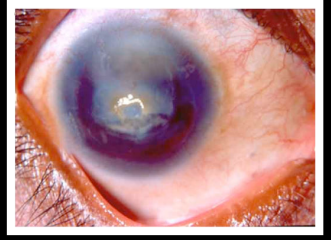
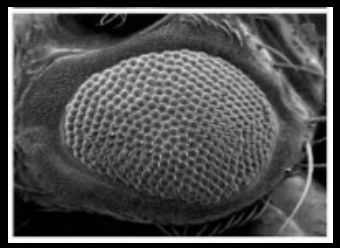
NATIONAL CENTER FOR BIOMEDICAL ONTOLOGY

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

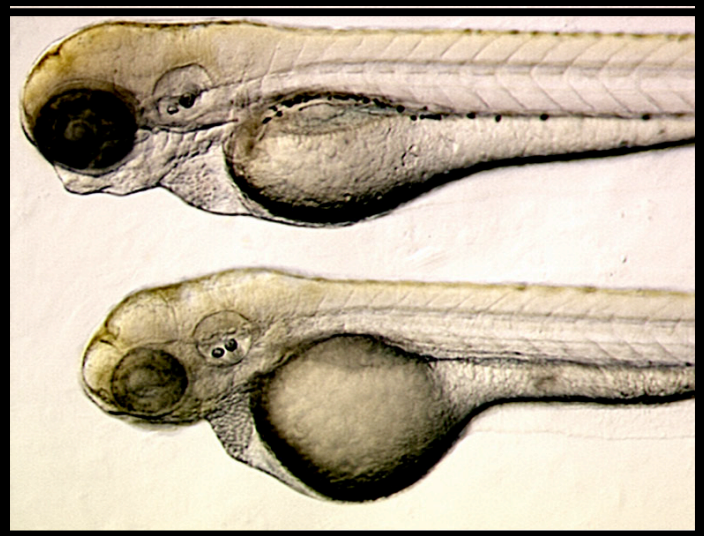
Mark Gibson
Suzi Lewis
Chris Mungall
Nicole Washington

Linking Animal Models and Human Diseases

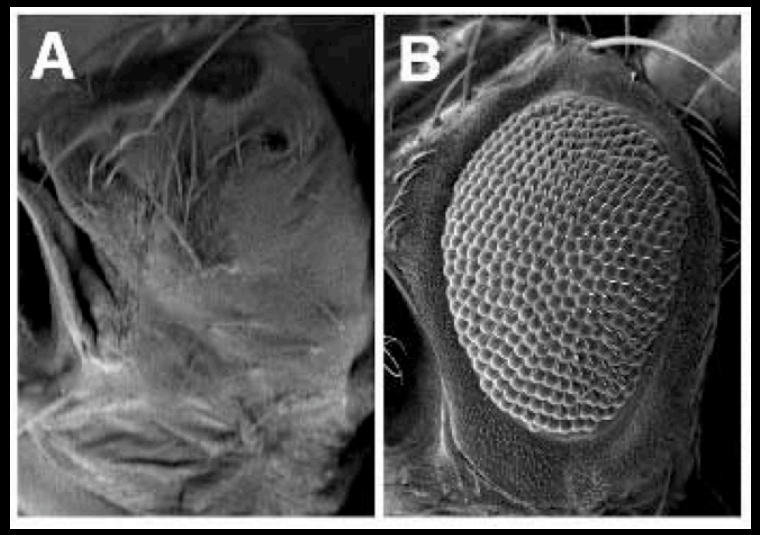
Develop methods to:

