

Advancing a Community-Led Zebrafish Toxicology Phenotype Atlas

Sabrina Toro, PhD
University of North Carolina at Chapel Hill

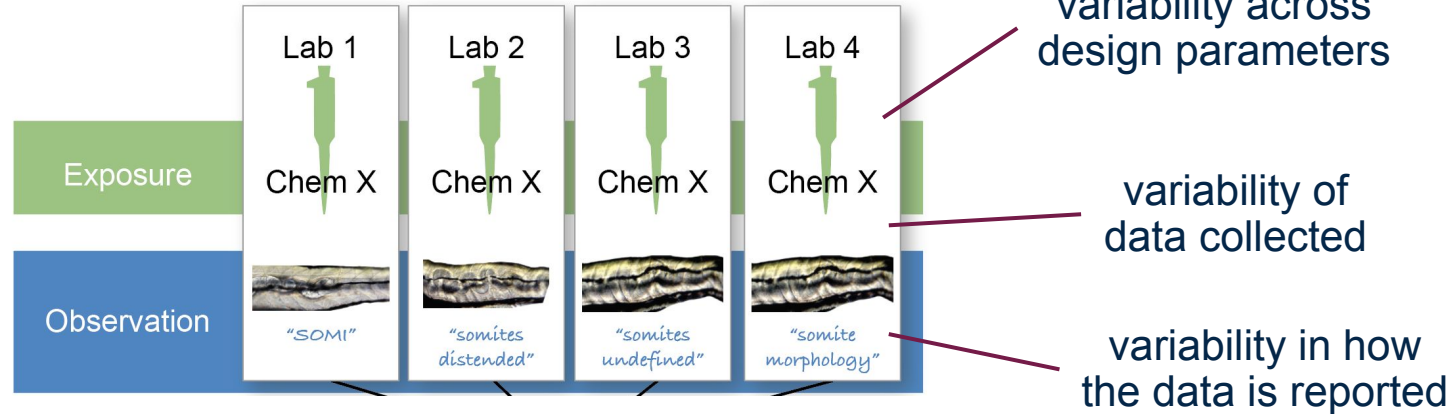


Alexa Burger, PhD
University of Colorado Anschutz Medical Campus



Lack of standards impedes data integration and reuse of zebrafish toxicology assay data.

Inter-laboratory study

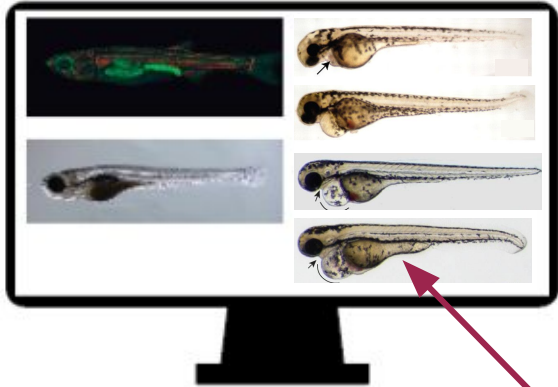


Community-led Zebrafish Toxicology Phenotype Atlas (ZAPP) will

- create/support **standards** for phenotypic and toxicology data
- make **standard adoption approachable**
- support **community-driven approaches**

The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Zebrafish Phenotype Atlas

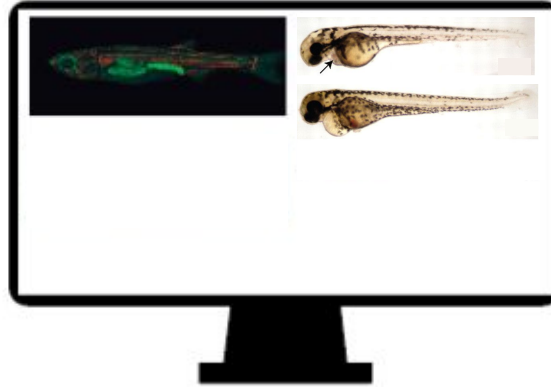


**Visual definition
of phenotypes**

Explore

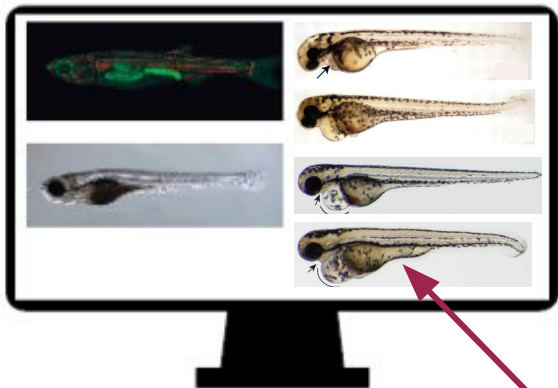
Search
Filter

Zebrafish Phenotype Atlas



The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Zebrafish Phenotype Atlas



Visual definition
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Explore

Search
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Zebrafish Phenotype Atlas



Images + Annotations

>Fish:

Strain: STRAIN

Genotype: GENOTYPE

Allele: ALLELE

...

