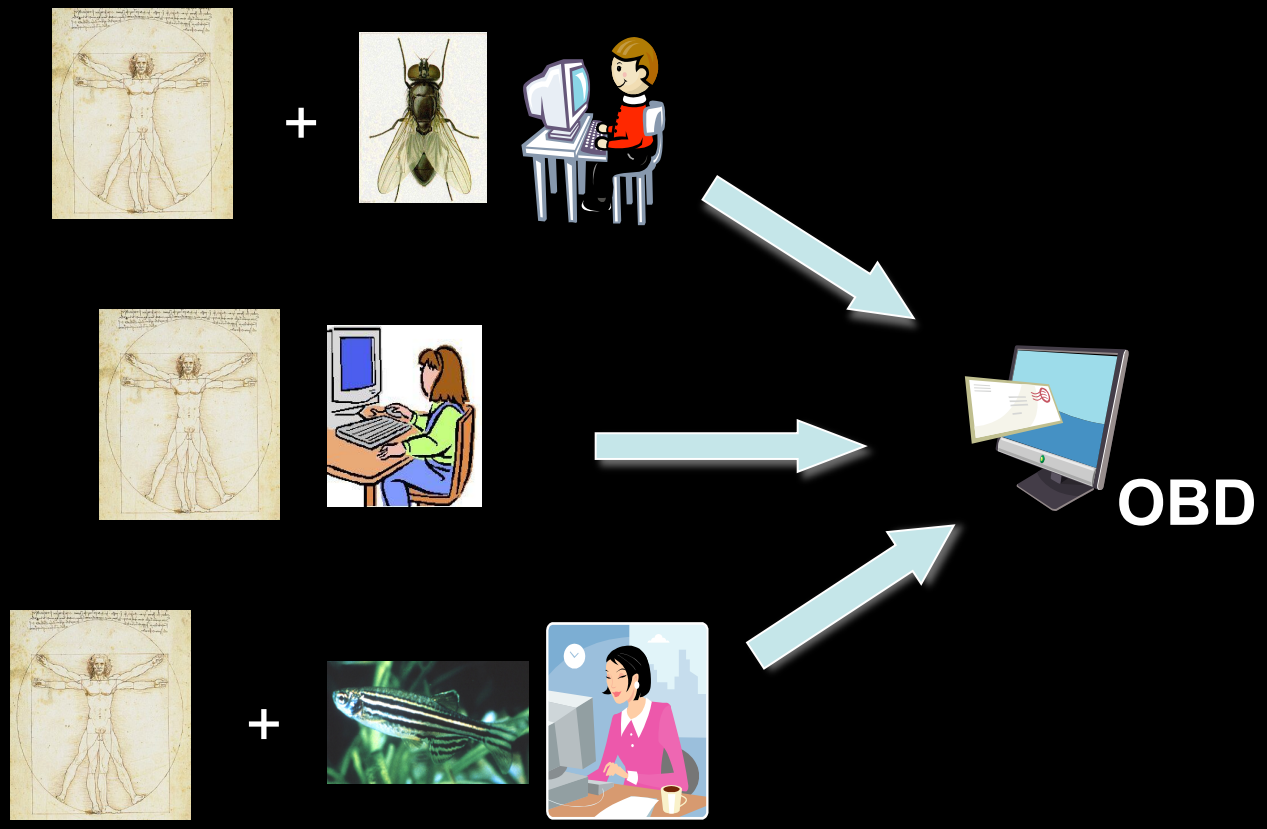
Strategy: use shared genes as proof of principle



Data type	Total
ZFIN genes	20,385
Genes with assigned human orthologs	2,884
Genes with OMIM links	2,174
ZFIN mutants	3,188
ZFIN mutants with OMIM links	720
Corresponding human genes	271
Drosophila homologs of these 271	187

Experimental design

- Annotate phenotypes in human, zebrafish, and fly
- Annotate human phenotypes triple blind
- Compare annotations



Results: Number of annotations added to OBD

Human

Curate OMIM gene and disease data into OBD using EQ syntax

10 genes
677 EQ annotations from ZFIN
314 EQ annotations from Flybase
507 EQ annotations from BBOP