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

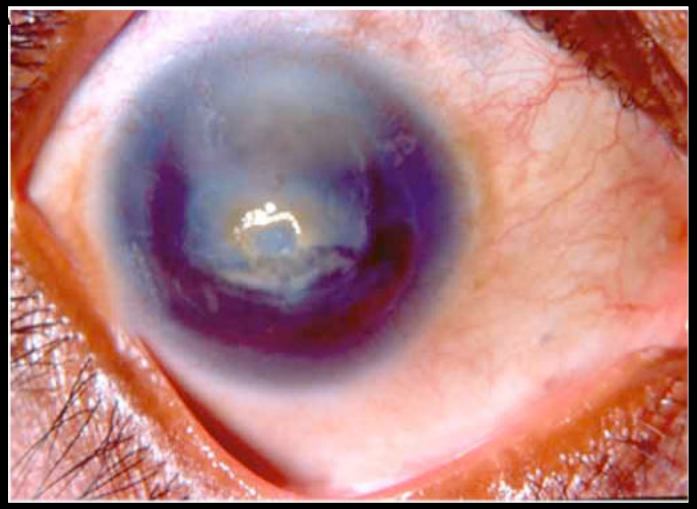
EYA gene mutants



zebrafish



fly

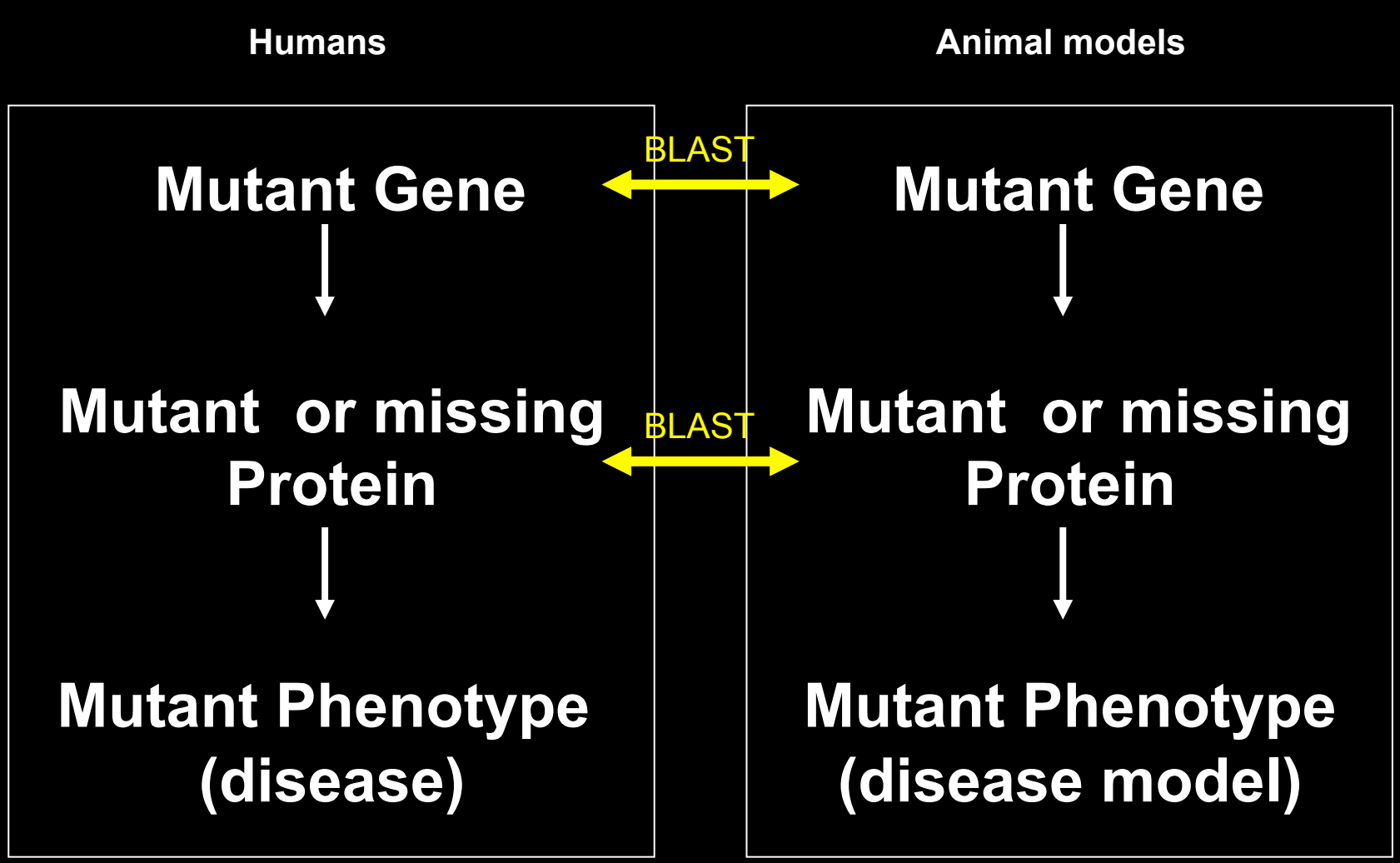


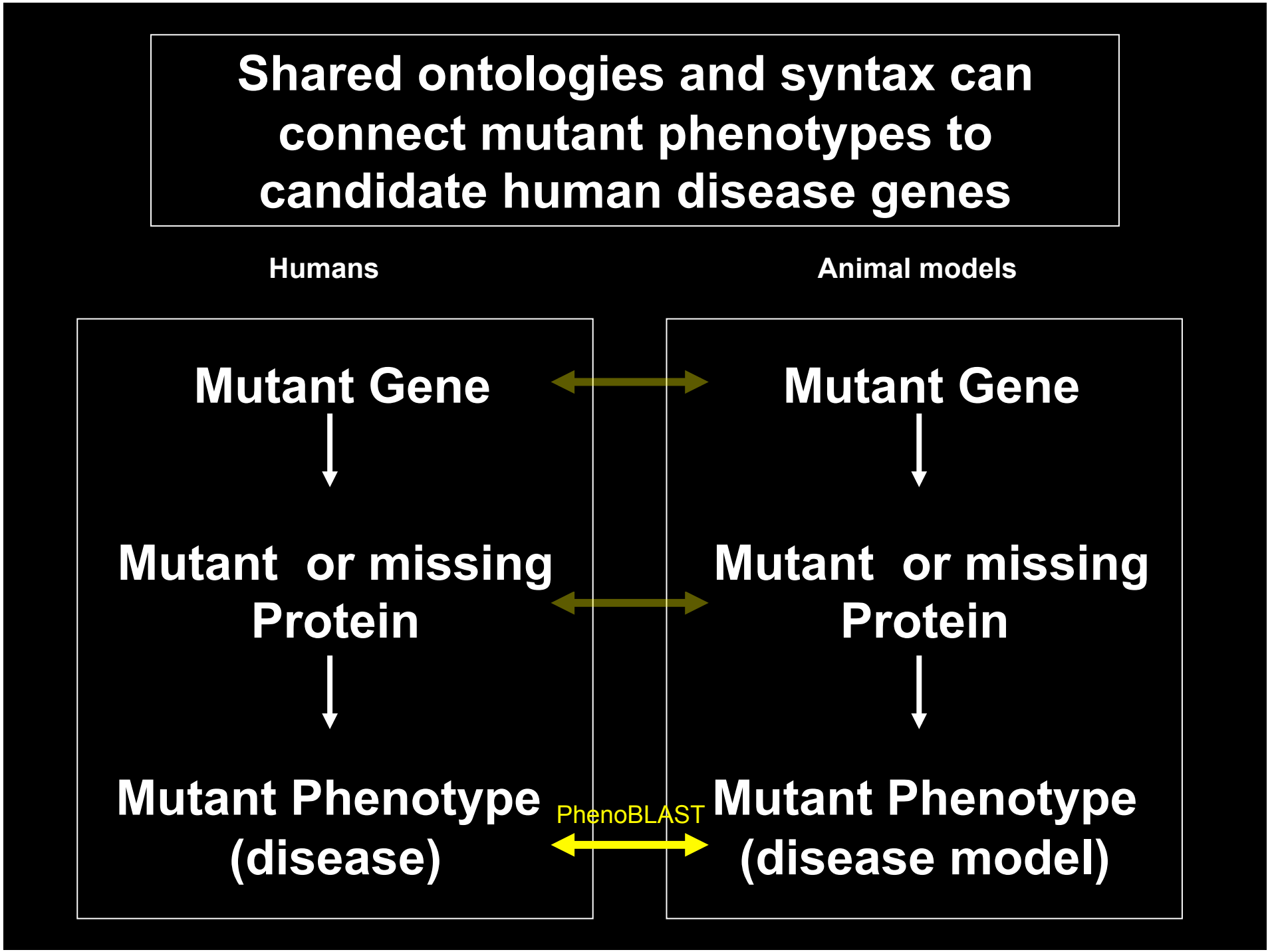
human

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)
PhenoBLAST

OMIM is a free-text disease description source

OMIM
Online Mendelian Inheritance in Man
Johns Hopkins University

My NCBI [Sign In] [Register]

All Databases PubMed Nucleotide Protein Genome Structure PMC OMIM

Search OMIM for Go Clear

Limits Preview/Index History Clipboard Details

Display Detailed Show 20 Send to

#113650

GeneTests, Links

BRANCHIOOTORENAL SYNDROME 1; BOR1

Alternative titles; symbols

BRANCHIOOTORENAL DYSPLASIA
MELNICK-FRASER SYNDROME

Gene map locus 8q13.3

TEXT

A number sign (#) is used with this entry because of evidence that this form of the branchiootorenal syndrome (BOR1) is caused by mutation in the EYA1 gene (601653). Another form, BOR2 (610896), is caused by mutation in the SIX5 gene (600963).

DESCRIPTION

Branchiootorenal syndrome is an autosomal dominant disorder characterized by sensorineural, conductive, or mixed hearing loss, structural defects of the outer, middle, and inner ear, branchial fistulas or cysts, and renal abnormalities ranging from mild hypoplasia to complete absence. Reduced penetrance and variable expressivity has been observed (Fraser et al., 1978).

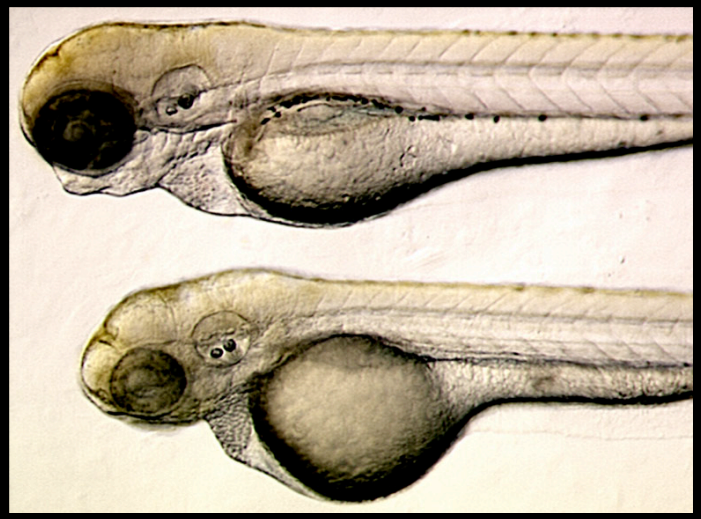
Information retrieval from text-based resources is difficult

OMIM Query	# of records
“large bone”	785
"enlarged bone"	156
"big bones"	16
"huge bones"	4
"massive bones"	28
"hyperplastic bones"	12
"hyperplastic bone"	40
"bone hyperplasia"	134
"increased bone growth"	612

