UNC SCHOOL OF MEDICINE Genetics

Anschutz

Zebrafish Atlas Phenotype Project (ZAPP): A Community-Driven Framework for Zebrafish Toxicology and Phenotype Data

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Alexa Burger, PhD University of Colorado Anschutz Medical Campus

EHLC webinar
January 23rd, 2026

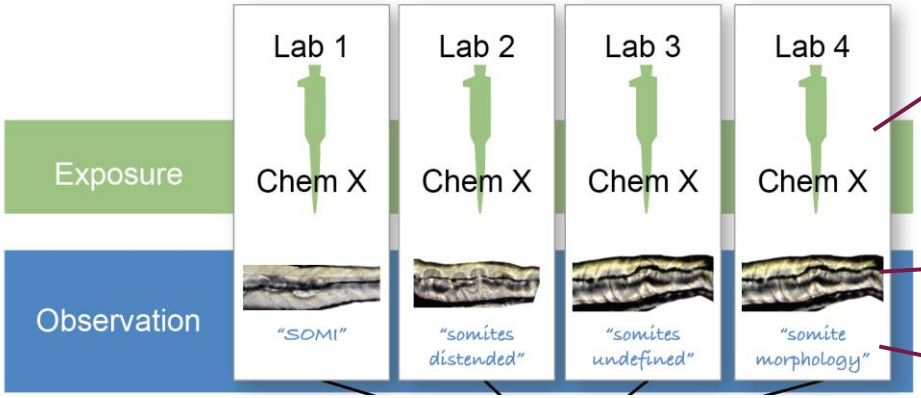
Lack of standards impedes data integration and reuse of zebrafish toxicology assay data

Systematic **E**valuation of the **A**pplication of **Z**ebrafish **i**n **T**oxicology (SEAZIT) project

SEAZIT Goals:

- Provide scientific basis to decide whether or not zebrafish can be used for toxicological screening
- Provide fundamental knowledge on the use of zebrafish in toxicology

Inter-laboratory study



variability across design parameters

variability of data collected

variability in how the data is reported

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

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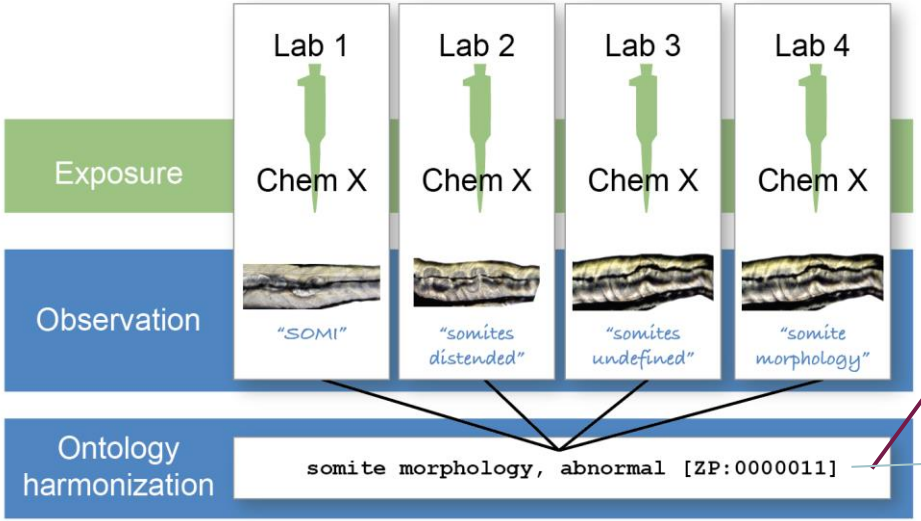
Inter-laboratory study



Use of standards (eg. ontology term to report phenotypes) reduces data variability

What does “abnormal somite morphology” phenotype look like?

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

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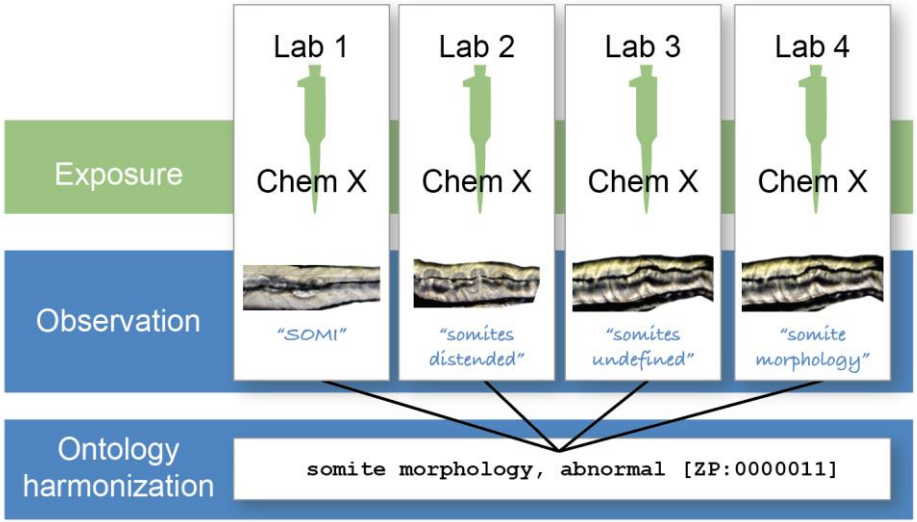
Inter-laboratory study



Reporting phenotypic and toxicology data **using standards** would improve data interoperability, sharing, reuse, and comparison.

https://ntp.niehs.nih.gov/whatwestudy/niceatm/test method evaluations/dev tox/seazit

Adoption of standards is limited by practical use

The Research Community understands and agrees that the need for standards is crucial. However, they **don’t know what to do in practice**.

- What are the standards and how to use them?
- Where to find the standards?
- What to do when what is needed is not available?
- How to use standards in existing research workflow?

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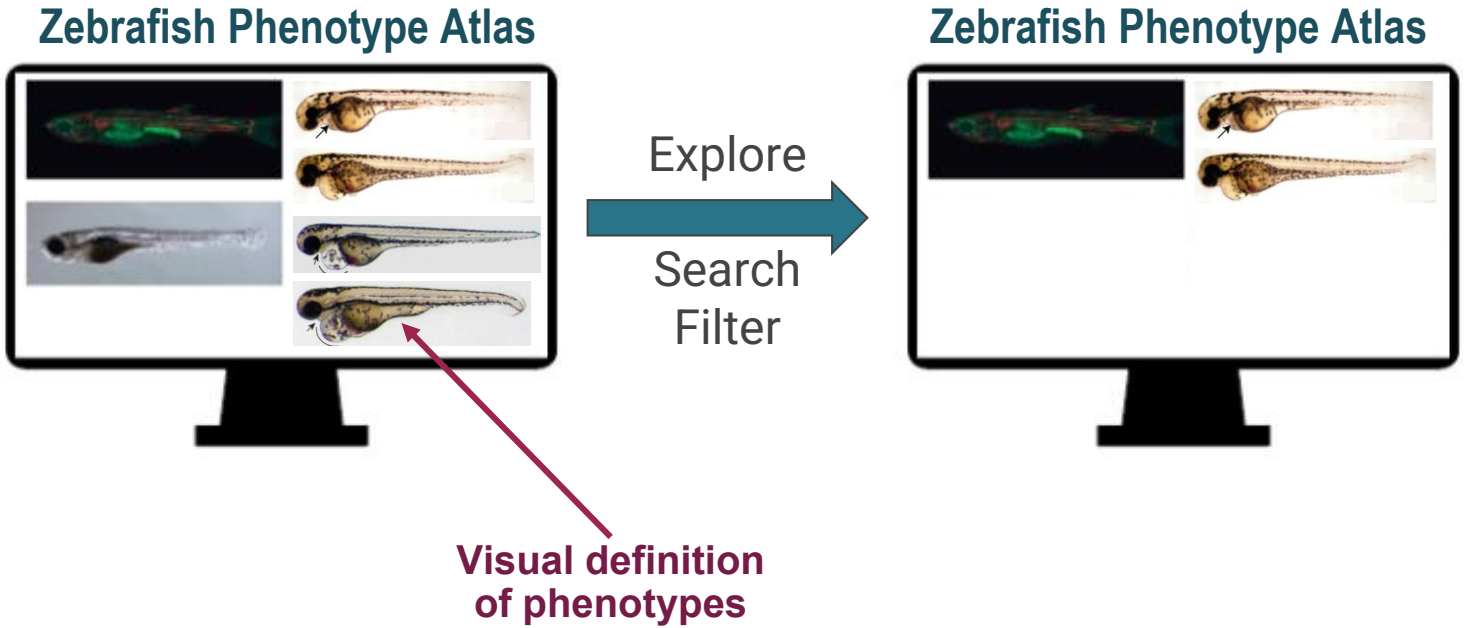
Community-led Zebrafish Toxicology Phenotype Atlas (ZAPP) will

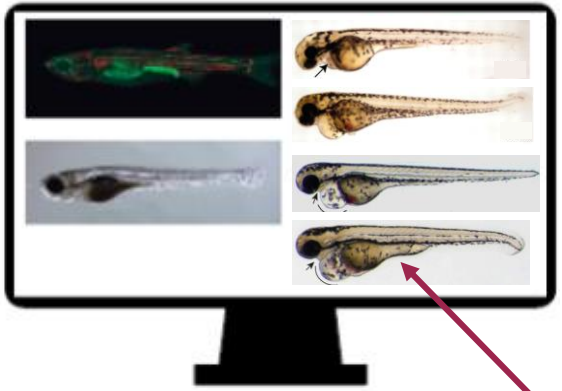
- **integrate existing standards, and develop new one when needed, for phenotypic and toxicology data**
- make **standard adoption approachable**
- support **community-driven** improvement

The Zebrafish Toxicology Phenotype Atlas (ZAPP)



The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Zebrafish Phenotype Atlas



Explore

Search
Filter

Zebrafish Phenotype Atlas

Visual definition of phenotypes

Images + Annotations

>**Fish**:

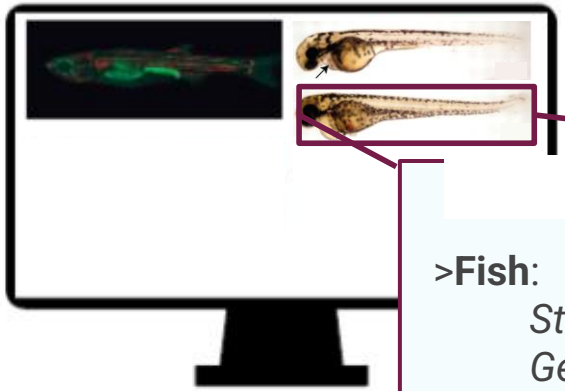
Strain: strain
Genotype: Genotype
Allele: Allele
…