Zebrafish

Curate zebrafish mutant phenotype data into OBD using EQ syntax

4,355 genes and genotypes into OBD
17,782 EQ annotations into OBD

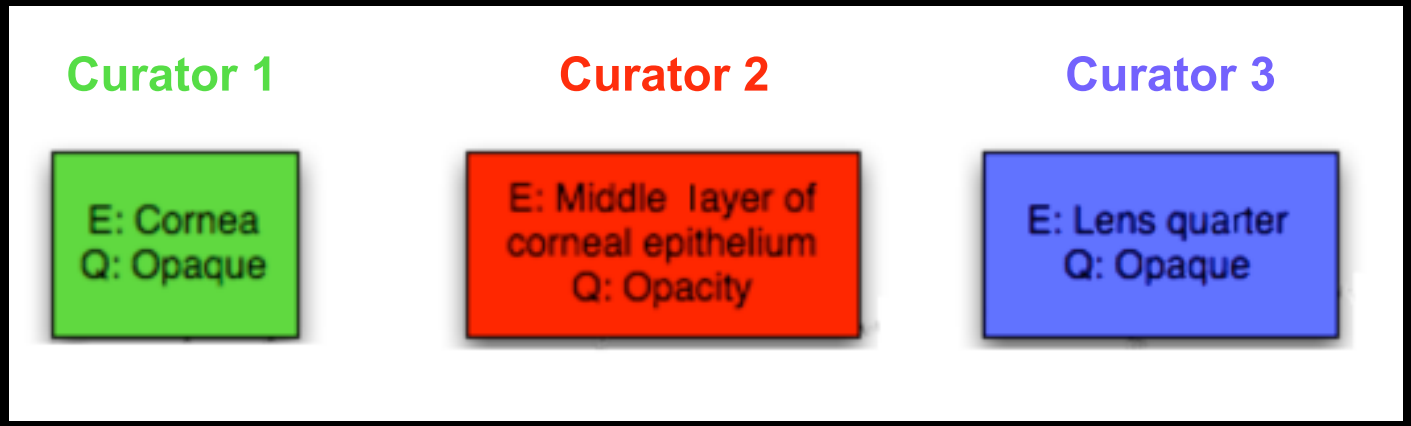
```
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000619 /*anterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000378 /*lateral cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000566 /*posterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000619 /*anterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000378 /*lateral cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000566 /*posterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000035) /*during(Larval:Protruding-mouth)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=GO:0021984 /*adenohypophysis development*/ Q=PATO:0000060 /*pattern*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000439 /*prolactin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000030) /*during(Pharyngula:Prim-15)*/ Tag=PATO:0000467 /*present*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000439 /*prolactin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000467 /*present*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000640 /*corticotrophin hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000440 /*melanocyte stimulating hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000476 /*thyroid stimulating hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000295 /*somatotrophin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=GO:0030916 /*otic vesicle formation*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000029) /*during(Pharyngula:Prim-5)*/ Tag=PATO:0000461 /*normal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000946 /*oblong*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000599 /*narrow*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000814 /*neuromasts opercular*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000039) /*during(Larval:Days 7-13)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000411 /*round*/ T=during(ZFS:0000039) /*during(Larval:Days 7-13)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0030916 /*otic vesicle formation*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000029) /*during(Pharyngula:Prim-5)*/ Tag=PATO:0000461 /*normal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000946 /*oblong*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000599 /*narrow*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000035) /*during(Larval:Protruding-mouth)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000386 /*maculae*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
```

PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:90
PUB=PMID:90
PUB=PMID:90
PUB=PMID:90
PUB=PMID:90
PUB=PMID:90
PUB=PMID:90