OMIM
Online Mendelian Inheritance in Man

Johns Hopkins University

Annotation of *eya* mutant phenotype using ontologies



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

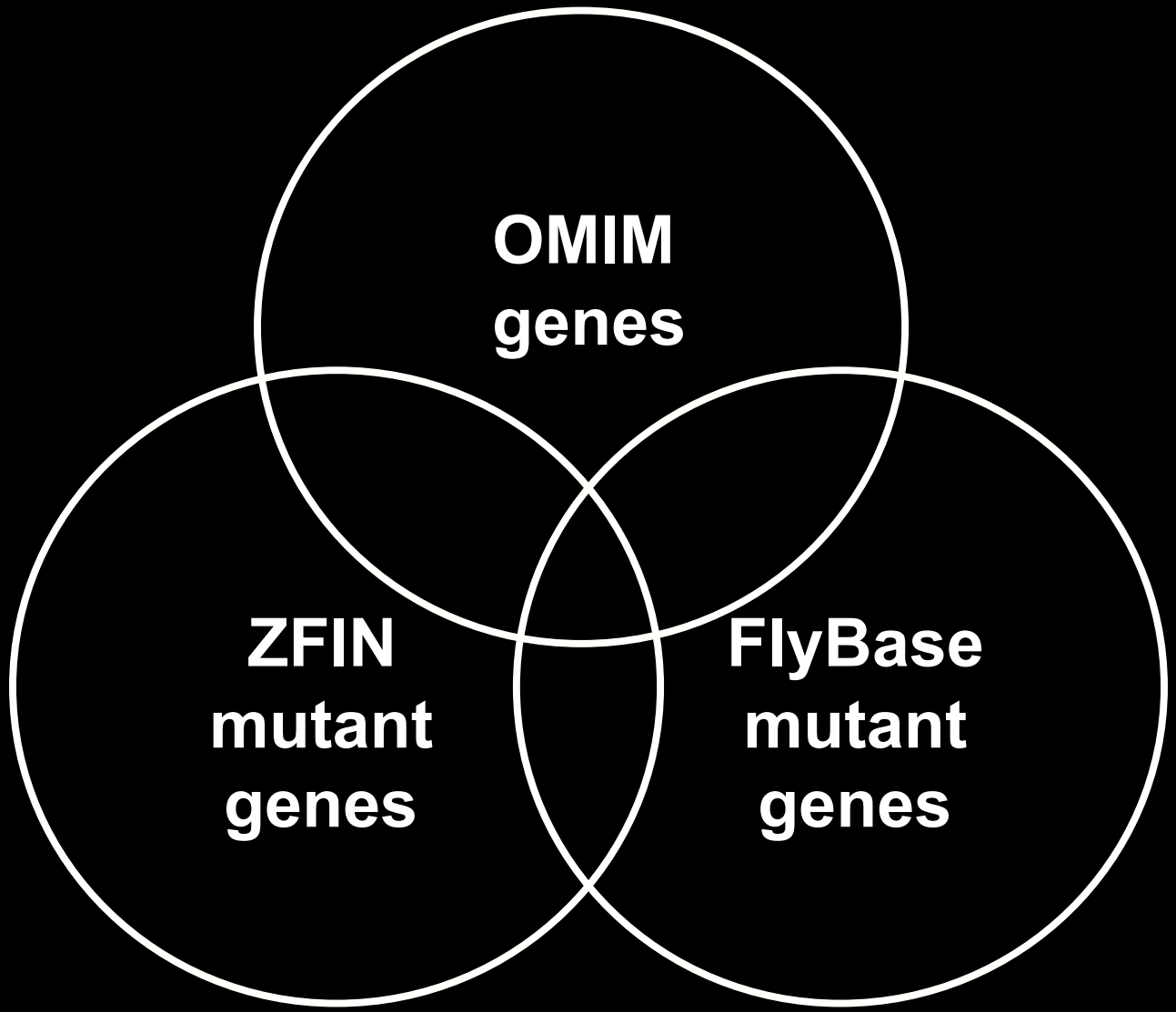
+ PATO

Linking Animal Models and Human Diseases

Develop methods to:

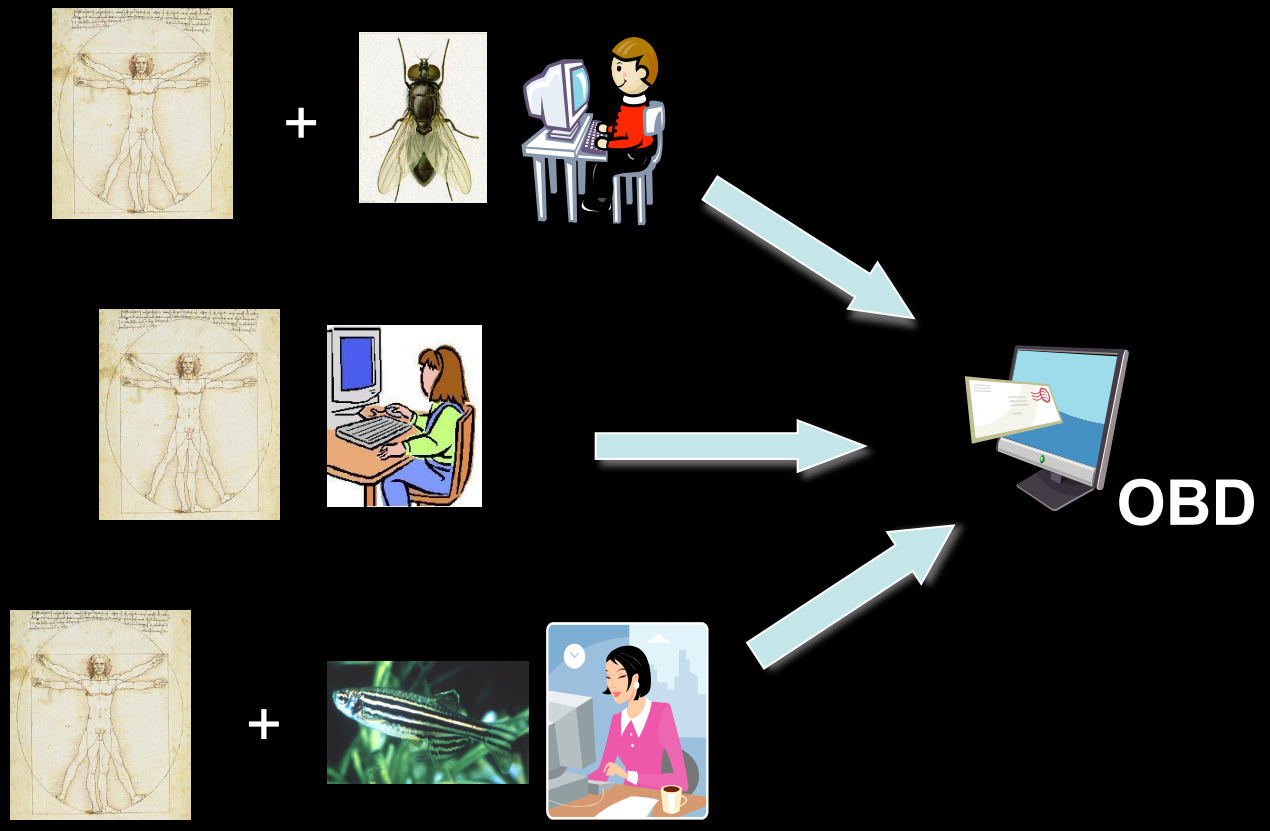
- Describe phenotypes
- Compare descriptions (annotations)
- Search phenotypes within and across species