>**Experimental conditions**

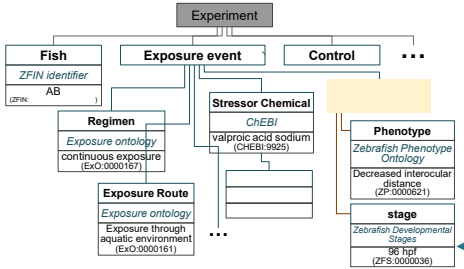
Toxicant: Toxicant
Concentration: mg/l
Timing of exposure: 2 h
…

The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Zebrafish Phenotype Atlas



Standards



Same standards
for all data in the atlas

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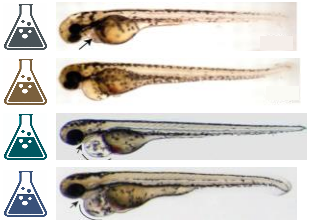
The Zebrafish Toxicology Phenotype Atlas (ZAPP)

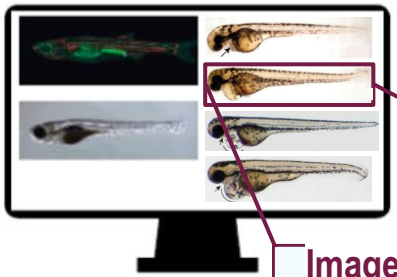
Data Collection

Zebrafish community



Submit to the Atlas

Zebrafish Phenotype Atlas



Images + Annotations

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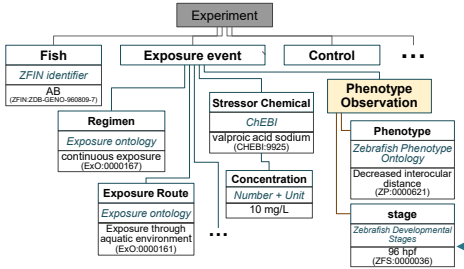
>**Phenotype**: Phenotype

Standards



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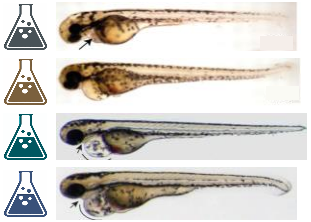
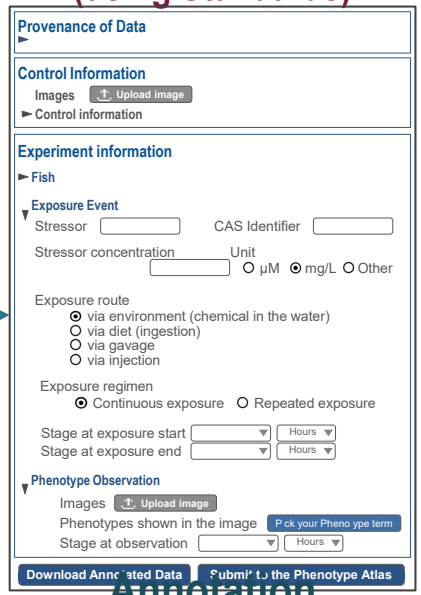


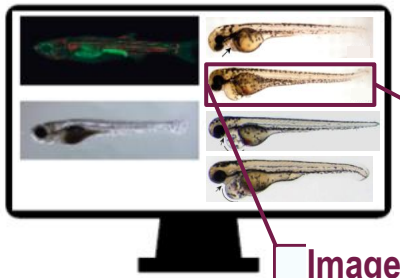
Data Annotation (using Standards)



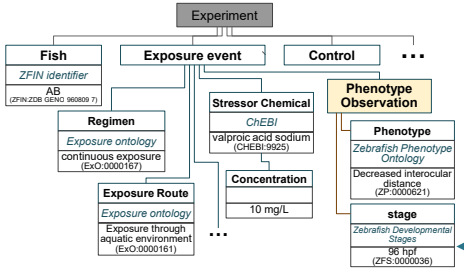
Annotation Toolkit

Submit to the Atlas

Zebrafish Phenotype Atlas



Standards



Images + Annotations

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>**Phenotype**: Phenotype

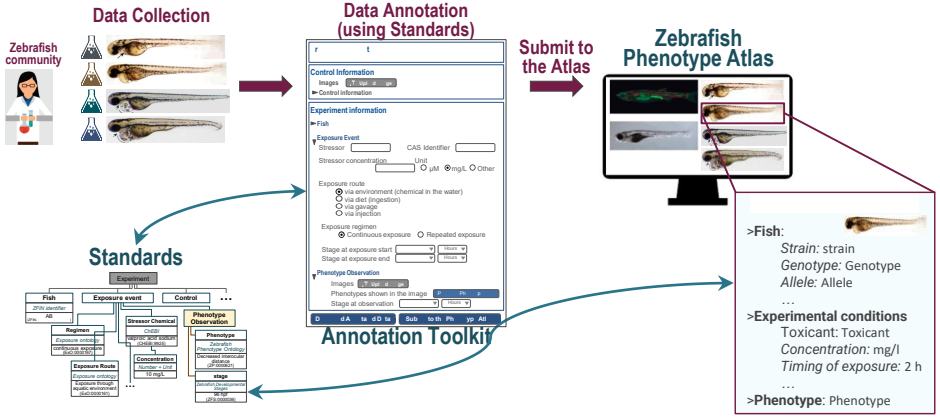
Community involvement is at the core of ZAPP

Community is involved in every part of the project

- Data annotation and submission
- Standards development
- Requirements gathering
- Governance

ZAPP community includes

- Zebrafish researchers
- Toxicologists
- Atlas experts
- Standards developers
- etc



A few caveats…

ZAPP is developed to be species agnostic

Though created to represent Zebrafish data, tools and standards can be adapted/reused, including

- Data model
- Annotation toolkit
- Ontology term picker

"Phenotypes? I am confused!"

Phenotype can be

- **Abnormal morphology** ← First iteration
- Change in gene expression
- Change in behavior

"Fish"

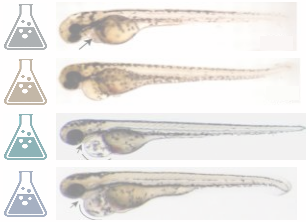
Fish can be

- **Wild-type** ← First iteration
- Transgenic
- Mutants

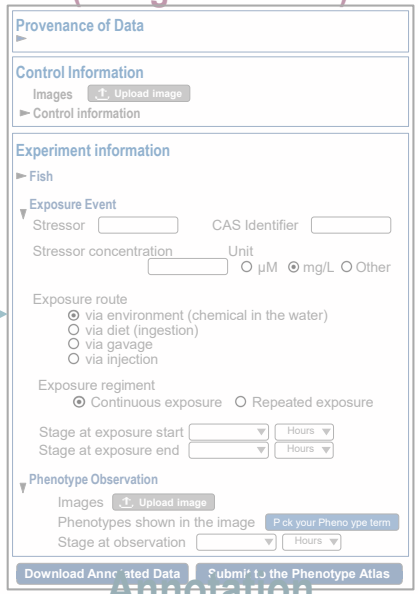
The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Data Collection

Zebrafish community



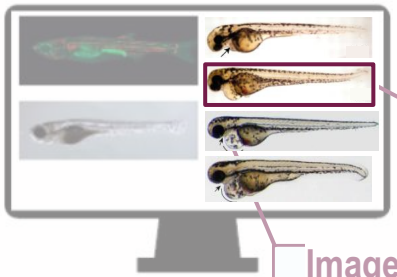
Data Annotation (using Standards)



Annotation Toolkit

Submit to the Atlas

Zebrafish Phenotype Atlas



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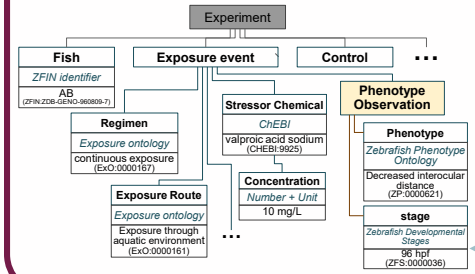

Images + Annotations

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Timing of exposure: 2 h

…

>**Phenotype**: Phenotype

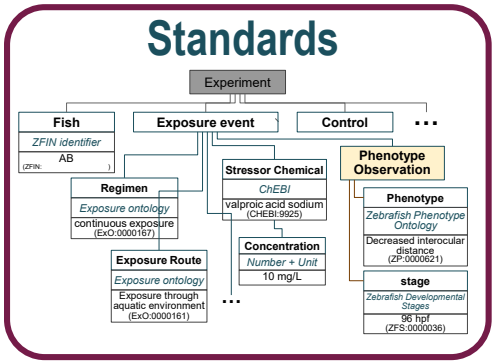
Standards for Toxicology Assay and Phenotype.