~10% of the annotations for 1 gene

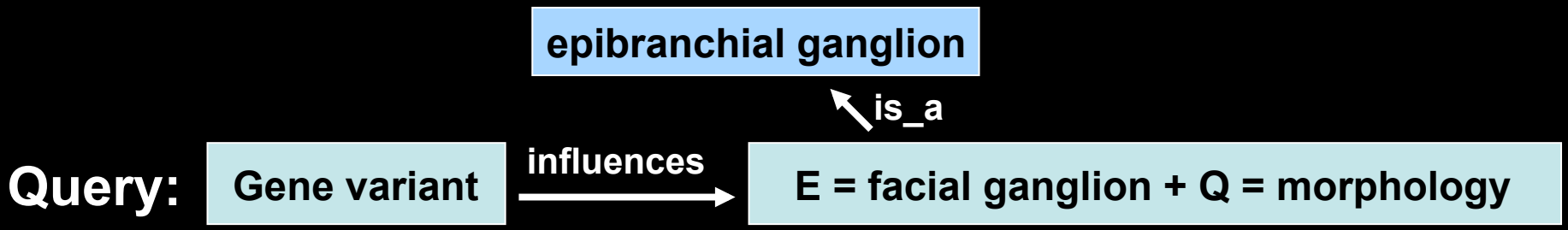
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000619 /*anterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000378 /*lateral cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[to15b/to15b] E=ZFA:0000566 /*posterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000095 /*pharyngeal arch 3-7 skeleton*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=GO:0007626 /*locomotory behavior*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0001094 /*whole organism*/ Q=PATO:0000718 /*lethal*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000619 /*anterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000378 /*lateral cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000566 /*posterior cristae*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000035) /*during(Larval:Protruding-mouth)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tp85b/tp85b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=GO:0021984 /*adenohypophysis development*/ Q=PATO:0000060 /*pattern*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000439 /*prolactin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000030) /*during(Pharyngula:Prim-15)*/ Tag=PATO:0000467 /*present*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000439 /*prolactin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000467 /*present*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000640 /*corticotrophin hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000440 /*melanocyte stimulating hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000476 /*thyroid stimulating hormone secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:14752054 GT=eya1[t22744/t22744] E=CL:0000295 /*somatotrophin secreting cell*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=GO:0030916 /*otic vesicle formation*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000029) /*during(Pharyngula:Prim-5)*/ Tag=PATO:0000461 /*normal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000946 /*oblong*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000599 /*narrow*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0000814 /*neuromasts opercular*/ Q=PATO:0001226 /*quantitative*/ T=during(ZFS:0000039) /*during(Larval:Days 7-13)*/ Tag=PATO:0000462 /*absent*/
PUB=PMID:15572137 GT=eya1[tc257e/tc257e] E=ZFA:0001227 /*pharyngeal arch 1 skeleton*/ Q=PATO:0000411 /*round*/ T=during(ZFS:0000039) /*during(Larval:Days 7-13)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0030916 /*otic vesicle formation*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000029) /*during(Pharyngula:Prim-5)*/ Tag=PATO:0000461 /*normal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000946 /*oblong*/ T=during(ZFS:0000033) /*during(Hatching:Long-pec)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000051 /*otic vesicle*/ Q=PATO:0000599 /*narrow*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000035) /*during(Larval:Protruding-mouth)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=GO:0048752 /*semicircular canal morphogenesis*/ Q=PATO:0000001 /*quality*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000585 /*sensory hair cells*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:15572137 GT=eya1[tm90b/tm90b] E=ZFA:0000386 /*maculae*/ Q=PATO:0000052 /*shape*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/