Strategy: use shared genes as proof of principle



Experimental design

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



Results: Number of annotations added to OBD

Human (from this project)

ATP2A1, EPB41, EXT2, EYA1*, FECH, PAX2*, SHH, SOX9*, SOX10*, TNNT2, TTN* (* annotated in triplicate)

268 genotypes

1669 annotations

Human (from NCBI:GAD)

2674 genes

23,744 annotations (using MP or DO)

Zebrafish (from ZFIN)

2911 genes and 4441 genotypes

17,494 annotations

Mouse (from MGI)

10,579 genes and 23,934 genotypes

116,609 annotations (using MP)

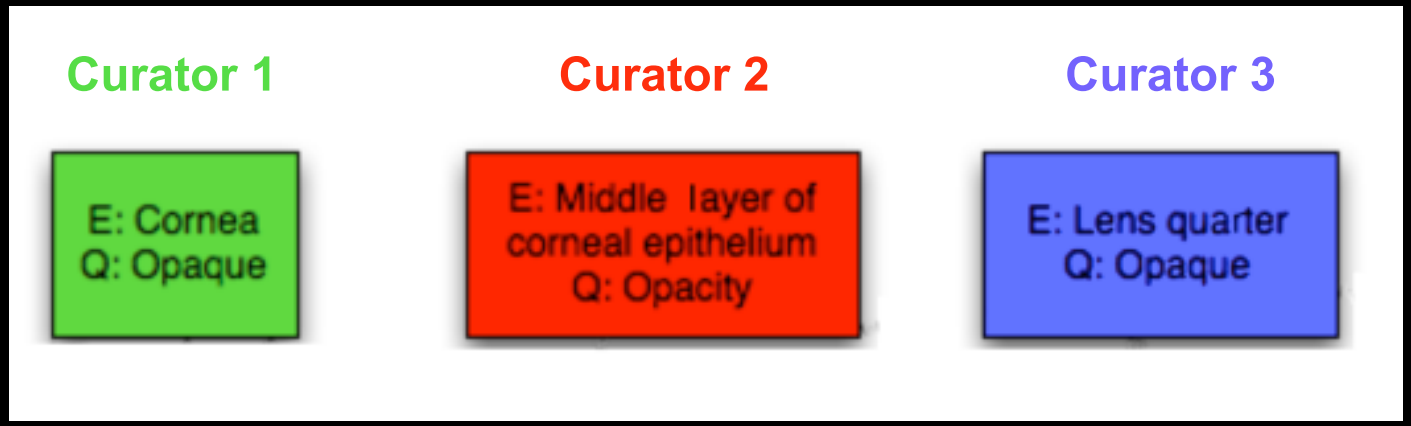
```
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000431 /*semicircular canals*/ Q=PATO:0000937 /*disorganized*/ T=during(ZFS:0000036) /*during(Larval:Day 