>Experimental conditions

Toxicant: TOXICANT

Concentration: MG/L

Timing of exposure: 2 H

...

>Phenotype: PHENOTYPE

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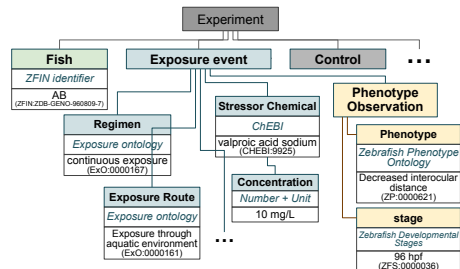
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Same standards
for all data in the atlas

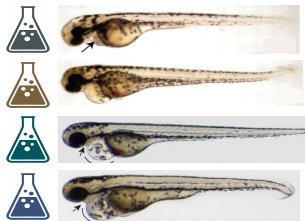
Standards



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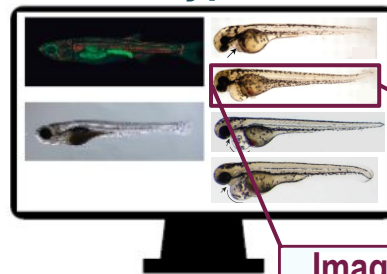
Data Collection

Zebrafish community



Submit to the Atlas

Zebrafish Phenotype Atlas



Images + Annotations

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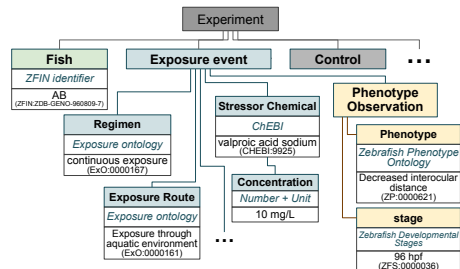
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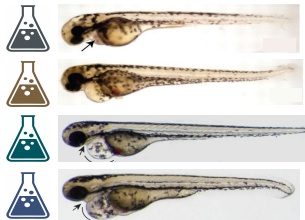
Standards



The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Data Collection

Zebrafish community



Data Annotation (using Standards)

Provenance of Data

Control Information

Images

Control information

Experiment information

Fish

Exposure Event

Stressor CAS Identifier

Stressor concentration Unit ☐ μ M ☒ mg/L ☐ Other

Exposure route

☒ via environment (chemical in the water)
☐ via diet (ingestion)
☐ via gavage
☐ via injection

Exposure regimen

☒ Continuous exposure ☐ Repeated exposure

Stage at exposure start Hours

Stage at exposure end Hours

Phenotype Observation

Images

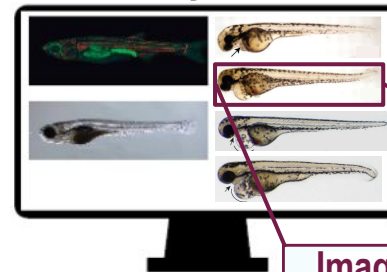
Phenotypes shown in the image

Stage at observation Hours

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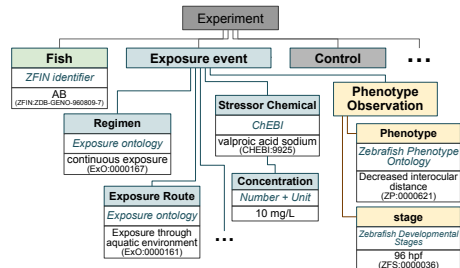
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Standards



Annotation Toolkit

The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Data Collection

Data Annotation (using Standards)