Annotations vary among curators

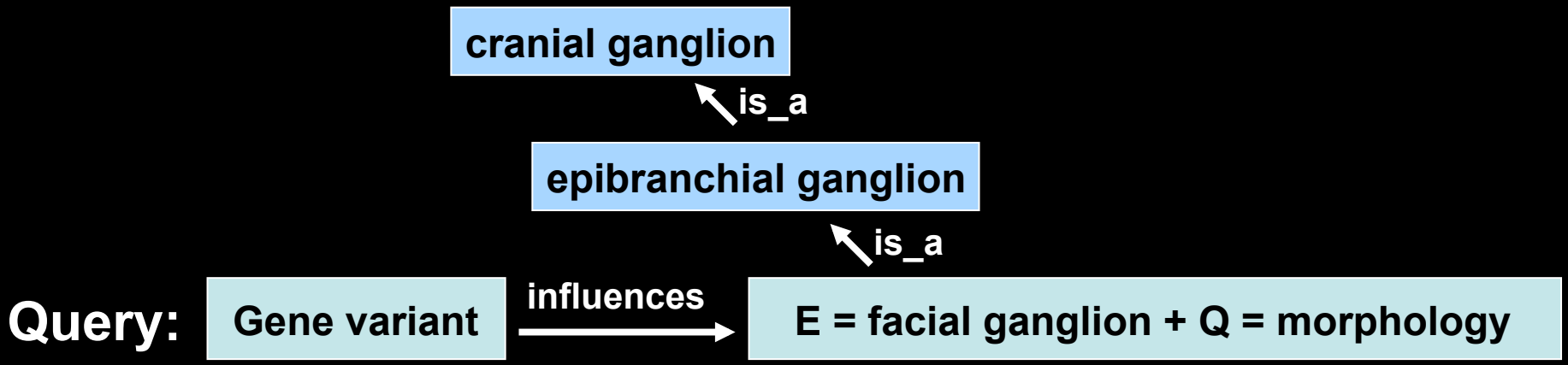


Example phenotype annotation

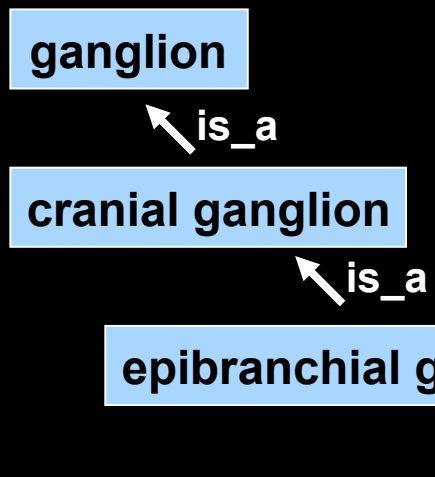
Terms are related by ontologies



Terms are related by ontologies



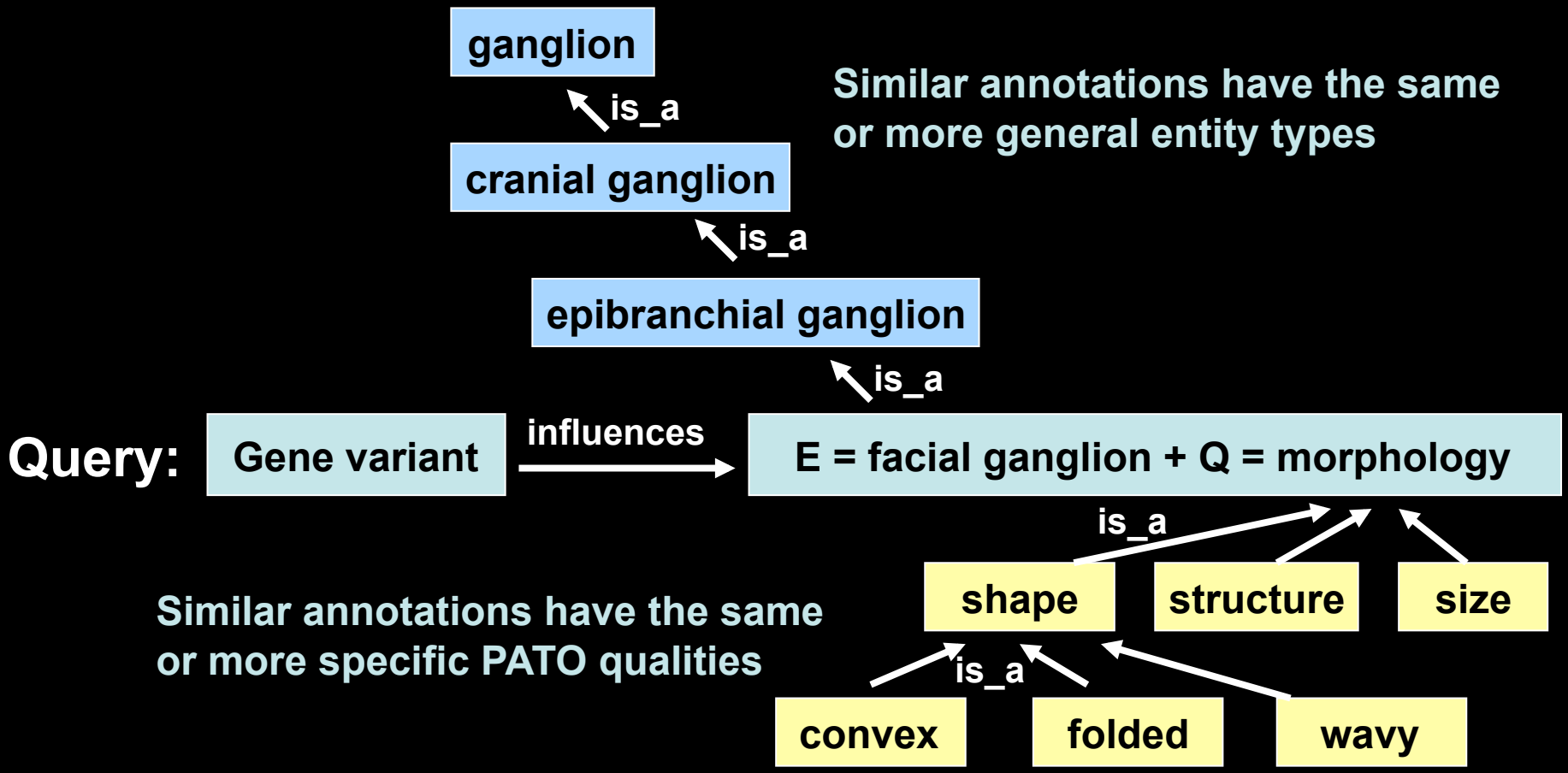
Terms are related by ontologies