4)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tc257e/tc257e] E=ZFA:0000139 /*immature otoliths*/ Q=PATO:0000587 /*small size*/ T=during(ZFS:0000036) /*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

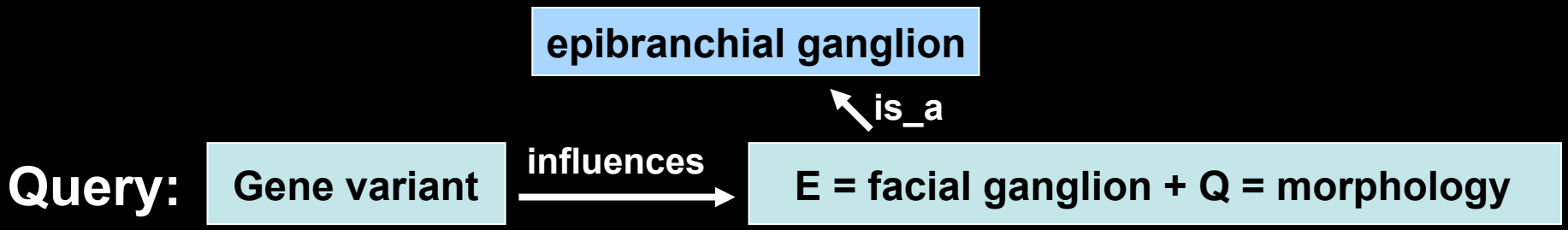
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000940 /*neuromasts posterior*/ Q=PATO:0000419 /*decreased number*/ T=during(ZFS:0000037) /*during(Larval:Day 5)*/ Tag=PATO:0000460 /*abnormal*/
PUB=PMID:9007244 GT=eya1[tm90b/tm90b] E=ZFA:0000034 /*lateral line*/ Q=PATO:0000001 /*quality*/ Tag=PATO:0000460 /*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

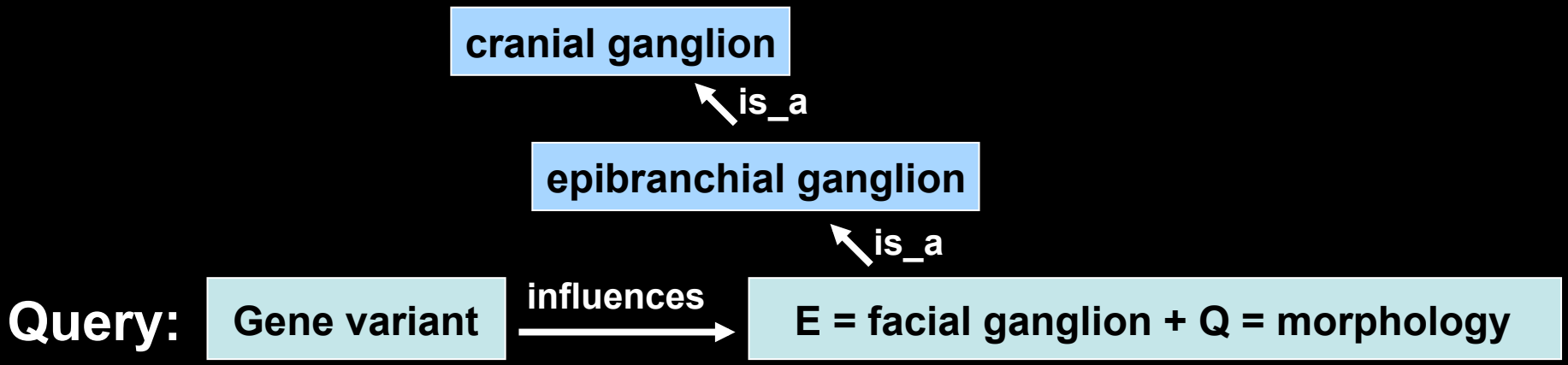


Example phenotype annotation

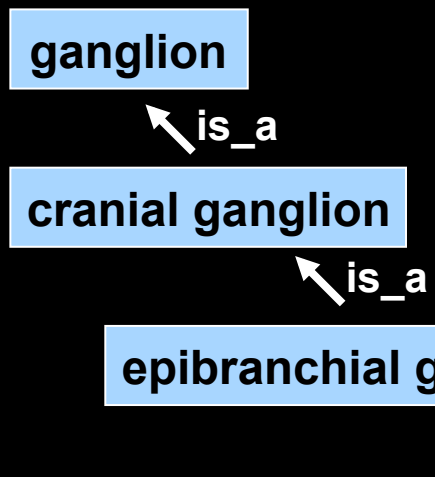