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Zebrafish Phenotype Atlas

Images + Annotations

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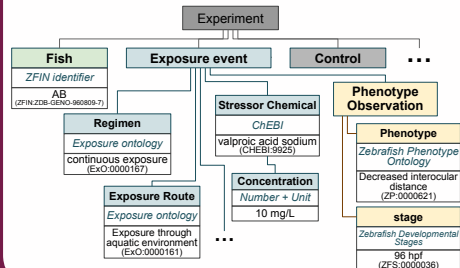
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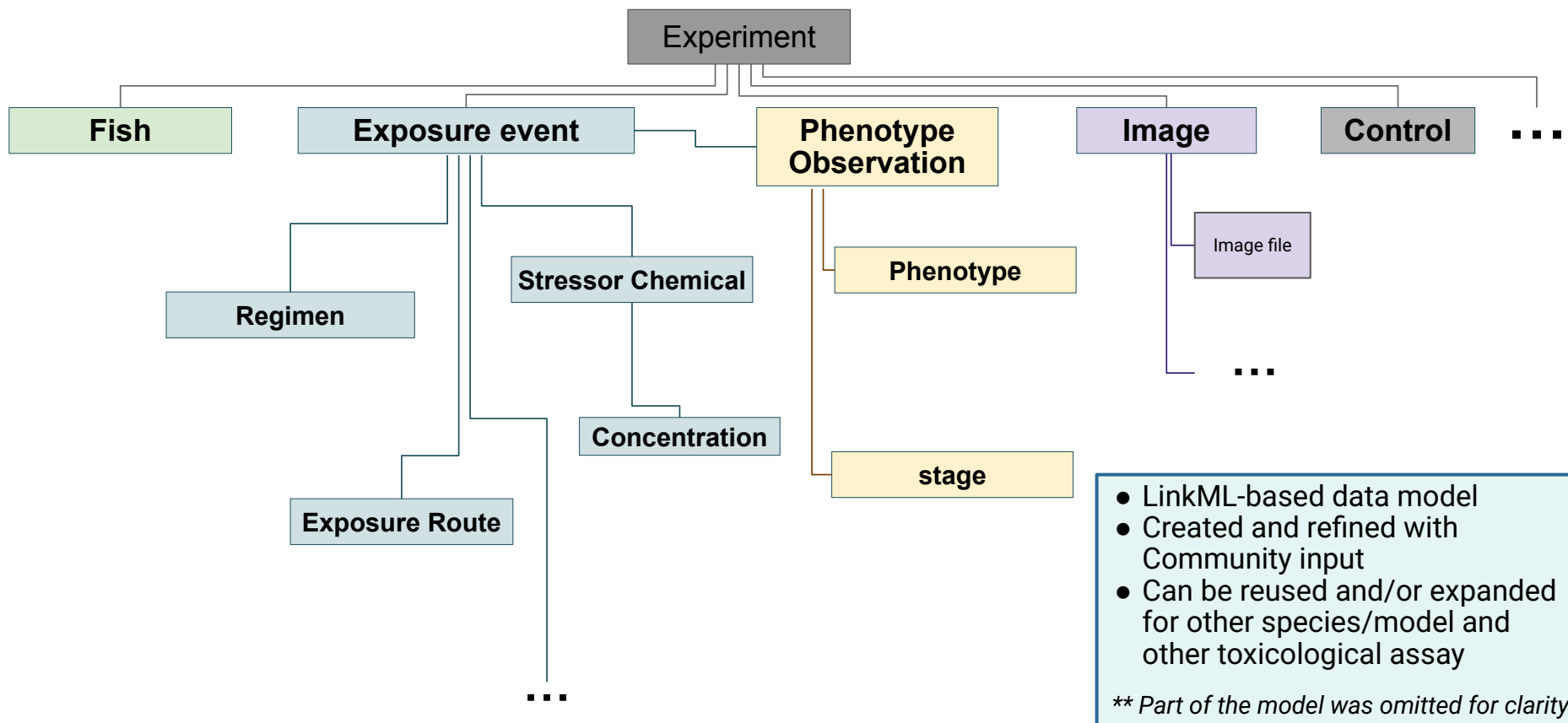
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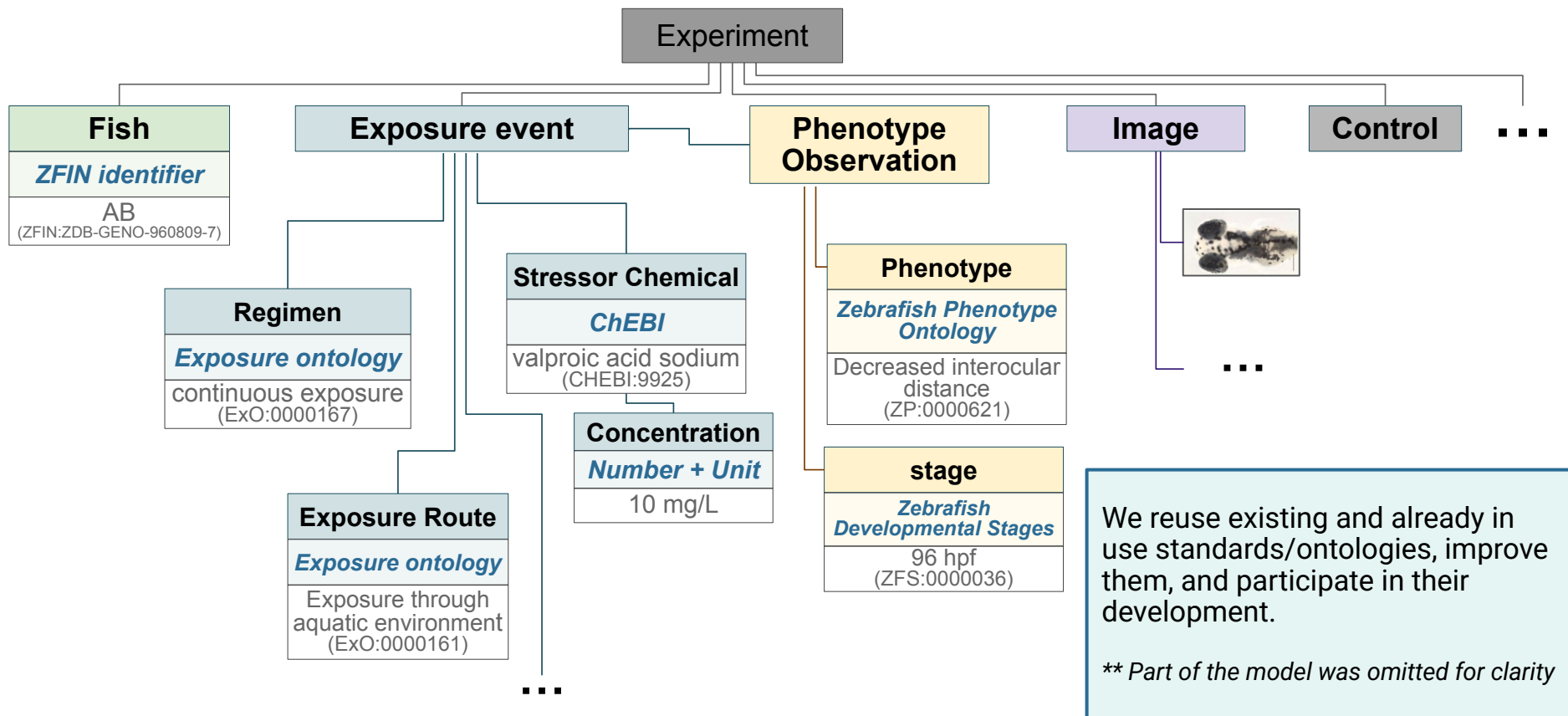
Phenotypes shown in the image