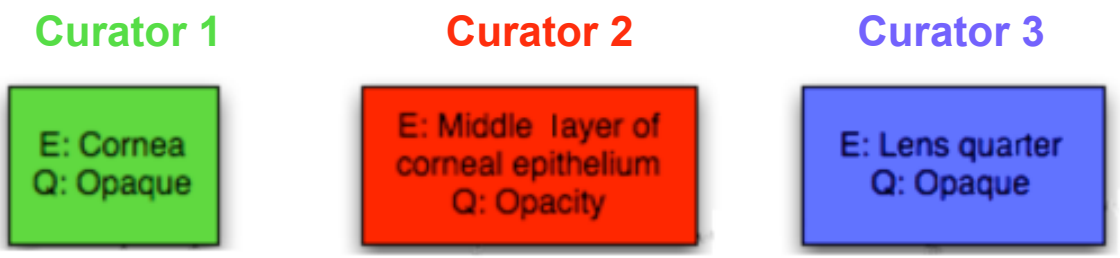
Similar annotations have the same or more general entity types

Query: Gene variant → influences → E = facial ganglion + Q = morphology

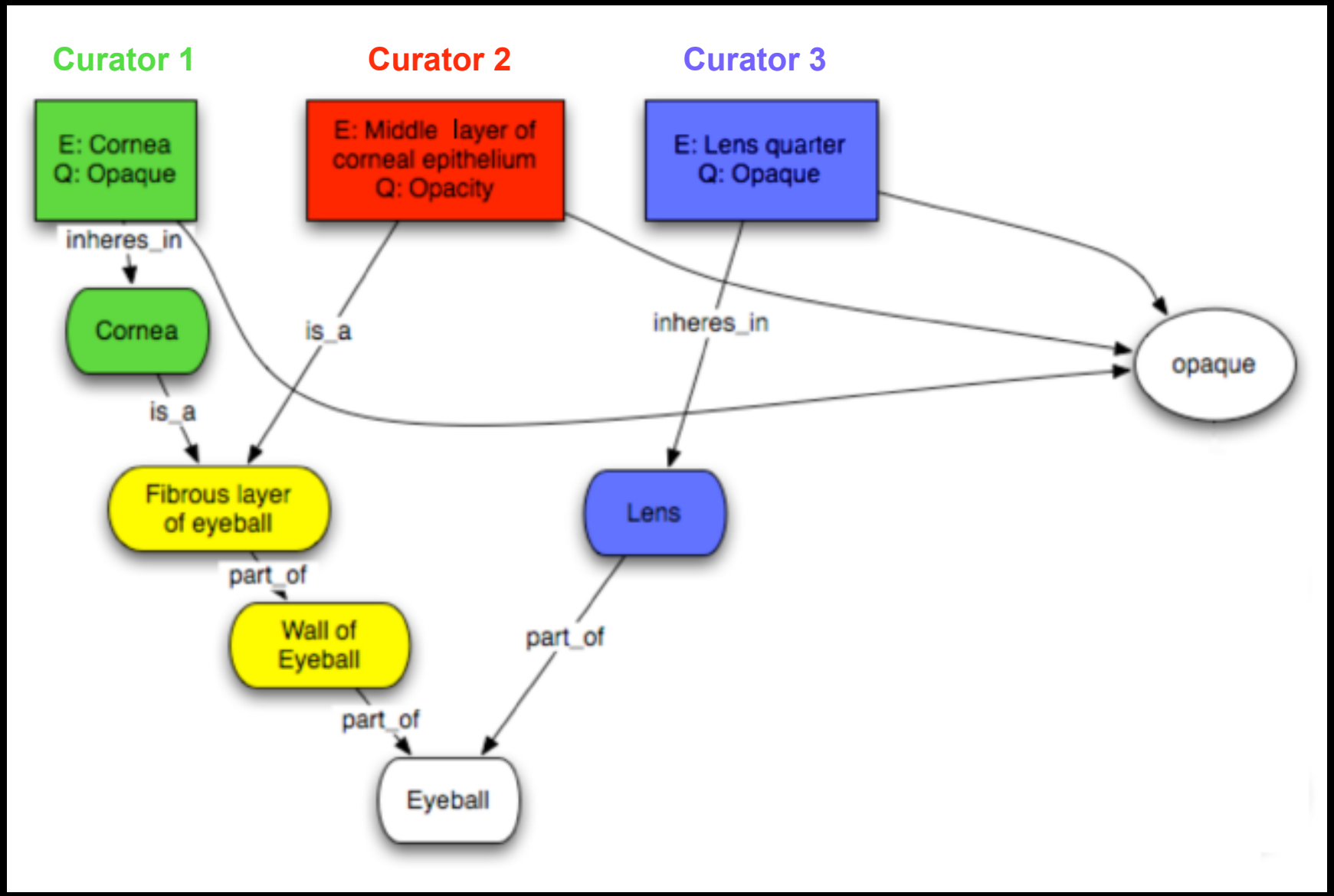
Similarity calculated by reasoning across ontologies



