Towards Understanding Craniofacial Abnormalities: The Ontology of Craniofacial Development and Malformation

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We introduce the Ontology of Craniofacial Development and Malformation (OCDM), a project of the NIH-funded FaceBase consortium, whose goal is to gather data from multiple species, at levels ranging from genes to gross anatomy, in order to understand the causes of craniofacial abnormalities. The OCDM is being developed in order to facilitate integration of these diverse forms of data in a central Hub. It currently consists of several components, including human adult and developmental anatomy, corresponding mouse structures, and malformations. Example queries show the potential of the OCDM for intelligent annotation and querying.

Over 50% of congenital anomalies involve defects in craniofacial structures such as the lip and palate, yet the specific genetic mutations and their causal mechanisms are often unclear. To help unravel the detailed genotype-phenotype correlations and causal mechanisms involved in these malformations the NIH-funded FaceBase Consortium[1] is gathering multi-institutional data, ranging from gene expression to clinical images, in a central Hub located at the University of Pittsburgh. The OCDM is being developed in order to relate these diverse forms of data within the Hub and elsewhere. Based on the Foundational Model of Anatomy (FMA) human structural ontology[2], the OCDM currently consists of several components: the Craniofacial Human Ontology (CHO) extracted from the FMA, the Craniofacial Mouse Ontology (CMO), also based on the FMA but which also includes all relevant anatomical entities from the Mouse Anatomy ontology (MA), the Craniofacial Human Mouse Mapping Ontology (CHMMO) mapping between homologous human and mouse structures, and the Craniofacial Human and Craniofacial Mouse Malformations Ontologies (CHMO, CMMO) CHECK. In addition we are currently adding developmental extensions to both the human and mouse ontologies, which not only list structures at different developmental time points (as is the case in developmental ontologies such as EMAP and GUDMAP), but also lists relations between structures, such as *transforms from* and *derives-from*. Whenever possible the OCDM uses terms from existing ontologies, although we have found that we generally have to add considerable detail.

The OCDM, which has been under development since CHECK, currently consists of CHECK terms and CHECK relations, largely because of the existing terminology from the FMA, and because of a systematic procedure for deriving and verifying mouse terms from the literature. The OCDM is authored in Protégé Frames, and an export is available in a version of OWL that is adequate for FaceBase needs. The development of the OCDM is driven by a series of use cases that also inform the creation of example SPARQL queries over the OWL export[3]. These queries will later be integrated into the Hub in order to facilitate such operations as ontology-based annotation as data are uploaded to the Hub, and intelligent search of existing data. An example search might be "Find all expression images from a specific mutated gene in a mouse structure that is a developmental precursor to another mouse structure, where that mouse structure is homologous to a human structure that is part of a specific malformation observed clinically, and the gene is known to be associated with the given malformation". As we develop these and other queries they will be integrated into the Hub and made accessible to researchers by graphical user interfaces that hide the details of the queries. The current released version of the OCDM is available on the FaceBase Hub[4].

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References

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