Stage at observation Hours

Formalized standards for reporting Toxicology data.



Formalized standards for reporting Toxicology data.



The annotation toolkit will allow the use of standards, without requiring expertise in ontologies or standards development.

Data Collection

Data Annotation (using Standards)

Submit to
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Zebrafish Phenotype Atlas

Standards + Annotations

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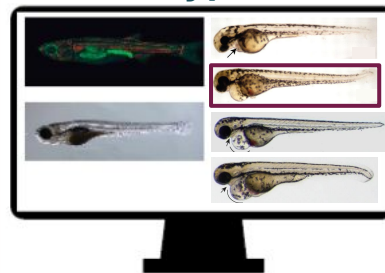
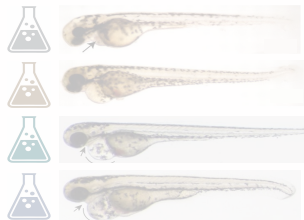
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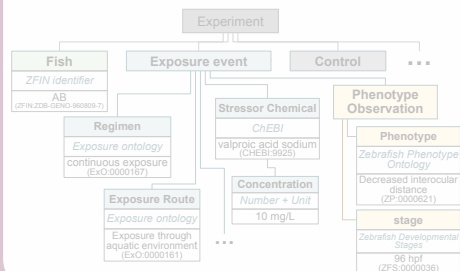
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Zebrafish
community



Standards



Provenance of Data

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Phenotypes shown in the image

Stage at observation Hours

Annotation Toolkit

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Data Collection

Data Annotation (using Standards)

Submit to
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Zebrafish Phenotype Atlas

Standards + Annotations

The ultimate goal is to encourage **reporting data in a standardized format**, so that the data is “born” unambiguous, comparable, reproducible, and reusable.