Terms are related by ontologies



Terms are related by ontologies



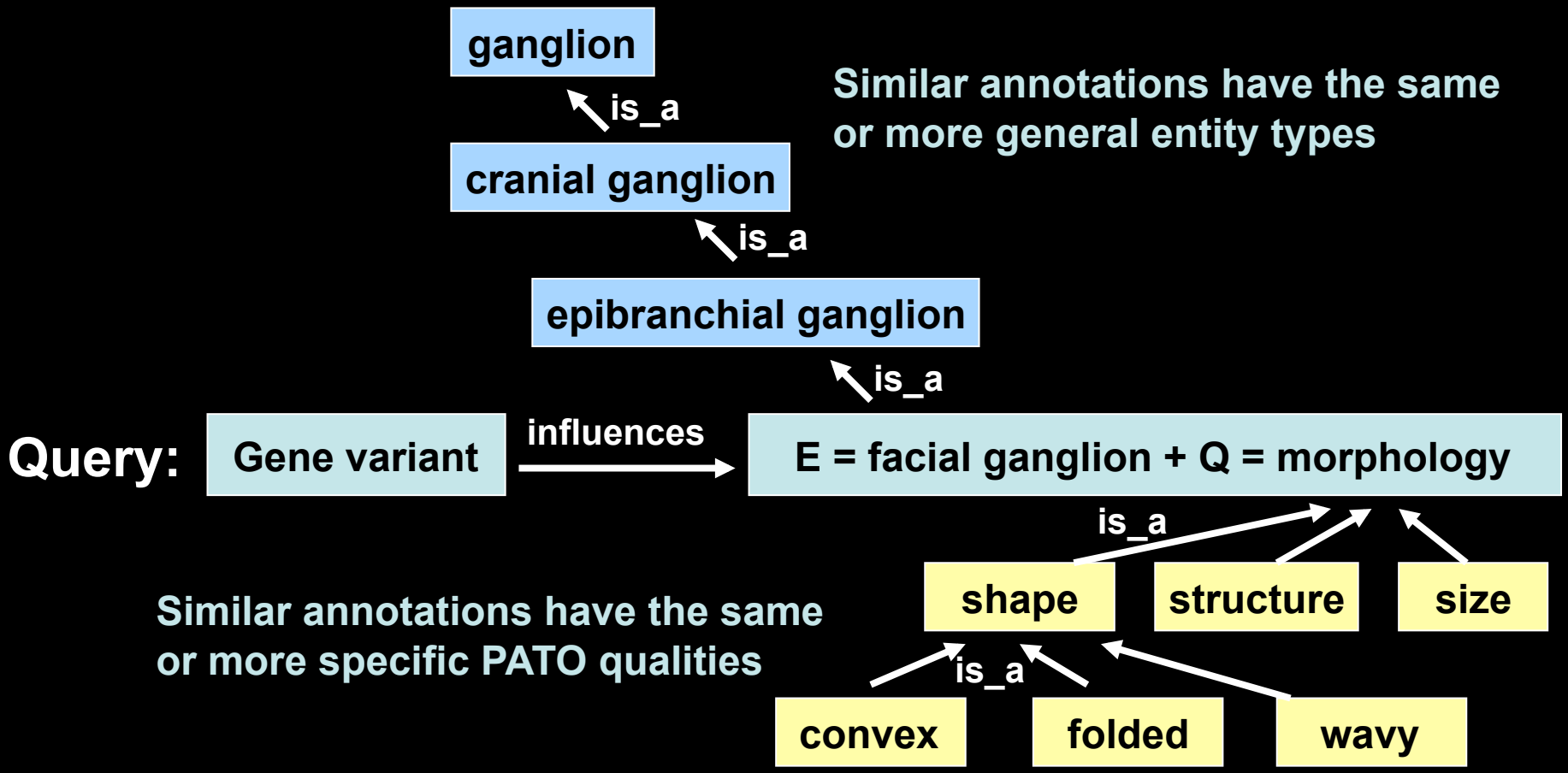
Terms are related by ontologies



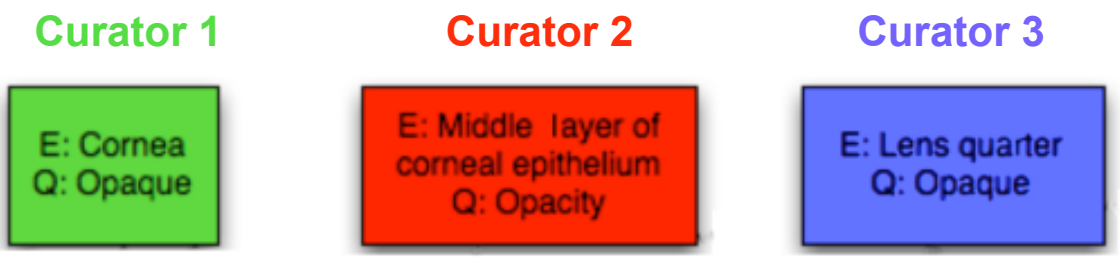
Similar annotations have the same or more general entity types

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

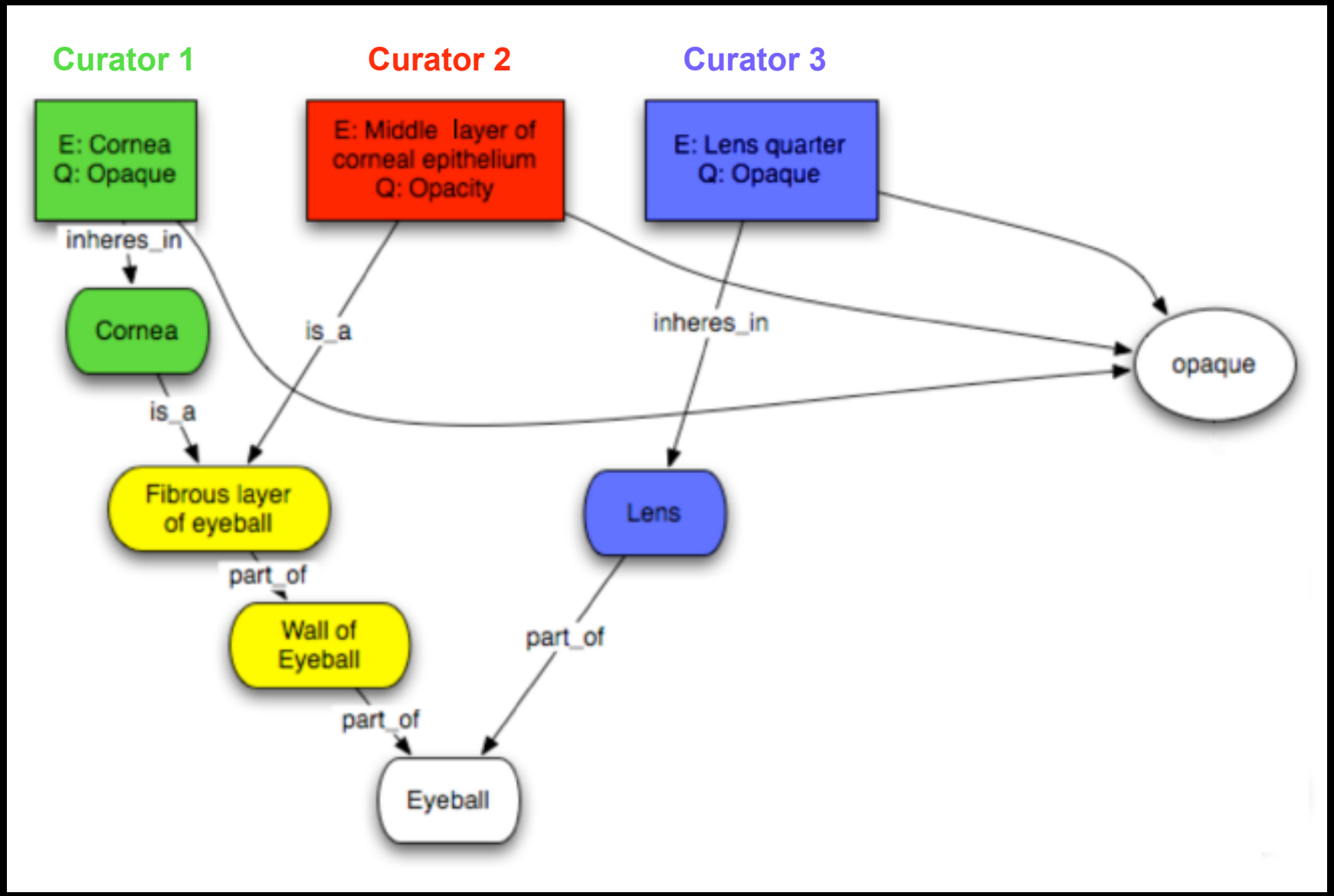
Similarity calculated by reasoning across ontologies



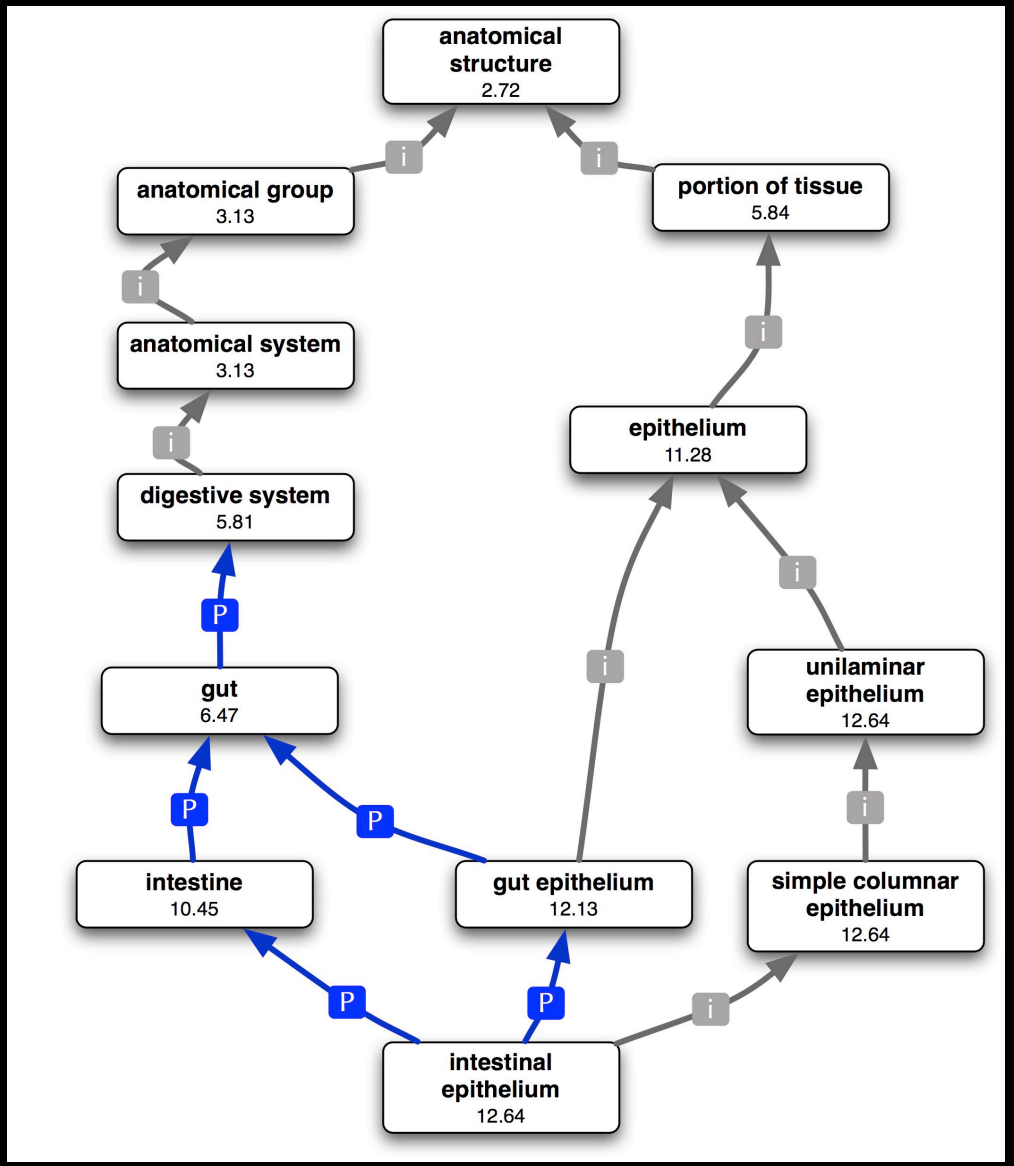
Ontologies support comparisons



Ontologies support comparisons

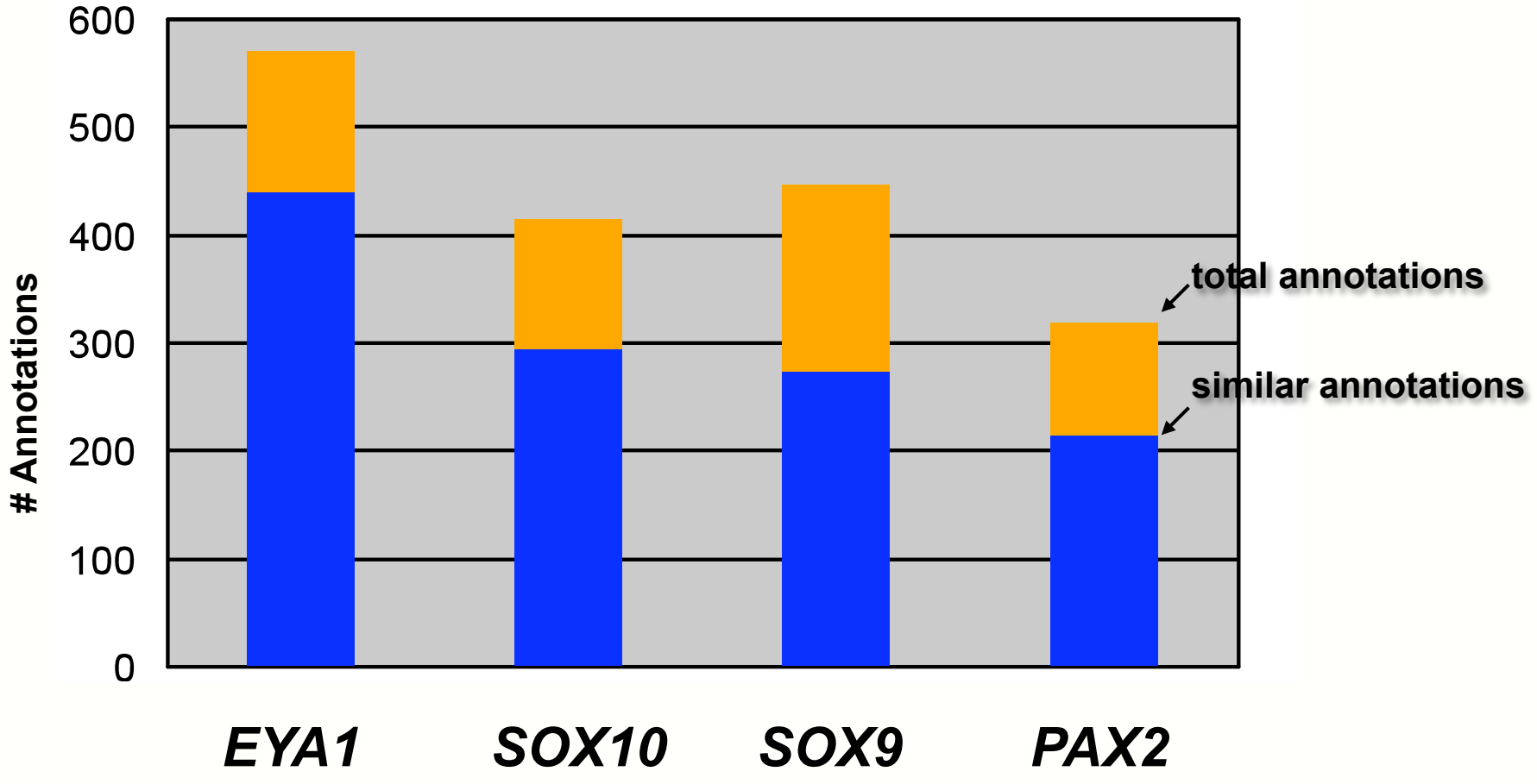


Subsumption reasoning for similarity scoring



Similarity is calculated based on depth within the ontology and annotation frequency

Average annotation consistency among curators



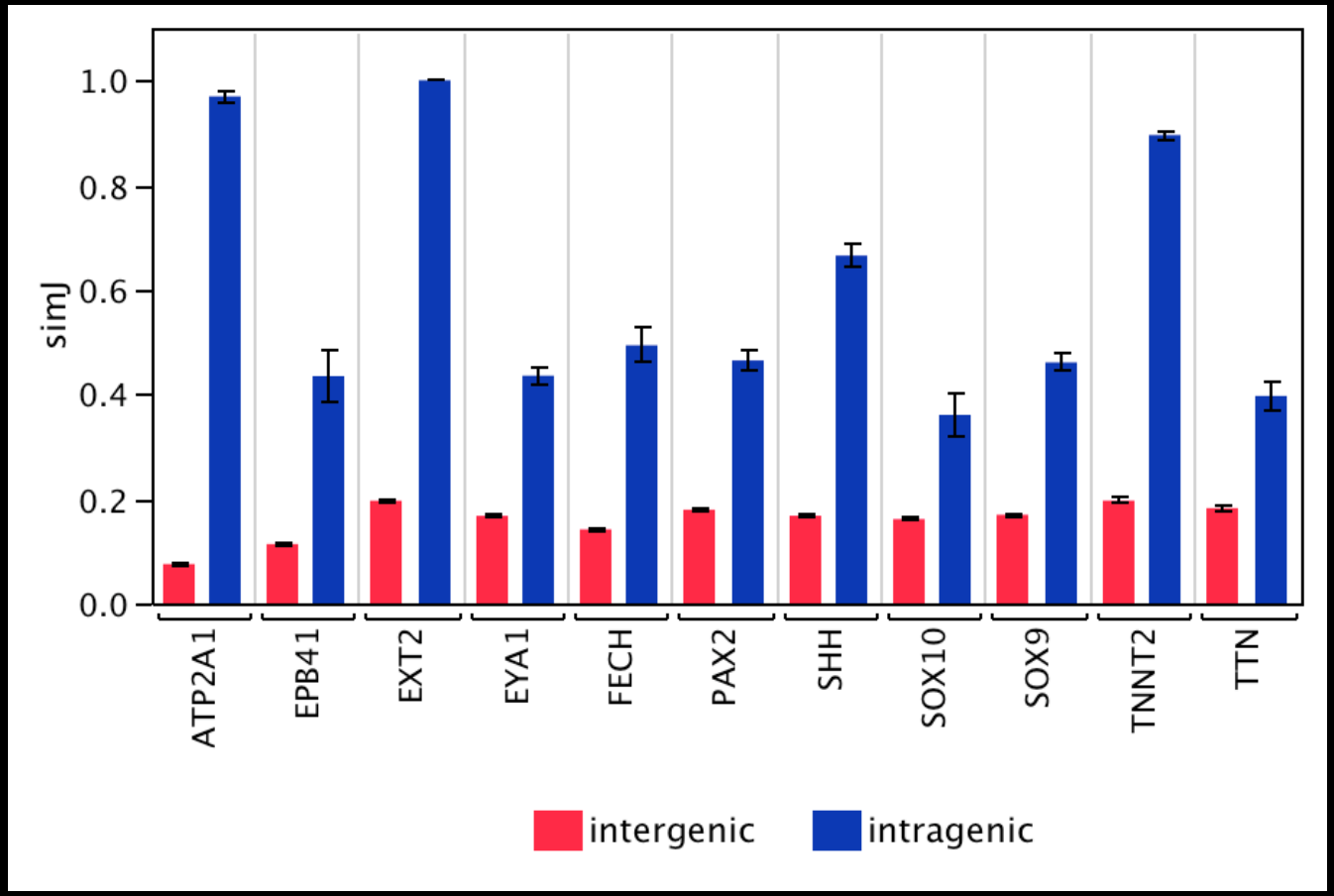