Ontologies support comparisons



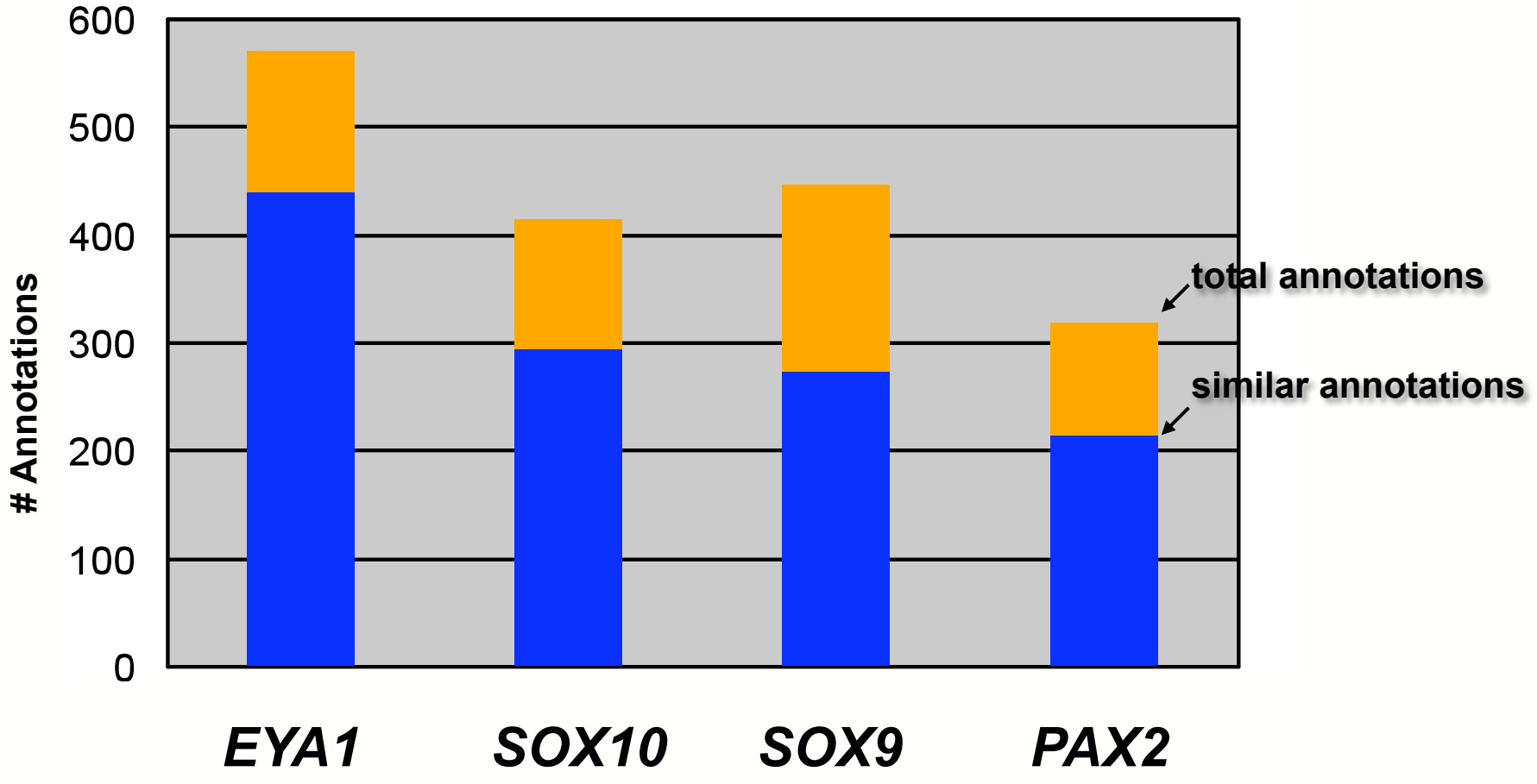
Ontologies support comparisons



Subsumption in similarity scoring

subsumption		←	←	←	←	←	←	←	←
Gene	Genotype	Quality *Anatomical Entity*	Morphology *Organ*	Shape *Part of organ*	Thickness *Cranial nerve*	Increased thickness *Vestibulo-cochlear nerve*	Increased thickness *Trigeminal nerve*	Perforated *Wall of heart*	Deformed *Retina*
GeneA	A-001	+		+				+	
	A-002	+	+		+	+			
	A-003	+	+		+	+			
Gene B	B-001	+	+		+		+		
	B-002	+		+				+	
	B-003	+		+					+
p value		0.99	0.6	0.3	1.1e-4	3.2e-5	6.1e-6	2.0e-7	1.9e-6
					Unlikely to match by chance				

Average annotation consistency among curators



	EYA1	SOX10	SOX9	PAX2
congruence	0.78	0.71	0.61	0.72

Linking Animal Models and Human Diseases

Develop methods to:

- Describe phenotypes
- Compare descriptions (annotations)
- Search phenotypes within and across species

Phenotypes identify other alleles of the **same** gene

Example: A search for phenotypes similar to each human *EYA1* allele returns other human *EYA1* alleles

Phenotypes identify other alleles of the **same** gene

Example: A search for phenotypes similar to each human *EYA1* allele returns other human *EYA1* alleles

