

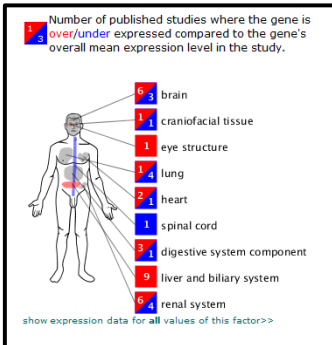
The Ontology of Craniofacial Development and Malformation

James Brinkley (PI)
Structural Informatics Group
University of Washington
Seattle

Goals

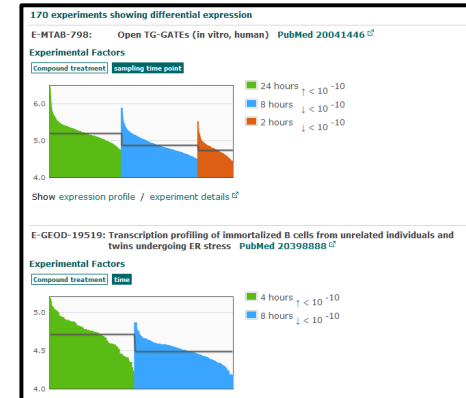
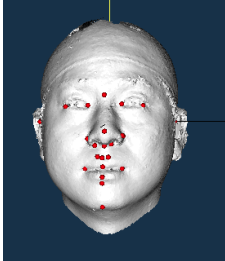
- Create an ontology for use by FaceBase
- Standardized terms
 - for annotation
 - retrieval by keyword search
- Relations
 - representation of knowledge
 - to allow intelligent integration