Data Model

= all the pieces of information required **AND** how they should be reported

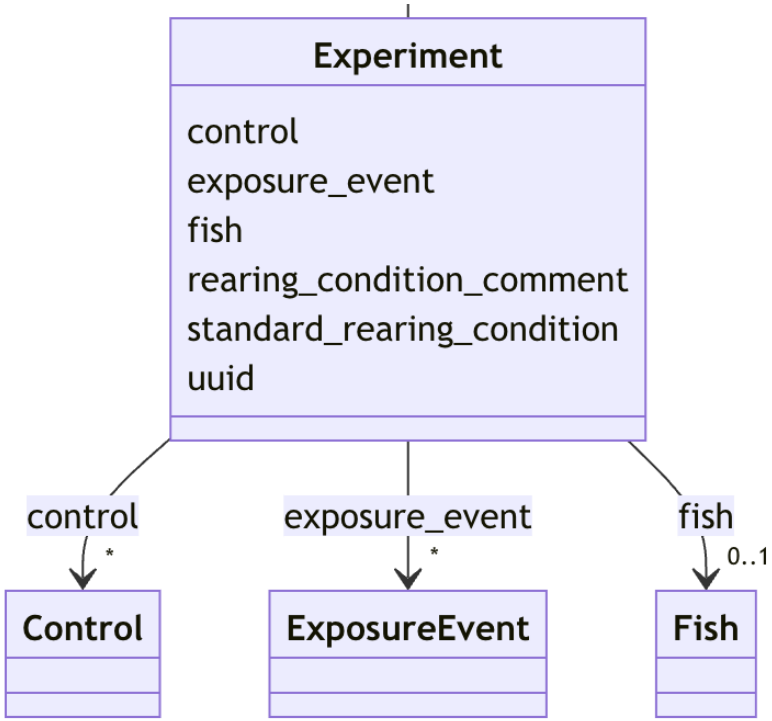
Ontologies and standard vocabularies

= standards to use to report the information



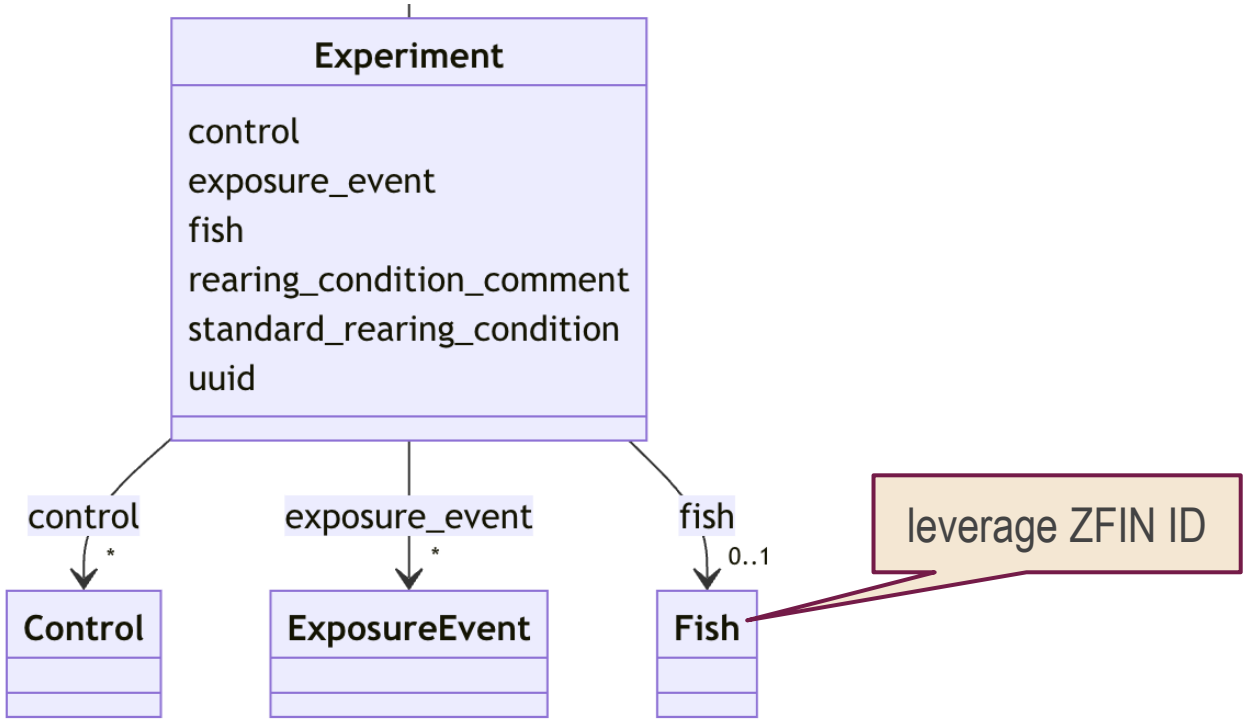
Zebrafish Toxicological Exposure Data Model

- Created based on community input
- Refined based on community feedback
- Created for Zebrafish toxicological assay, but can be reused and/or expanded for other species/model and other toxicological assay



LinkML-based ; https://github.com/zappfish/zebrafish-toxicology-atlas-schema

Zebrafish Toxicological Exposure Data Model



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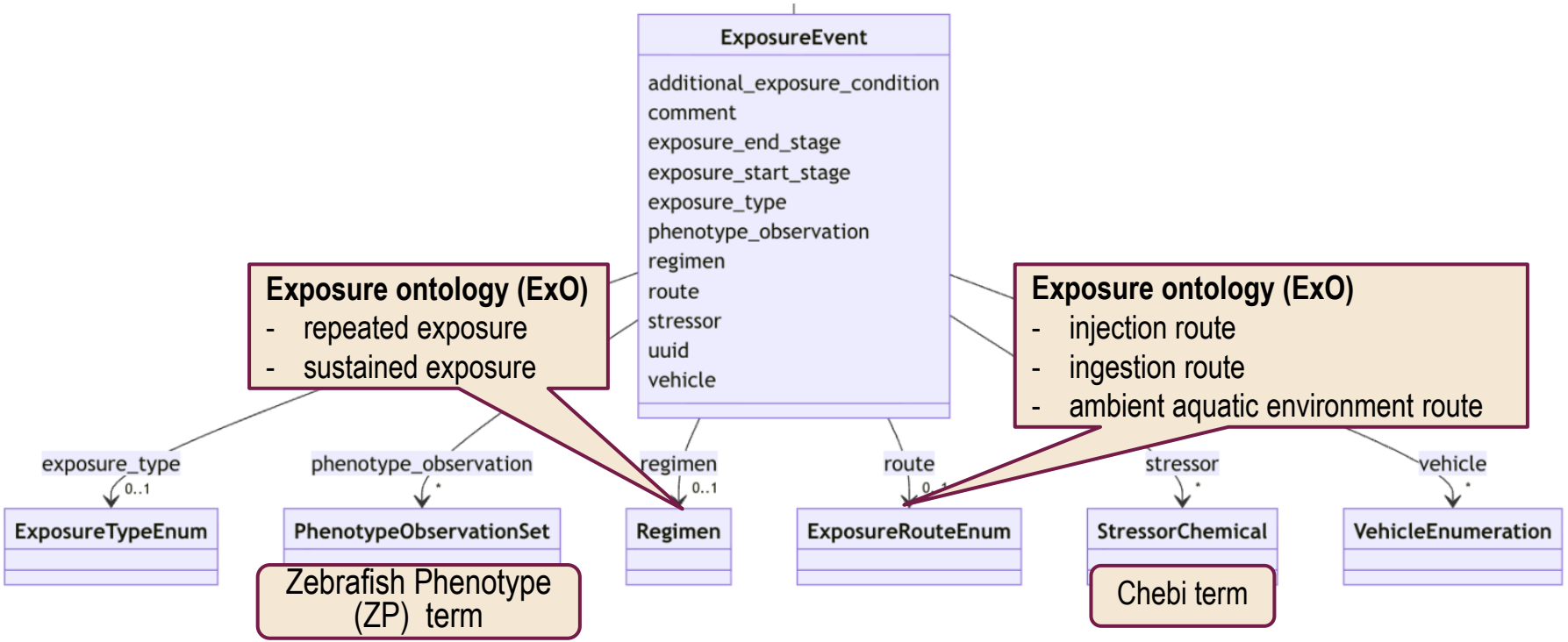


LinkML-based ; https://github.com/zappfish/zebrafish-toxicology-atlas-schema

Annotations following the data model: example

- **Fish**: AB — ZFIN:ZDB-GENO-960809-7
- **Exposure event**
  - **Regimen**: continuous exposure — ExO:0000167
  - **Exposure Route**: Exposure through aquatic environment — ExO:0000161
  - **Stressor Chemical**: valproic acid sodium — CHEBI:9925
    - **Concentration**: 10 mg/L
  - **Stage at exposure start**: 3 hpf — ZFS:0000011
  - **Stage at exposure end**: 96 hpf — ZFS:0000036
- **Phenotype Observation**
  - **Phenotype**: Decreased interocular distance — ZP:0000621
  - **stage**: 96 hpf — ZFS:0000036

Part of the model omitted for clarity.

Data from PMID: 38977114 (https://doi.org/10.1016/j.etap.2024.104500)

Ontologies and Standard Vocabularies

We **reuse existing** ontologies/terminologies, and **improve/enhance them** as needed.

- Exposure ontology (ExO)
  - Species non-specific
  - We created new terms to represent exposure route and exposure regimen
- Environment Exposure Ontology (ECTO)
  - Species non-specific
  - We currently use the term “exposure to chemical” (ECTO:0000231)
  - ECTO allows for the representation of other exposure type (eg: exposure to smoke - ECTO:7000059)
- Zebrafish Phenotype Ontology (ZP)
  - Specific to Zebrafish, but already integrated into uPheno (species non-specific phenotype ontology)
  - Computationally created from ZFIN phenotype annotations
    - Represented by concatenation of different ontology terms
    - Terms names are cumbersome and non-intuitive
  - We are improving ZP by:
    - creating user friendly names
    - adding definition to terms

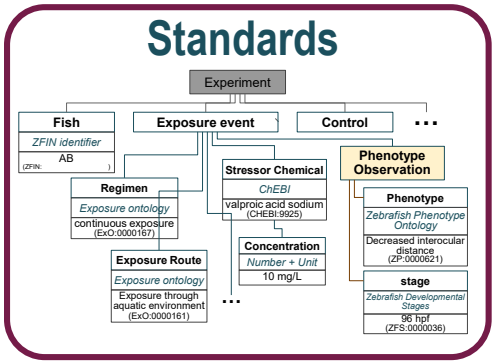
Standards for Toxicology Assay and Phenotype.