	EYA1	SOX10	SOX9	PAX2
congruence	0.78	0.71	0.61	0.72

Linking Animal Models and Human Diseases

Develop methods to:

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

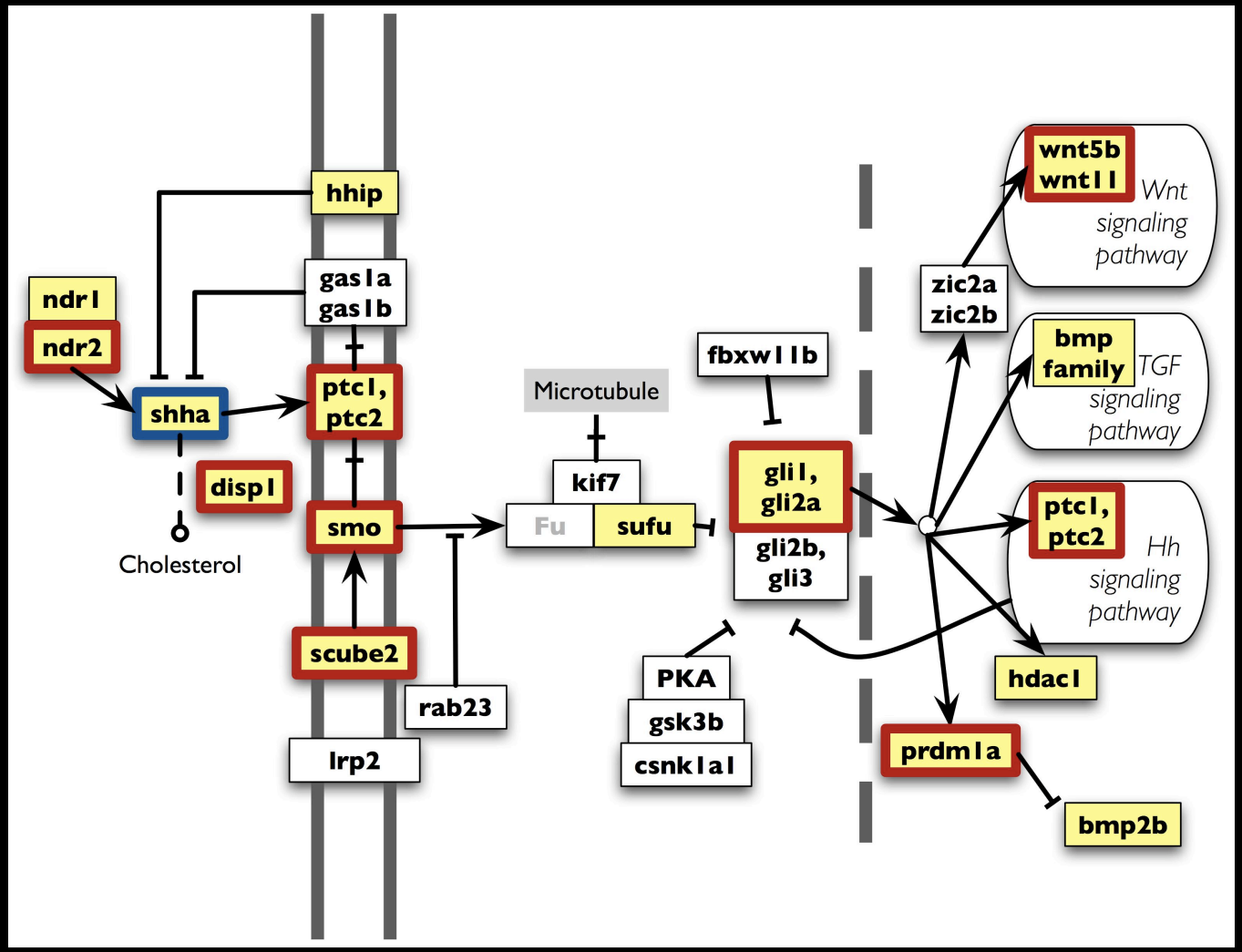
Phenotypes identify other alleles of the **same** gene



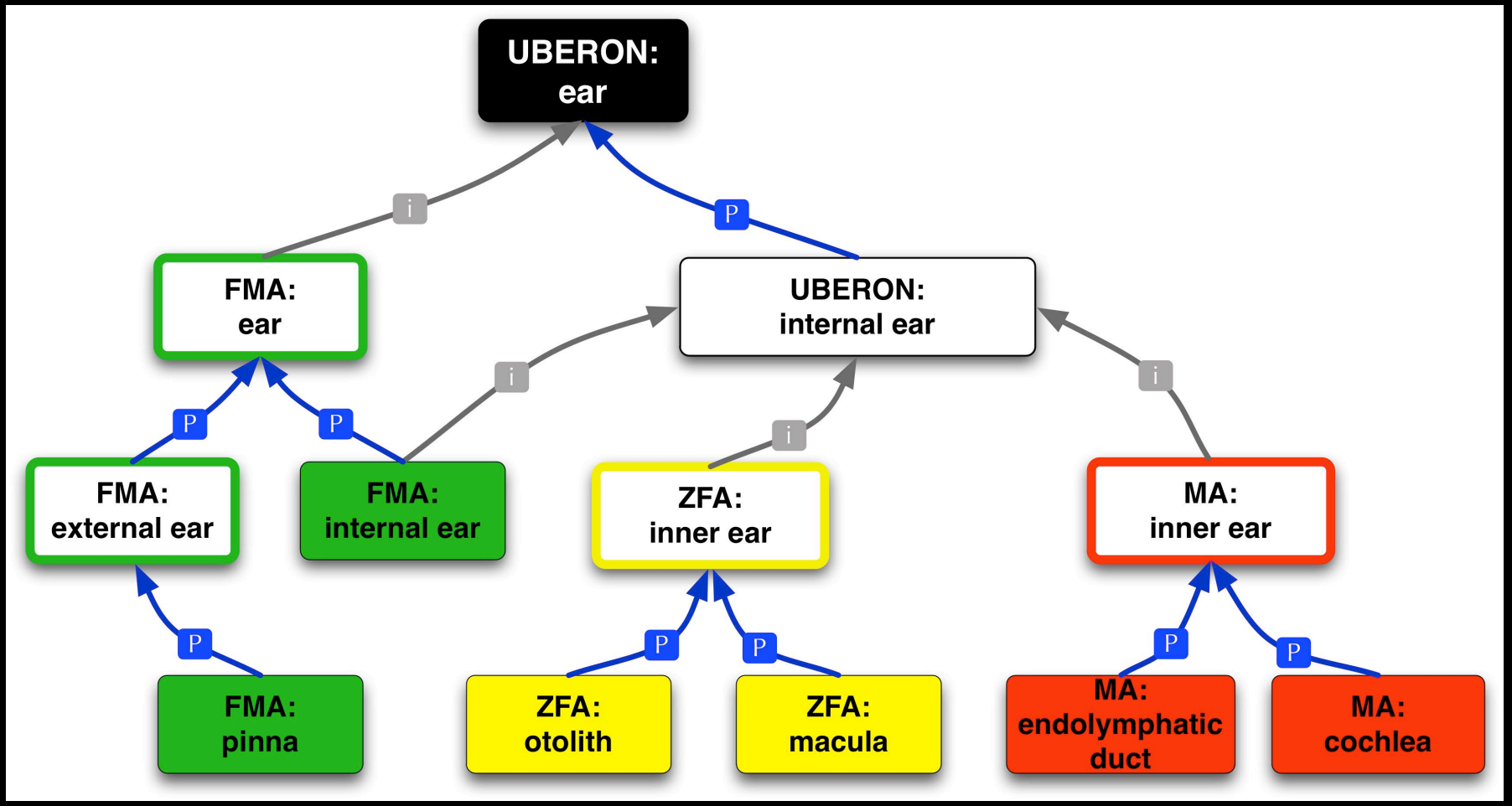
All alleles are significantly more similar to alleles of the same gene than to alleles of other genes $p<0.0001$

Annotations can identify other pathway members

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



Cross-species comparisons require linking species-specific anatomy ontologies



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:

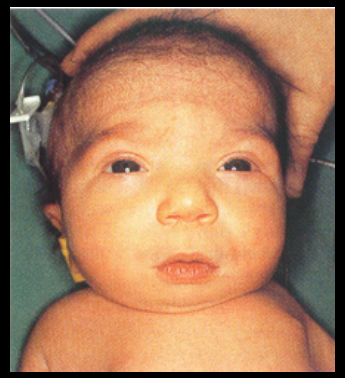
Human *EYA1* variant OMIM:601653