EYA1 query	target / Allele number	1	2	3	4	5	6	7
Allele number	1	9.E-34	6.E-29	7.E-19	7.E-19	6.E-29	6.E-29	6.E-29
	2	6.E-29	6.E-29	7.E-19	7.E-19	6.E-29	6.E-29	6.E-29
	3	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19
	4	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19	7.E-19
	5	6.E-29	6.E-29	7.E-19	7.E-19	6.E-29	6.E-29	6.E-29
	6	6.E-29	6.E-29	7.E-19	7.E-19	6.E-29	5.E-37	6.E-29
	7	6.E-29	6.E-29	7.E-19	7.E-19	6.E-29	6.E-29	6.E-29

(The smaller the number, the more similar)

Human phenotypes identify mutations in orthologous model organism genes

A search for phenotypes similar to:

Human *EYA1* variant OMIM:601653

MP:deafness = E = Sensory perception of sound Q = absent

Human phenotypes identify mutations in orthologous model organism genes

A search for phenotypes similar to:

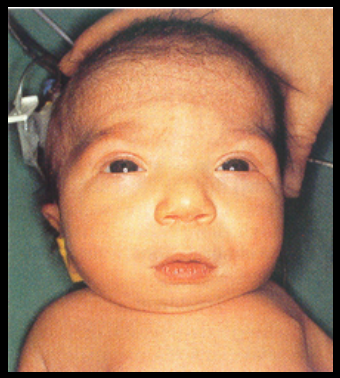
Human *EYA1* variant OMIM:601653
MP:deafness = E = Sensory perception of sound Q = absent

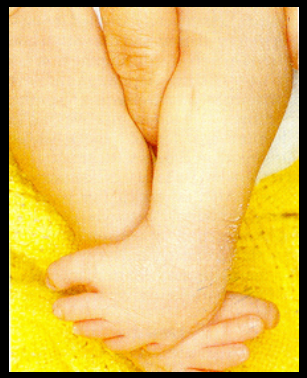
returns:

Mouse *Eya1*$^{bor/bor}$ and *Eya1*$^{tm1Rilm/tm1Rilm}$
E = Sensory perception of sound Q = decreased

Animal annotations can identify human diseases

Human, *SOX9*
(Campomelic dysplasia)