Data Model

LinkML-based Zebrafish Toxicological Exposure Data Model — https://github.com/zappfish/zebrafish-toxicology-atlas-schema

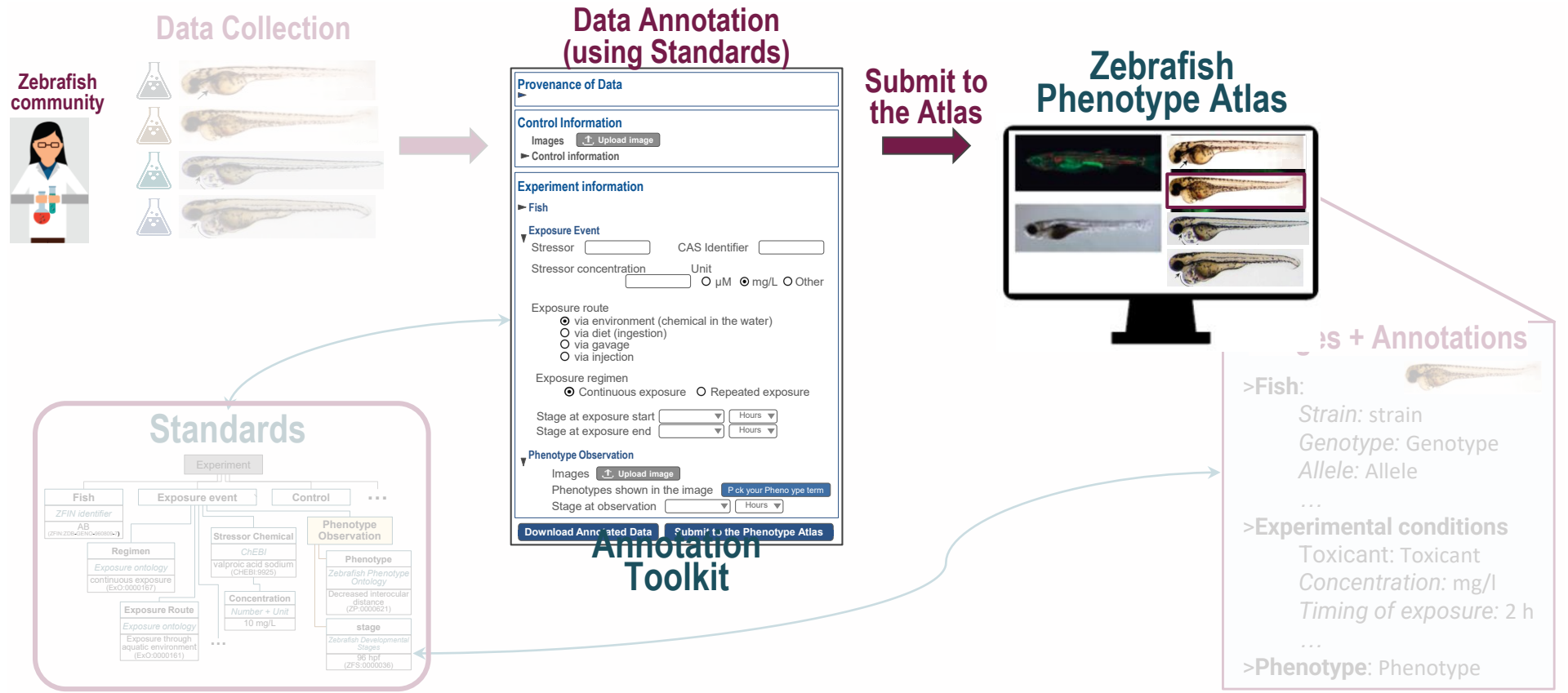
Ontologies

- Exposure ontology (ExO) — https://github.com/CTDbase/exposure-ontology
- Environment Exposure Ontology (ECTO) — https://github.com/EnvironmentOntology/environmental-exposure-ontology
- Zebrafish Phenotype Ontology (ZP) — https://github.com/obophenotype/zebrafish-phenotype-ontology
- Zebrafish Anatomy Ontology (ZFA) — https://github.com/ZFIN/zebrafish-anatomical-ontology



Standards are created for Zebrafish toxicological assay, but planned to be reusable or extendable to other species/model and other toxicological assay

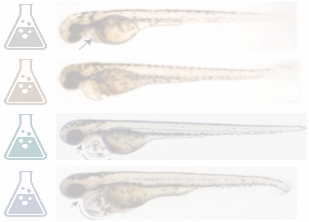
Standards adoption



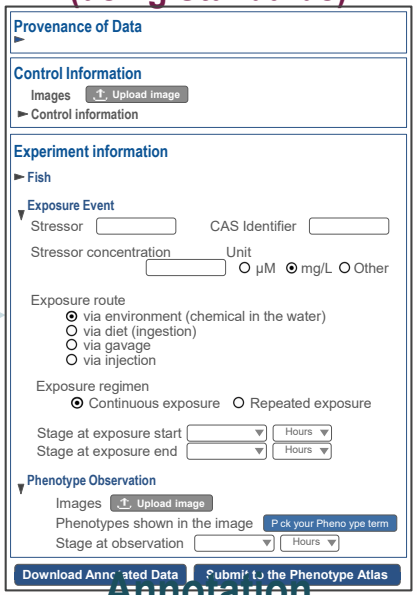
Standards adoption

Data Collection

Zebrafish community



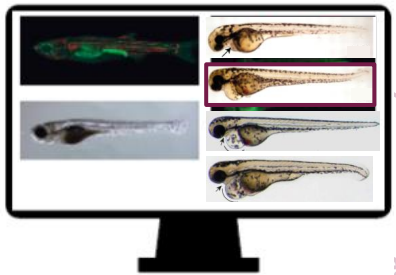
Data Annotation (using Standards)



Annotation Toolkit

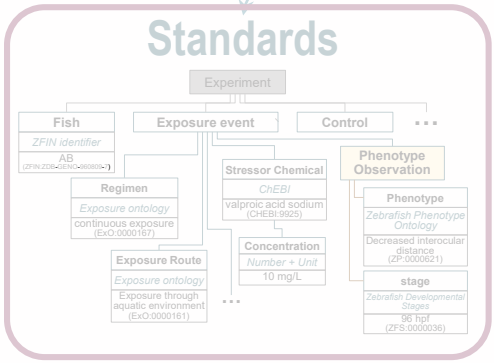
Submit to the Atlas

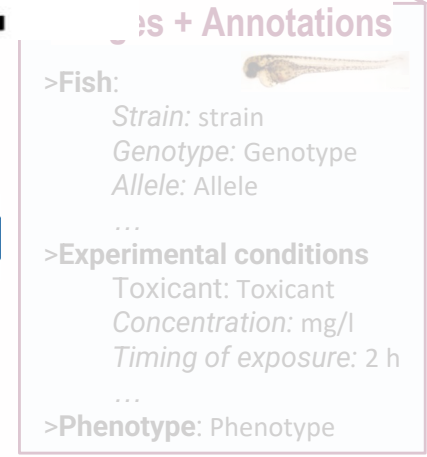
Zebrafish Phenotype Atlas



Publish standardized data

PubMed





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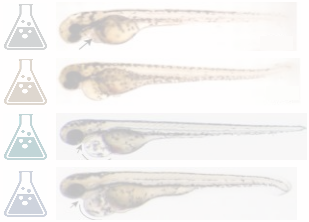

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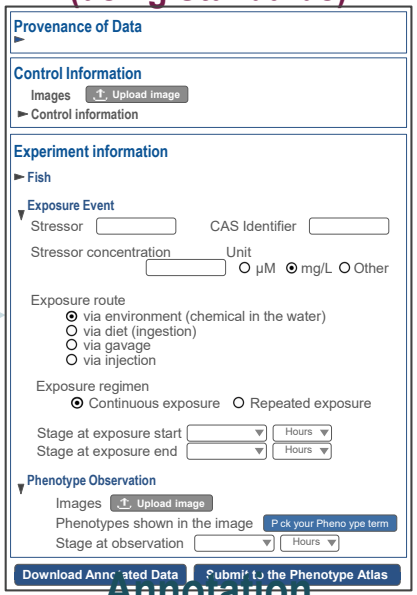

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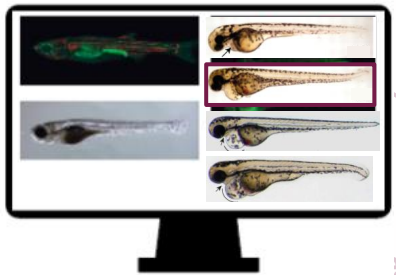

Publish standardized data

PubMed

The ultimate goal is for the reported data to be unambiguous, comparable, reproducible, and reusable.

…s + Annotations

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Strain: strain
Genotype: Genotype
Allele: Allele
…
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Toxicant: Toxicant
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Timing of exposure: 2 h
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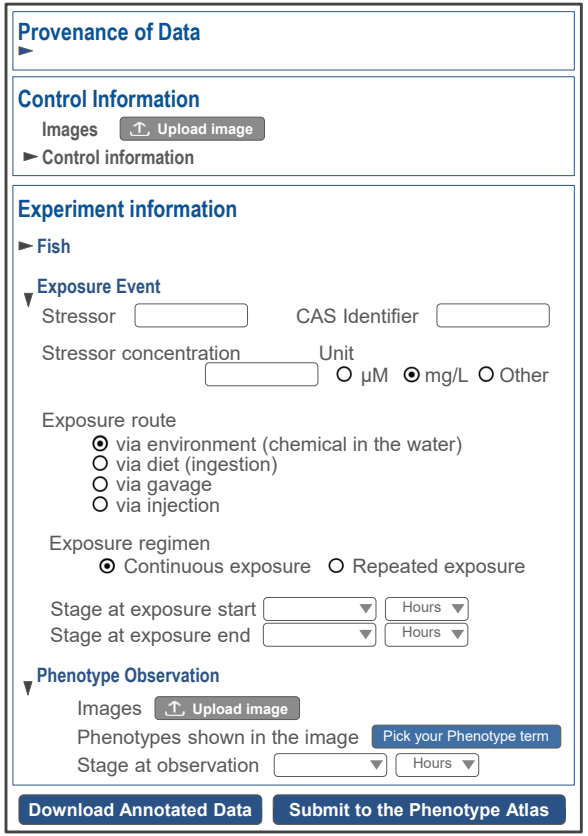
>**Phenotype**: Phenotype

