Growth of the Zebrafish Anatomy Ontology

Expanded to support adult morphology and dynamic changes in the early embryo

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***Abstract*—The Zebrafish Anatomy Ontology (ZFA) is an application ontology used by ZFIN to support curation of expression and phenotype. The research community also uses the ontology to support annotation of high throughput studies. As the research focus of the zebrafish community evolves it drives changes in the ZFA. Here we provide an update on the changes made to support research carried out in adult fish and describe the changes in modeling of the neural crest in the ontology in order to bring the structure of the ontology into closer accordance with the morphological changes that occur during development.**

***Keywords*—ZFA; ZFS; anatomy; neural crest**

I. Introduction

The Zebrafish Anatomy Ontology (ZFA)[1, 2] is an OBO Foundry [3] ontology that is used in conjunction with the Zebrafish Stage Ontology (ZFS) [4] to describe the developmental progression of the gross and cellular anatomy of the zebrafish, *Danio rerio*, from single cell zygote to adult. Zebrafish share many anatomical and physiological characteristics with other vertebrates, including humans, and have emerged as a premiere organism to study vertebrate development and genetics. The Zebrafish Model Organism Database (ZFIN) [5] uses the ZFA and ZFS to annotate zebrafish phenotype and gene expression data from the primary literature and from contributed data sets. By using the ZFA and ZFS to annotate gene expression and phenotypic data, ZFIN is able to provide efficient querying and analysis across ZFIN data as well as cross-species inference[6].

II. Current Status

The ZFA and ZFS are developed utilizing OBO Foundry principles[7] to ensure orthogonality, accessibility, and interoperability. The ZFA is designed to model anatomy using a largely structure-based subclass hierarchy, featuring a strong partonomy (using the part_of relation) and developmental hierarchy (using the develops_from relation). Each anatomical class in ZFA is defined using these relationships to other classes in ZFA as well as to stage classes in ZFS. The relations used between the ZFA and ZFS are start_stage and end_stage. The start_stage utilized is equivalent to Relation Ontology (RO) [8] 'starts_during' and end_stage is equivalent to RO 'ends_during'. In this way, each anatomical entity can be defined in terms of what it is a type of, what it is a part of, what it develops from, and during which stages it exists. The ZFA has 2977 classes, 85% with text definitions, representing anatomical structures from different anatomical systems across the zebrafish developmental series.

III. Current Work

The current focus of development of the ZFA has been extending the tree as new research on anatomy is published and to build an extensible framework for future work. Improved modelling of transient structures present for only a short period early in zebrafish development has been an area of active development. Toward this end, work has been done to improve modeling of neural crest based on outcomes of the Neural Crest Workshop held at the National Evolutionary Synthesis Center (NESCent) during the Phenotype RCN meeting 2012 (http://www.phenotypercn.org/?page_id=54). The changes to the neural crest branch better reflect the development of neural crest and its constituent cells from the neural plate border, their gross location along the axis, as well as differentiation of pre-migratory and migratory populations (14 classes). To effectively model the neural crest there was coordination with appropriate CL classes[9] to allow for proper cross referencing with in the ZFA. The hierarchy implemented in ZFA should be applicable for all vertebrates and is intended to be in a format UBERON[10, 11] can generalize across species.

Additional development of ZFA classes has been varied and driven by the focus of research in the zebrafish community. Active development has focused on structures that develop in older fish as adult processes are being increasingly investigated by the zebrafish community. To support this research discrete updating across the ontology was done to reflect adult structures and includes the adult surface structures: maxillary barbels, with supporting vasculature (10 classes) [12]; breeding tubercles (11 classes) [13, 14]; adult fin musculature (12 classes) [15]; heart muscles (4 classes) [16]. To better extend the developmental modeling of larval and juvenile fish to adult stages, we extended the vasculature branch by centering on vasculature development of organs with a particular attention on the lymph vasculature. To that end we added branchial, facial and visceral lymph vasculature classes (22 classes) [17] and blood vasculature (8 classes)[12, 18]. In addition, updates to the nervous system (21 classes) and modelling of replacement teeth were implemented. Overall the ZFA has expanded the hierarchical modeling of the zebrafish anatomy by 121 classes.

IV. Future Work

The ZFA will continue to be built to meet the needs of the zebrafish research community. ZFIN curators are actively involved in the zebrafish and ontology research communities to improve the ZFA through addition of classes, definitions, relations, and the continued support for interoperable ontologies. The neural crest branch will undergo continued development to model the various migratory streams and their development contributions to defined structures.

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