Provenance of Data

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Stage at observation Hours

Annotation Toolkit

Publish
standardized
data

PubMed

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Exposure Route Exposure ontology Exposure through aquatic environment (EXO:0000181) ...	Concentration Number + Unit 10 mg/L	Decreased interocular distance (ZP:3000621) stage Zebrafish Developmental Stages 96 hpf (ZFS:0000036)
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Ontology term picker tool allows users to find phenotype terms without the need to understand how ontologies work.

Filter by Anatomy

- ☒ nervous system
 - ☐ autonomic nervous system
 - ☒ central nervous system
 - ☒ brain
 - ☐ brain nucleus
 - ☐ brain vasculature
 - cephalic flexure
 - ☐ choroid plexus
 - choroidal fissure
 - ☐ forebrain
 - forebrain midbrain boun...
 - ☐ granule cell
 - ☐ hindbrain
 - ☐ midbrain
 - ☐ midbrain hindbrain bou...
 - supraoptic tract
 - ☐ brainstem

Find term
using
anatomy

Showing the
ontology tree
suggests a more
specific terms

Phenotypes for brain

Filter within results...

Showing 50 of 118 phenotypes

abnormal brain morphology

ZP_0000100

• 356 ZFIN references



abnormal brain

ZP_0000032

• 343 ZFIN references



microencephaly

ZP_0000711

• 307 ZFIN references



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Phenotypes for brain

4 phenotypes matching "increased size"

increased size of the macrophage in brain

ZP_0148851

• 2 ZFIN references



increased size of the proliferative region in brain

ZP_0007309

• 1 ZFIN references



macroencephaly

ZP_0003410

• 16 ZFIN references



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Find term using anatomy

Showing the ontology tree suggests a more specific terms

Phenotypes for brain

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ZP_0148851

• 2 ZFIN references



FROGPOT (From Graphs, Pick Out Terms) is developed to accommodate 'any' ontologies, especially ontologies using 2 types of concepts (e.g., *phenotype and anatomy; breed and taxon; disease and gene*)



Other ongoing work

Standards and Tools

- Standards improvements
 - Zebrafish Phenotype ontology (ZP)
 - Exposure ontology (ExO)
 - Environment Exposure Ontology (ECTO)
- Tool to identify chemicals based on any identifier (CAS, ChEBI, PubChem) or name.
- Data annotation tool
- Atlas Web Application

Community Outreach

- Workshops
- Materials
 - Website
 - Blog posts
 - Tutorials
- Governance documents

Resources (i.e. Offers)



- Standards:
 - [Toxicology data model](#): *can be modified to any animal model or specimen*
 - Ontologies:
 - [Environment Exposure Ontology](#) (ECTO) - Species non-specific
 - [Exposure ontology](#) (ExO) - Species non-specific
 - [Zebrafish Phenotype Ontology](#) (ZP) - Specific to Zebrafish, but already integrated into uPheno (species non-specific phenotype ontology)
- Website: <https://zappfish.org/>
 - [Governance documents](#)
 - [ZAPP Blog](#)
- [ZAPP Zenodo Community](#)

- FROGPOT (Ontology term picker tool)
- Annotation toolkit
- Atlas web application



How to participate (ie. Asks)



- Join the ZAPP community (*no commitment required*):
 - tislabs.org/ZebraPhenoAtlas-signup
 - Slack channel on Zebrafish Rock!: #zapp-fish
- Participate in the workshops
 - Gather information about data standards, all information required
 - Gather feedback, community needs, etc
- Send us feedback
 - About what you need, what you want
 - About how we can make the use of standard easier (ie with minimal disruption of every day research)
 - Error, misrepresentation, changes
- Use our tools and submit your data (*when available*)



Acknowledgements

Sabrina Toro, MPI
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MeeSiing Ngu, Curator



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Raéden Gray, Post-Doctoral Fellow



Collaborators:

Sierra Moxon (LBNL)

Advisory Team:

Anne Thessen (UNC)
Jonathan Hamm (Inotiv)
Melissa Haendel (UNC)

 **zappfish.org**

 **info@zappfish.org**



tislab.org/ZebraPhenoAtlas-signup