The Annotation Toolkit simplifies standards adoption

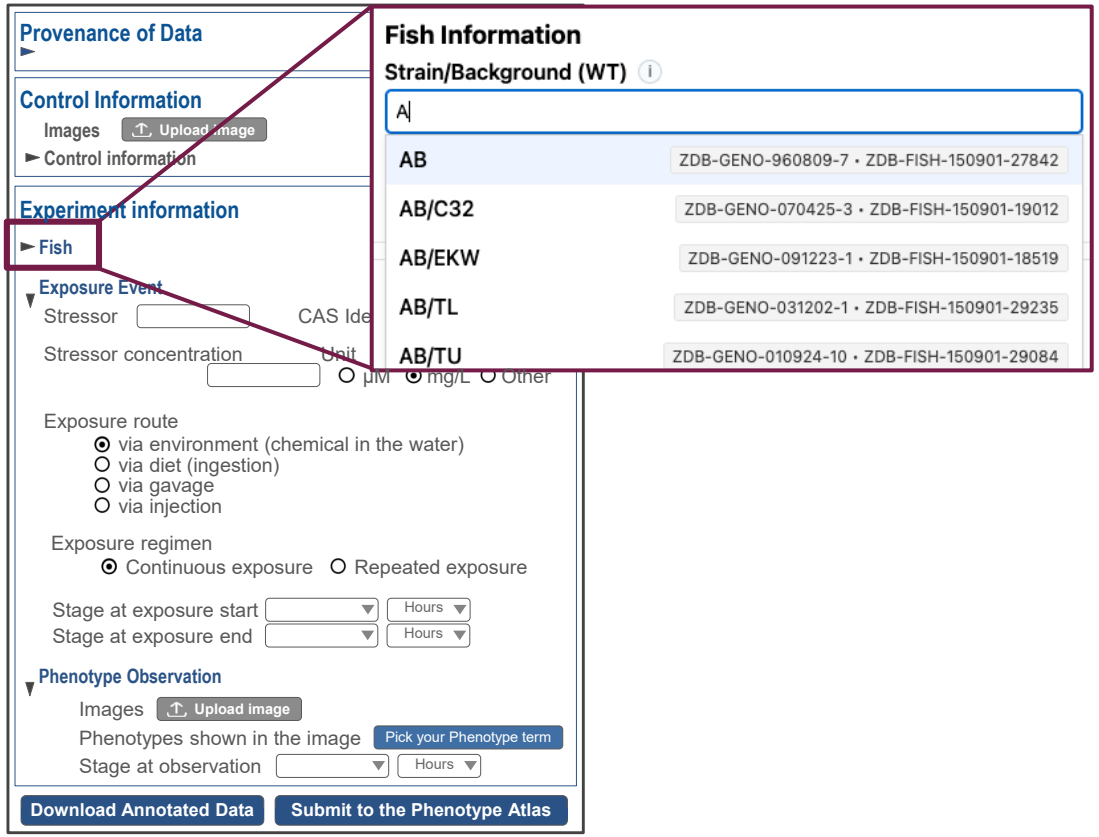


The annotation toolkit allows the use of standards, without requiring expertise in ontologies or standards development.

The research community can use the tool to **annotate** their data using standards, and

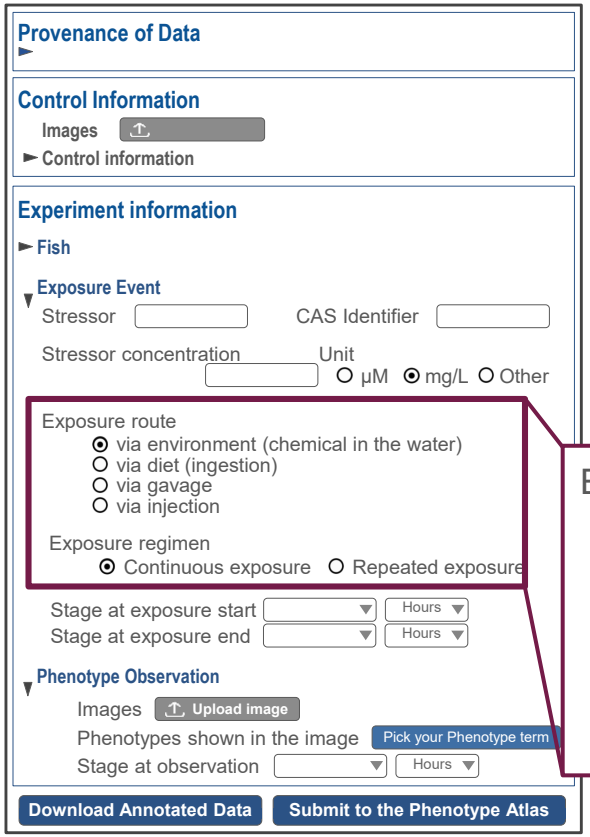
- **submit** their annotated data to the Atlas
- **download** their annotated data for publication submission (e.g. supplementary data of a manuscript)