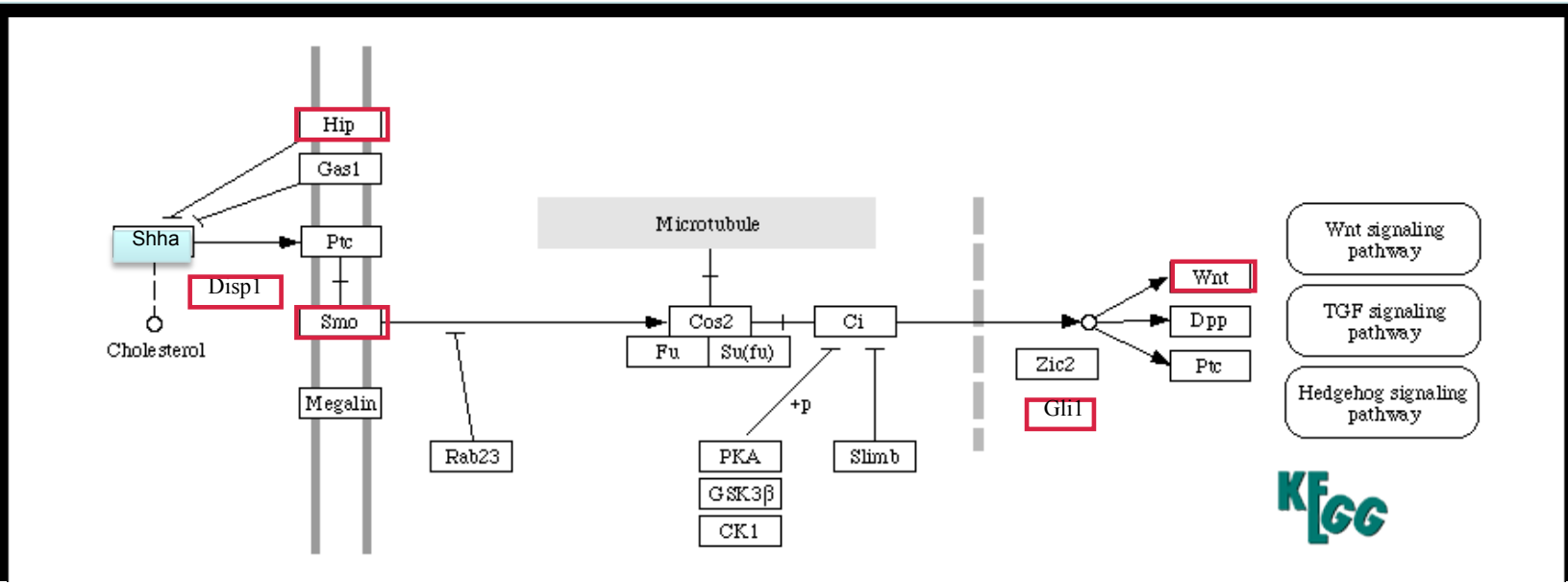
Zebrafish, *sox9a*
(*jellyfish*)

Scapula: hypoplastic	⟷	Scapulocorocoid: aplastic
Lower jaw: decreased size	⟷	Cranial cartilage: hypoplastic
Heart: malformed or edematous	⟷	Heart: edematous
Phalanges: decreased length	⟷	Pectoral fin: decreased length
Long bones: bowed	⟷	Cartilage development: disrupted

Annotations can identify other pathway members

Similarity search for zebrafish *shha*$^{t4/t4}$ identifies pathway members

Genotype	Congruence	# of alleles	Function
disp1^{ty60}	9.6E-19	6	regulates long range Shh signaling
gli1^{ts269}	6.6E-13	2	downstream transcriptional repressor
wnt5b^{te1c}	4.3E-11	5	downstream target gene
smo^{hi1640Tg}	4.1E-11	4	membrane protein mediates Shh intracellular signaling pathway
hhip^{hu540a}	3.1E-5	2	binds Shh in membrane



Linking Animal Models and Human Diseases

Develop methods to:

- Describe phenotypes
- Compare descriptions (annotations)
- Search phenotypes within and across species

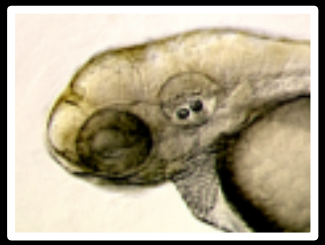
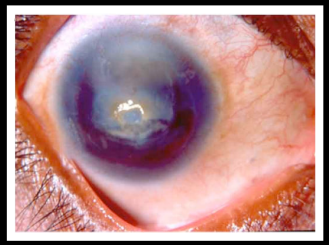
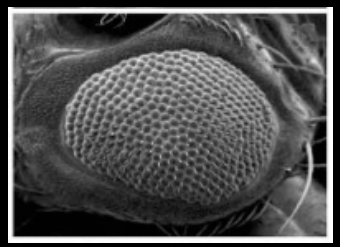
NATIONAL CENTER FOR BIOMEDICAL ONTOLOGY

ZFIN The Zebrafish Information Network

PHENOSCAPE

FlyBase

Linking Animal Models and Human Diseases

Supported by NIH P41 HG002659 and U54 HG004028

Cambridge University & the University of Oregon