MP:deafness = E = Sensory perception of sound Q = absent

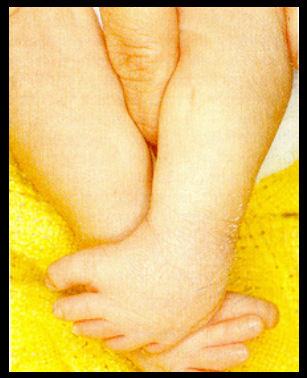
returns:

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

Annotations of animal phenotypes can identify candidate human disease genes

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

Linking Animal Models and Human Diseases

Develop methods to:

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

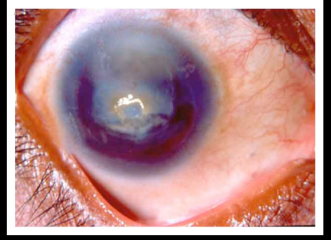
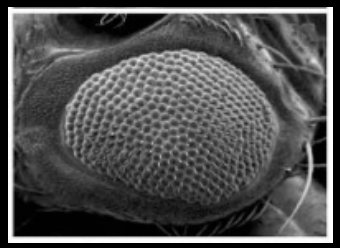
NATIONAL CENTER FOR BIOMEDICAL ONTOLOGY

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

Vocabulary

Anatomical system
Cornea
Embryo
Eye
Nervous system
Visual system

Ontology

Embryo

- Anatomical system
  - Nervous system
    - Visual system
      - Eye
        - Cornea