The Annotation Toolkit simplifies standards adoption

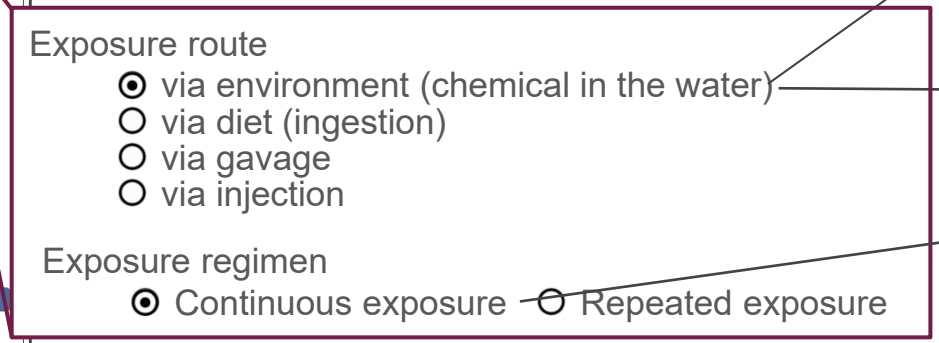


- Common names found with **autocomplete**
- IDs are shown to bring awareness

The Annotation Toolkit simplifies standards adoption



Limited options when constraints in data model



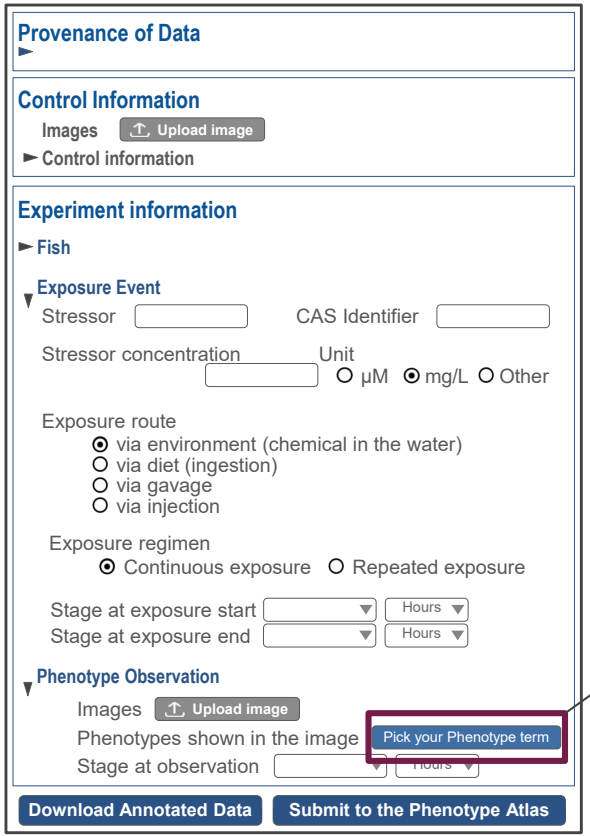
User friendly names

Translation to ID behind the scenes

ExO:0000161
ambient aquatic environment route

ExO:0000167
sustained exposure

The Annotation Toolkit simplifies standards adoption

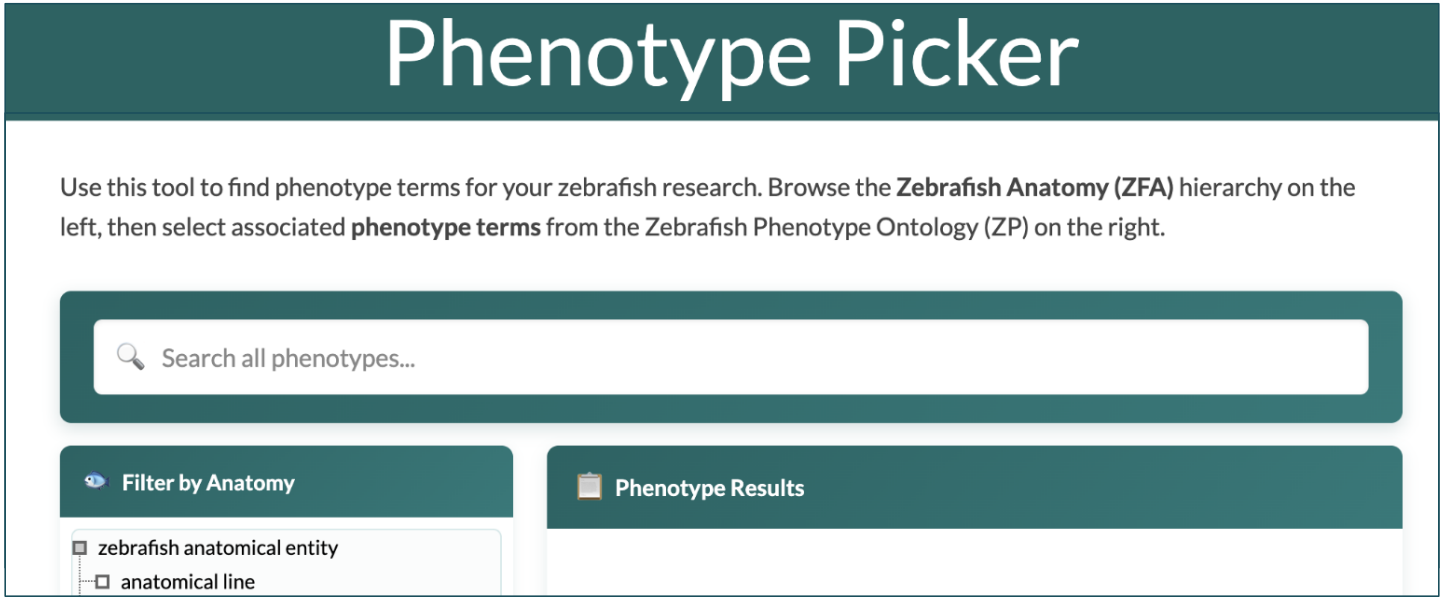


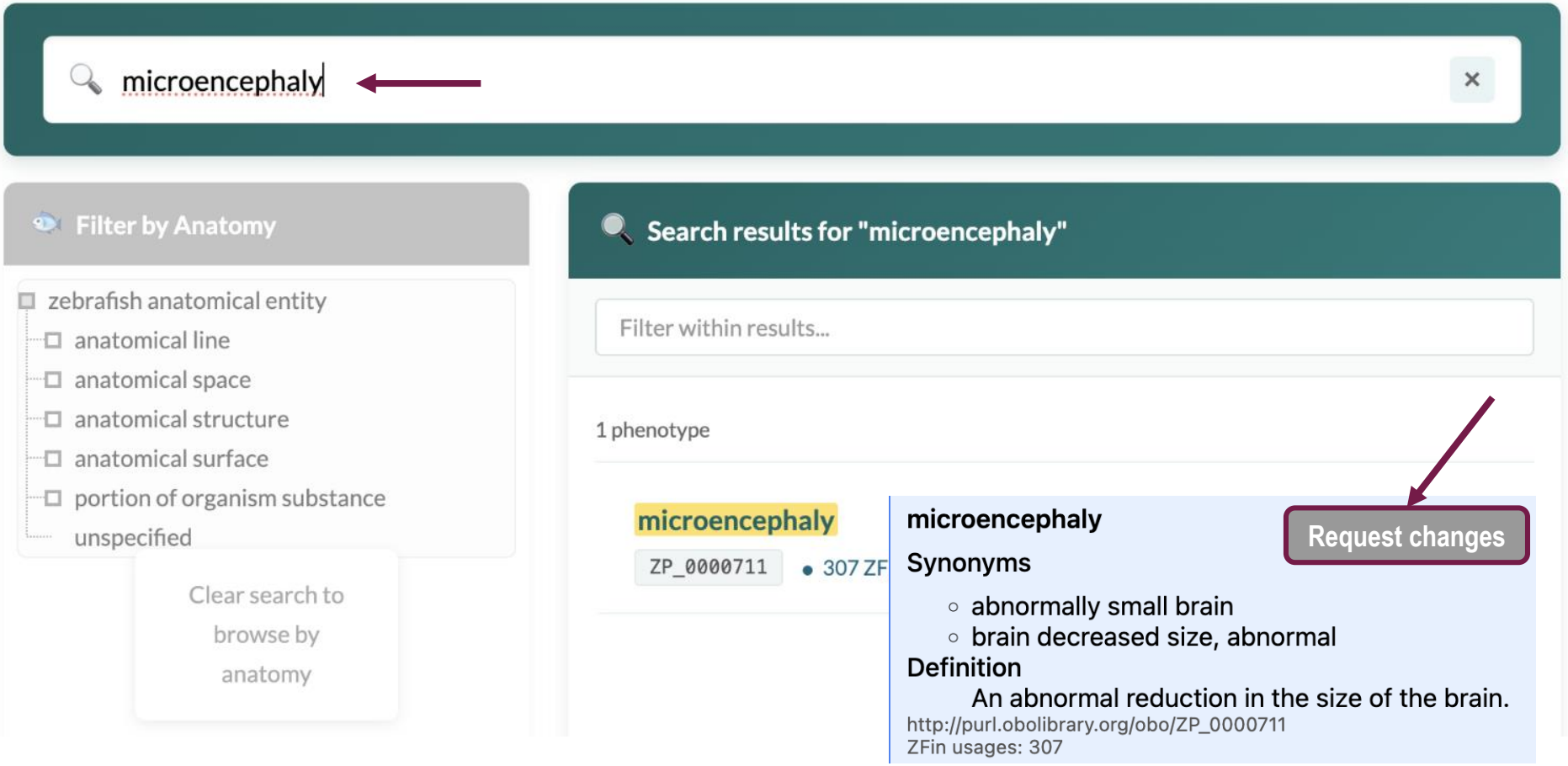
Pick a term from the Zebrafish Phenotype Ontology

Ontology Term Picker Tool

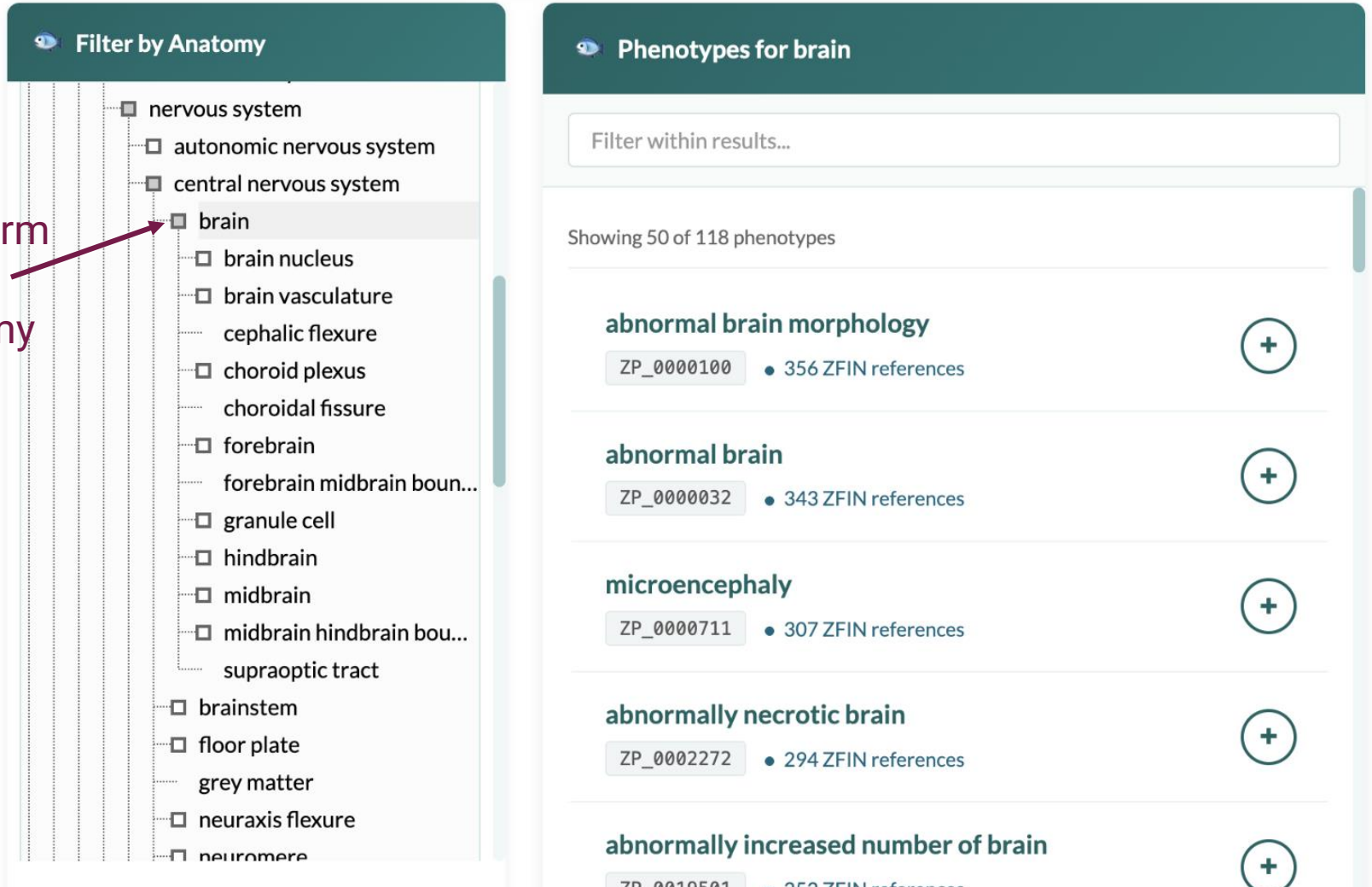
NEW

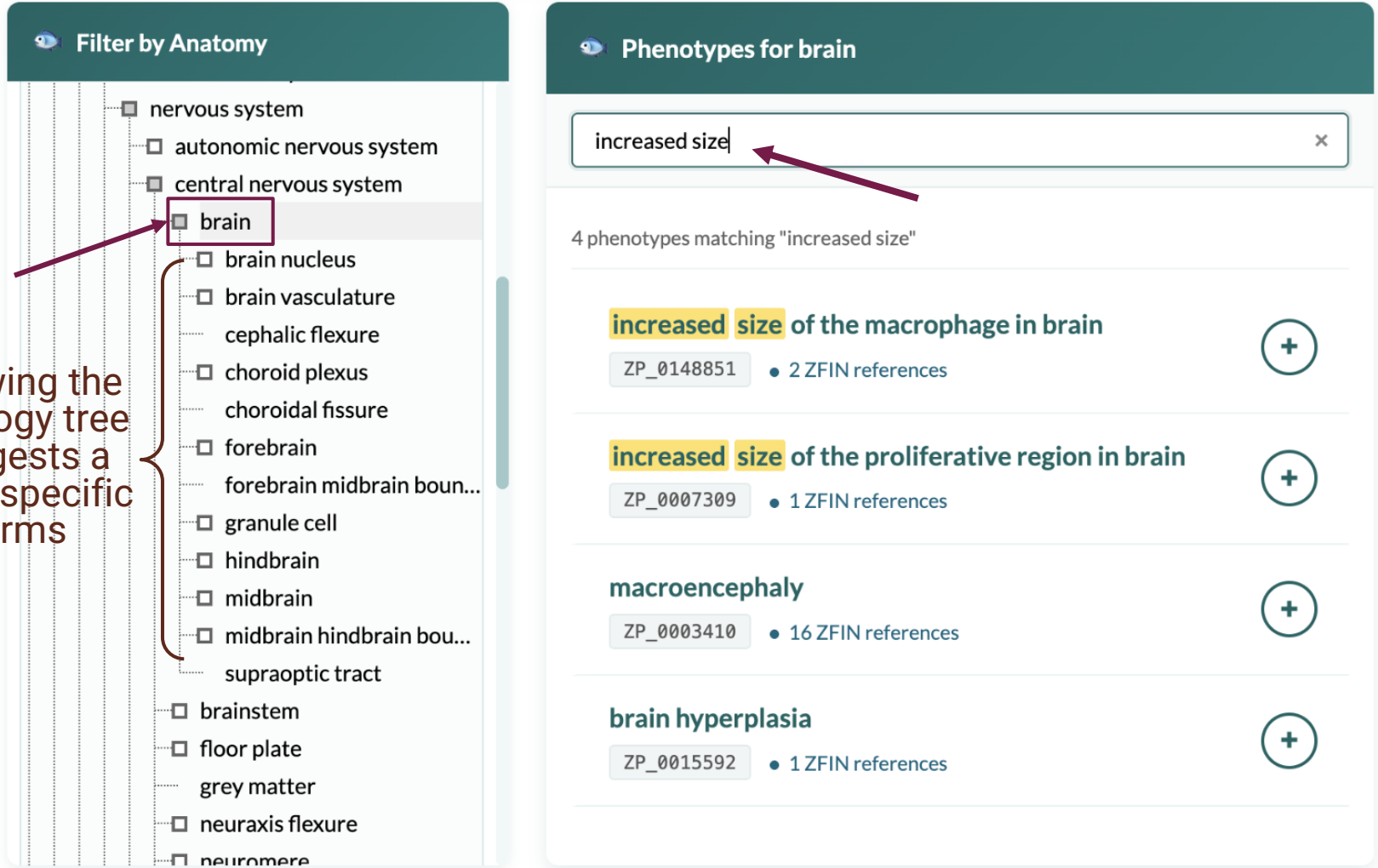
The **Ontology Term Picker allows users to find phenotype** terms without the need to understand how ontologies work.

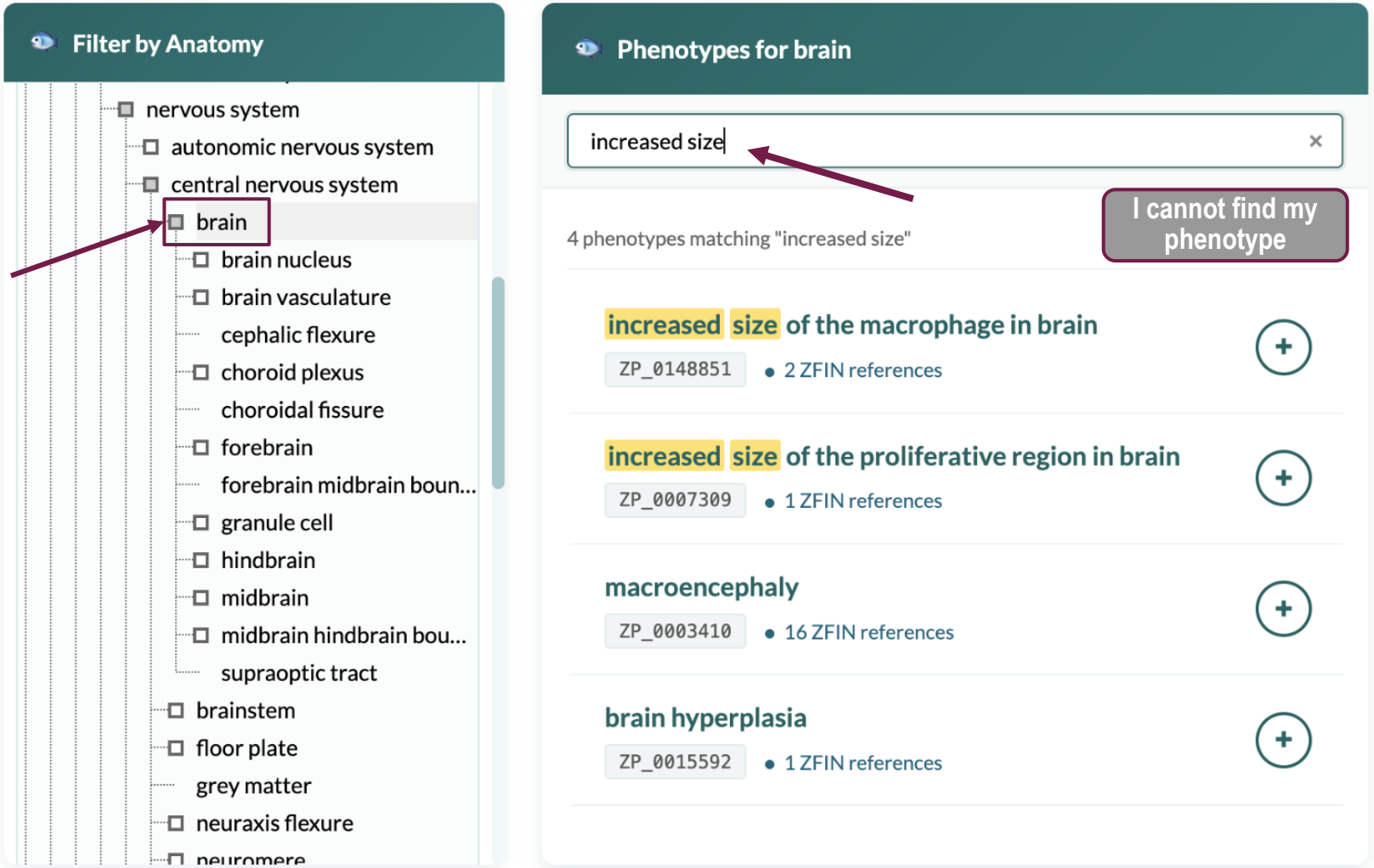



microencephaly
Filter by Anatomy
zebrafish anatomical entity
anatomical line
anatomical space
anatomical structure
anatomical surface
portion of organism substance
unspecified
Clear search to browse by anatomy
Search results for "microencephaly"
Filter within results...
1 phenotype
microencephaly
ZP_0000711
307 ZF
microencephaly
Request changes
Synonyms
abnormally small brain
brain decreased size, abnormal
Definition
An abnormal reduction in the size of the brain.
http://purl.obolibrary.org/obo/ZP_0000711
ZFin usages: 307

Find term using anatomy




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
floor plate
grey matter
neuraxis flexure
neuromere
Showing the ontology tree suggests a more specific terms
Phenotypes for brain
increased size
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
brain hyperplasia
ZP_0015592 • 1 ZFIN references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choroid plexus
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forebrain
forebrain midbrain boun...
granule cell
hindbrain
midbrain
midbrain hindbrain bou...
supraoptic tract
brainstem
floor plate
grey matter
neuraxis flexure
Phenotypes for brain
increased size
4 phenotypes matching "increased size"
I cannot find my phenotype
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
brain hyperplasia
ZP_0015592
1 ZFIN references

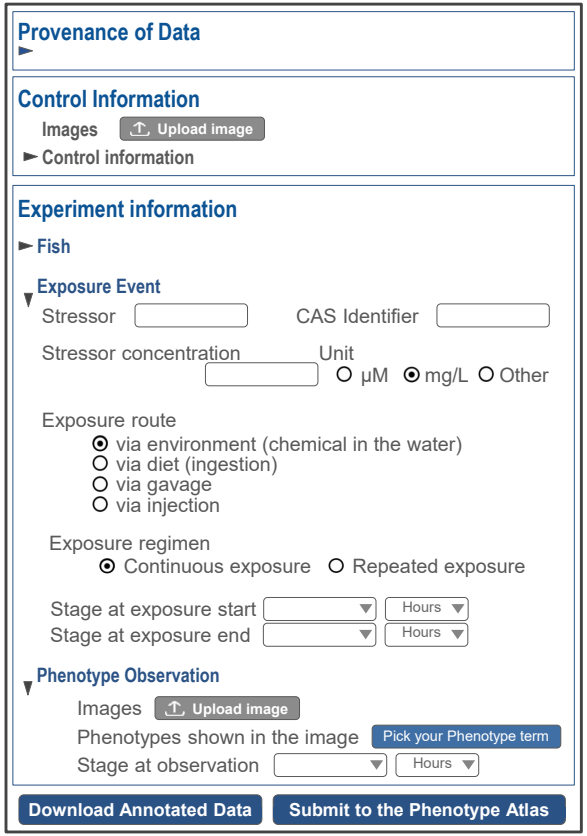
Ontology Term Picker Tool

The **Ontology Term Picker allows users to find phenotype** terms without the need to understand how ontologies work.

This tool is developed to **accommodate 'any' ontologies**, especially ontologies using 2 types of concepts

Examples: phenotype and anatomy
breed and taxon
disease and gene

The Annotation Toolkit simplifies standards adoption



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

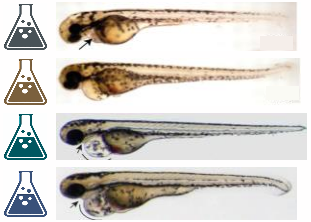
The research community can use the tool to **annotate** their data using standards, and

- **submit** their annotated data to the Atlas
- **download** their annotated data for publication submission (e.g. supplementary data of a manuscript)

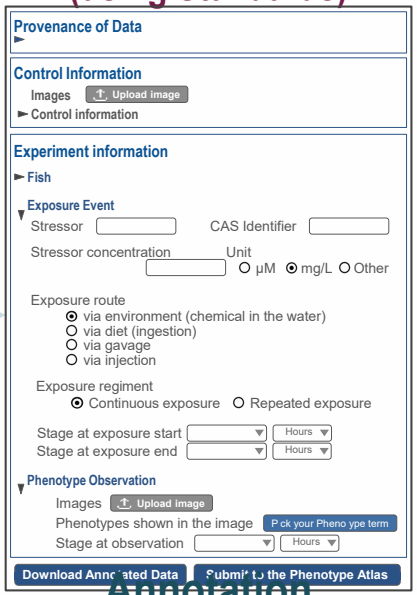
Zebrafish Phenotype Web Application

Data Collection

Zebrafish community



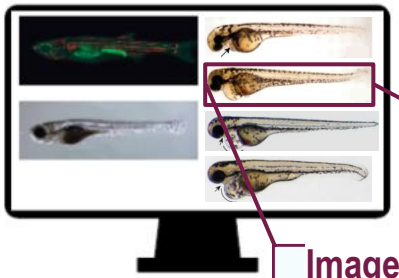
Data Annotation (using Standards)



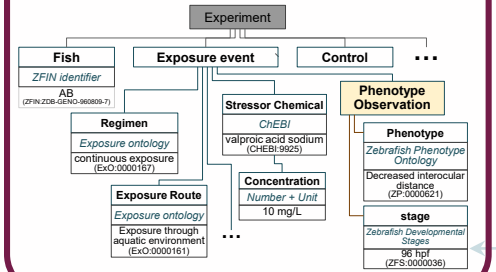
Annotation Toolkit

Submit to the Atlas

Zebrafish Phenotype Atlas



Standards



Images + Annotations

>**Fish**:

Strain: strain

Genotype: Genotype

Allele: Allele

…

>**Experimental conditions**

Toxicant: Toxicant

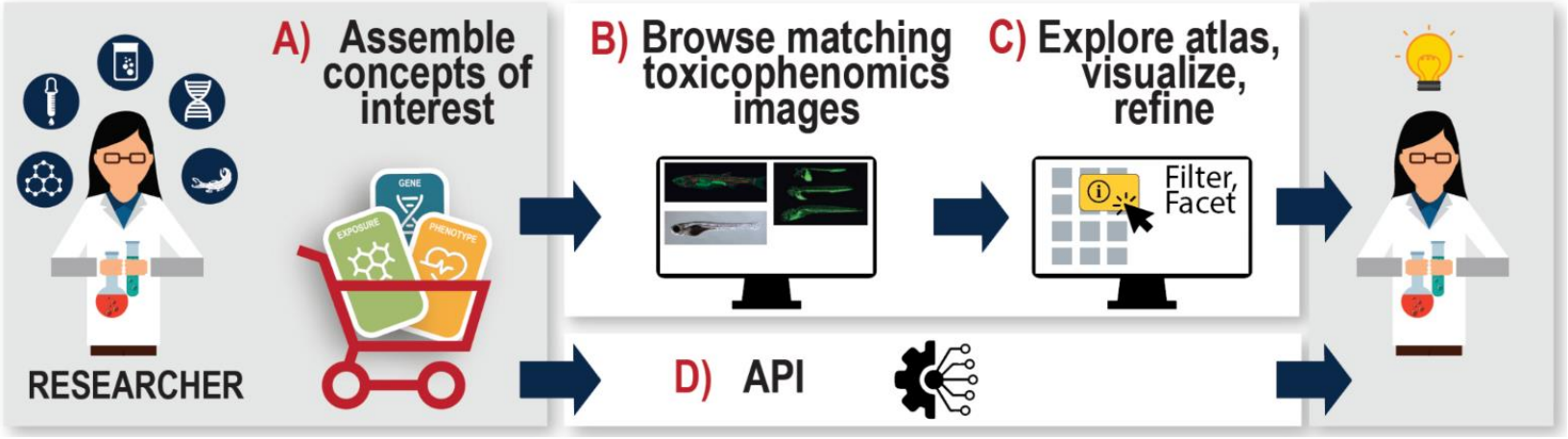
Concentration: mg/l

Timing of exposure: 2 h

…

>**Phenotype**: Phenotype

Zebrafish Phenotype Web Application



Functionality

- Browsing
- Filtering
- *TBD based on community requirements*

Features

- Open access
- All data attributed and provenanced
- Content submitted by the community
- All data standardized
- Data “peer reviewed” - *process TBD*

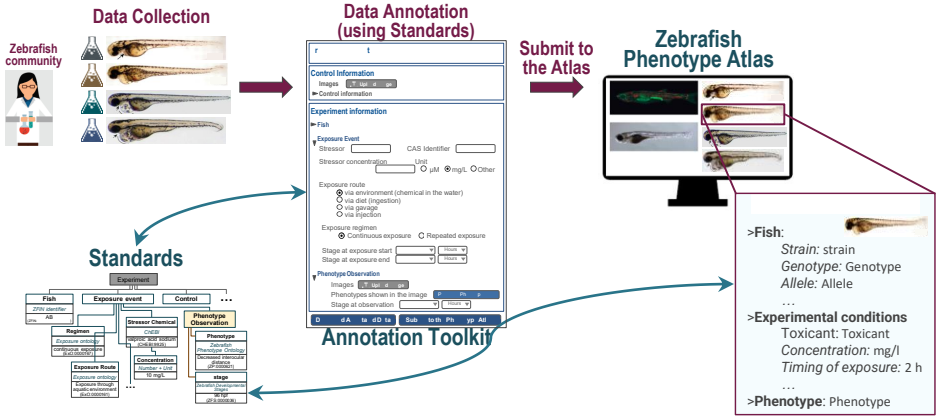
Community involvement is at the core of ZAPP

Community is involved in every part of the project

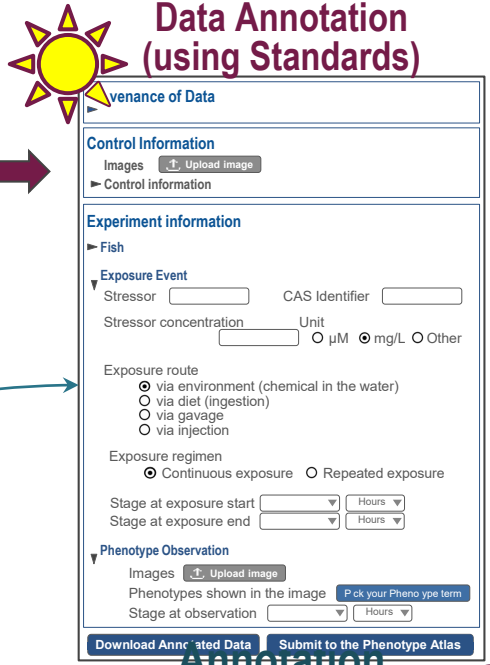
- Data annotation and submission
- Standards development
- Requirements gathering
- Governance

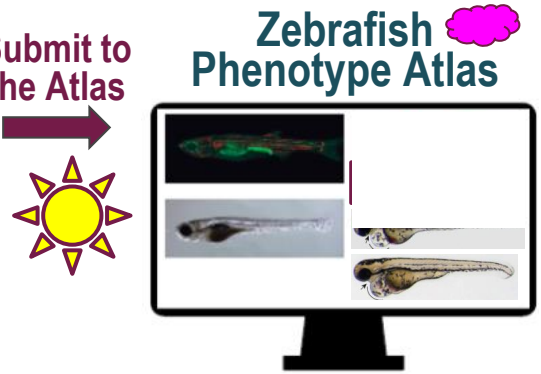
ZAPP community includes

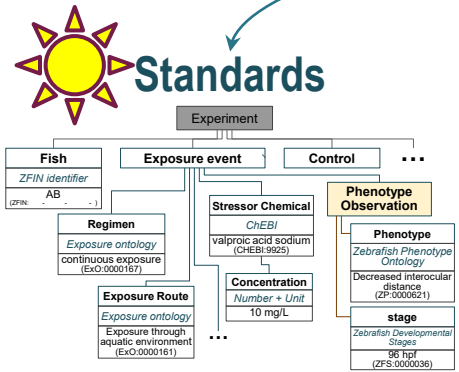
- Zebrafish researchers
- Toxicologists
- Atlas experts
- Standards developers
- etc



Community involvement is at the core of ZAPP







Community involvement

- Requirements gathering
- **Governance**

The Zebrafish Research Community is our primary community

The Research Community understands and agrees that the need for standards is crucial. However, they **don't know what to do in practice**.

- How to use standards in existing research workflow?
- What are the standards and how to use them?
- Where to find the standards?
- What to do when what is needed is not available?

We meet the community where they are, and we "nudge them" into understanding standards and adopting them.

Engaging with the community: Meeting the community where it is

- Speak “their” language: communication style and vocabulary
  - *e.g avoid using the words “data model”*
  - *e.g workshops and hands-on exercises to gather requirements*
- Develop tools that allow standards adoption without the need to understand what standards are and how they are developed

Engaging with the community: Fostering community awareness

- “Standards” is not a commonly discuss topic in the research community.
- We bring awareness through: workshops, posters, presentations at conferences.
- We partner with conference organizers** to create working groups and dedicated sessions to
  - highlight standards and community projects (which are rarely discussed at zebrafish research conferences)
  - promote how (and why) the research community can (and should) get involved

*** This has been possible thanks to Alexa Burger’s connections with the Zebrafish research community and position on the International Zebrafish Society (IZFS) board of directors*

Engaging with the community: Clearly communicating how people can participate

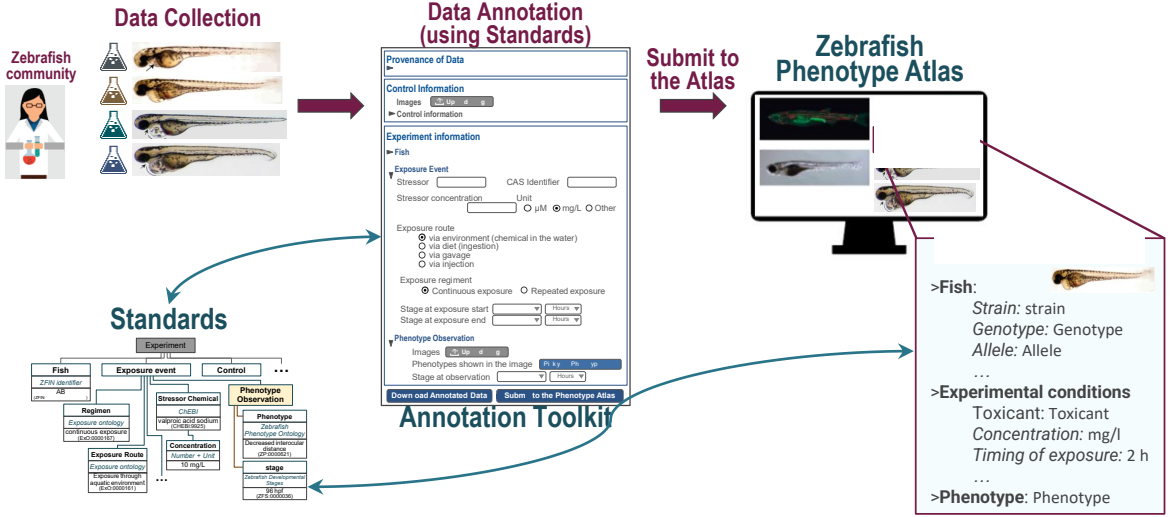
- Join the ZAPP community:
  - tislab.org/ZebraPhenoAtlas-signup
  - Slack channel on Zebrafish Rock!: #zapp-fish
- Participate in the workshops
  - Gather information about data standards, all information required
  - Gather feedback, community needs, etc
- Send us feedback
  - About what you need, 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 the tools** (annotation tools and atlas) and submit your data

** when available

The Zebrafish Toxicology Phenotype Atlas (ZAPP)

Community-led Zebrafish Toxicology Phenotype Atlas (ZAPP) will

- **integrate existing standards, and develop new one when needed, for phenotypic and toxicology data**
- make **standard adoption approachable**
- support **community-driven** improvement



The ultimate goal is for the reported data to be unambiguous, comparable, reproducible, and reusable.

Acknowledgements

Sabrina Toro, MPI
Sarah Gehrke, Project Manager
Patrick Golden, Developer
Aaron Odell, Developer
MeeSiing Ngu, Curator

Alexa Burger, MPI
Raéden Gray, Post-Doctoral Fellow

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Advisory Team:
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Jonathan Hamm (Inotiv)
Kevin Schaper (UNC)
Melissa Haendel (UNC)

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info@zappfish.org

tislab.org/ZebraPhenoAtlas-signup

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