FaceBase



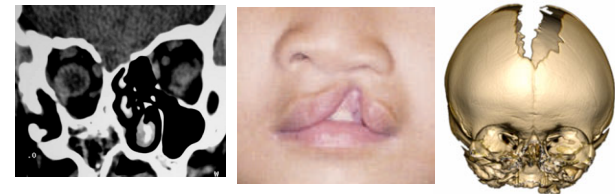
Genomic studies

Medical imaging

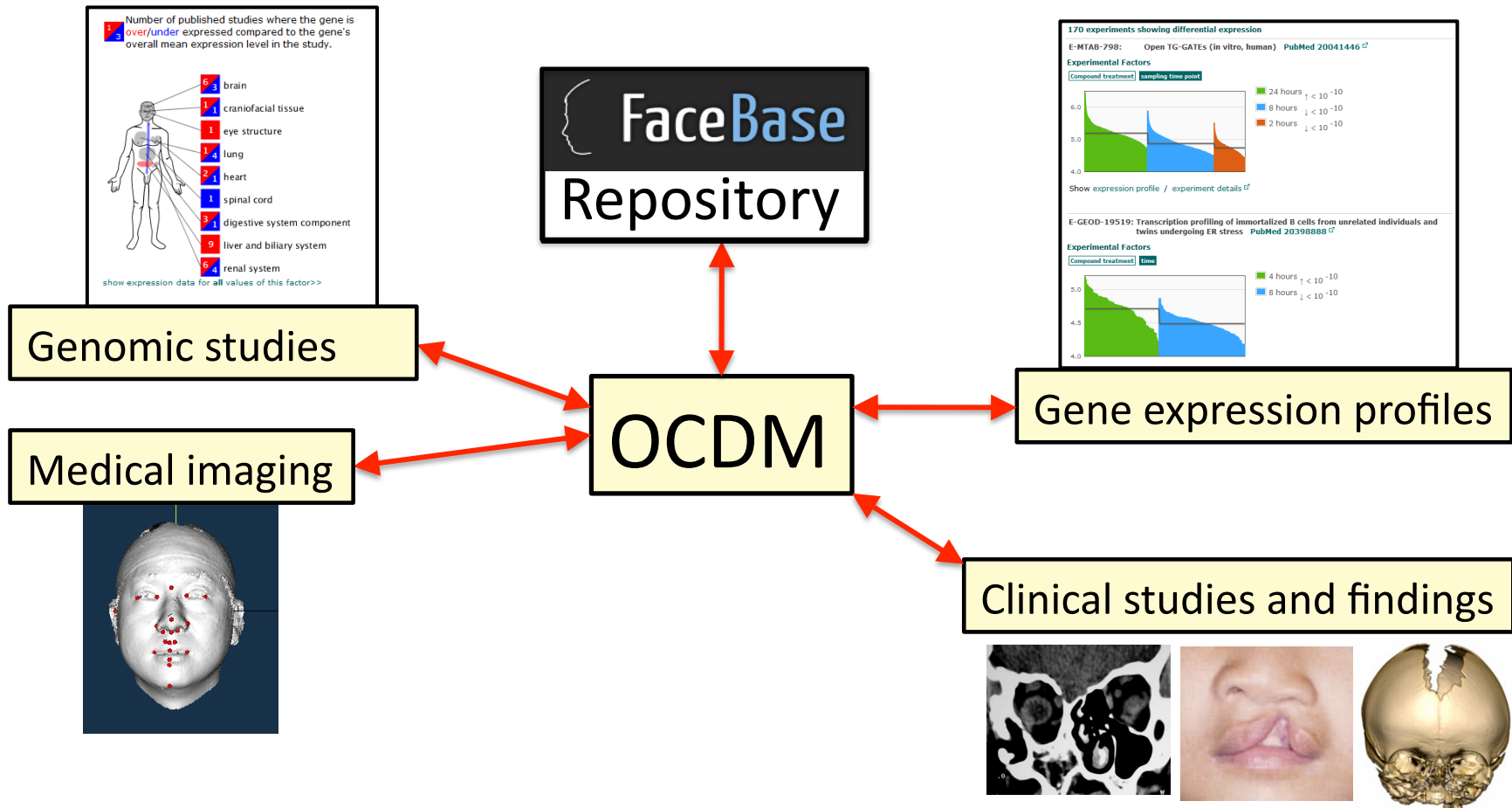


Gene expression profiles

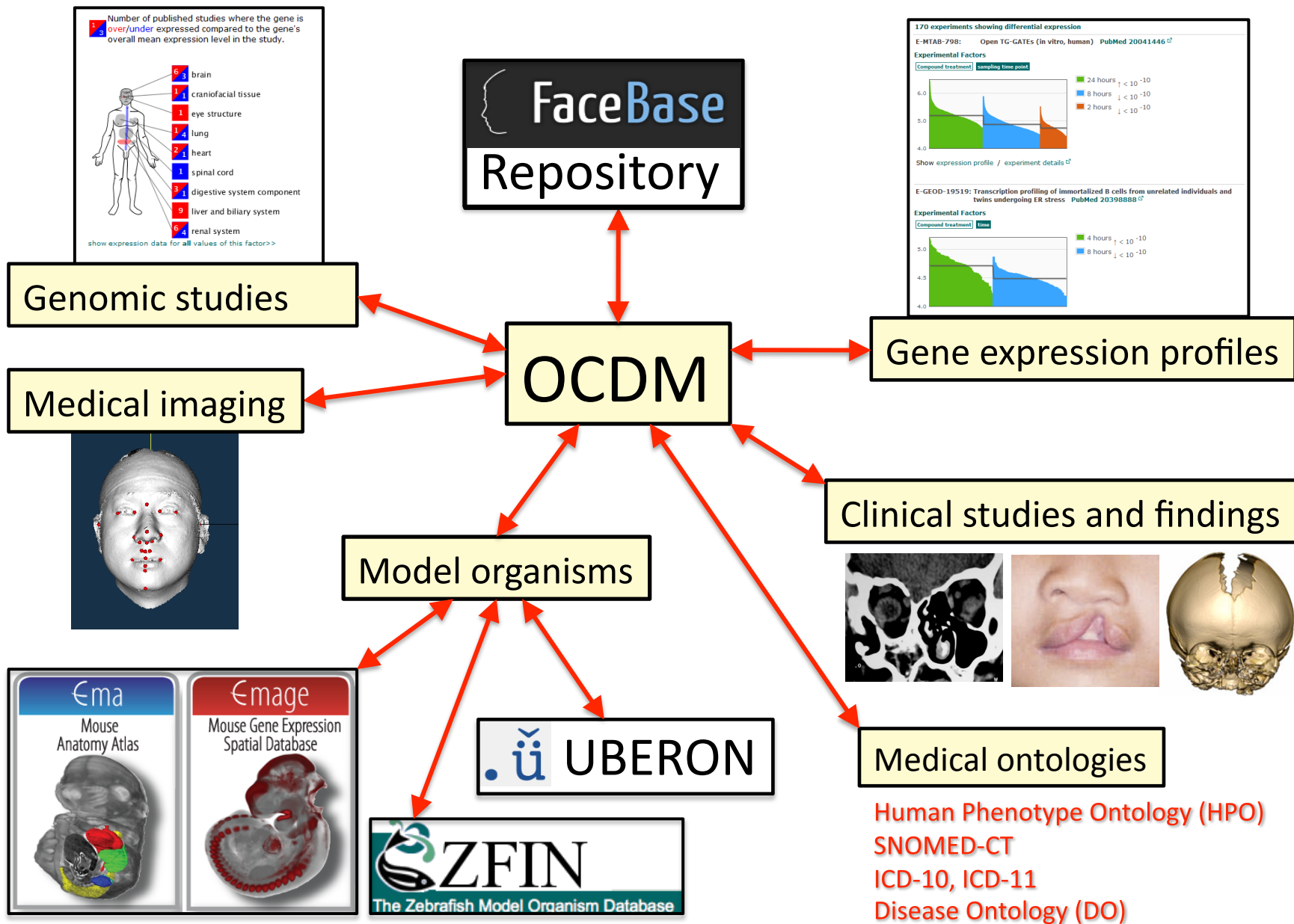
Clinical studies and findings



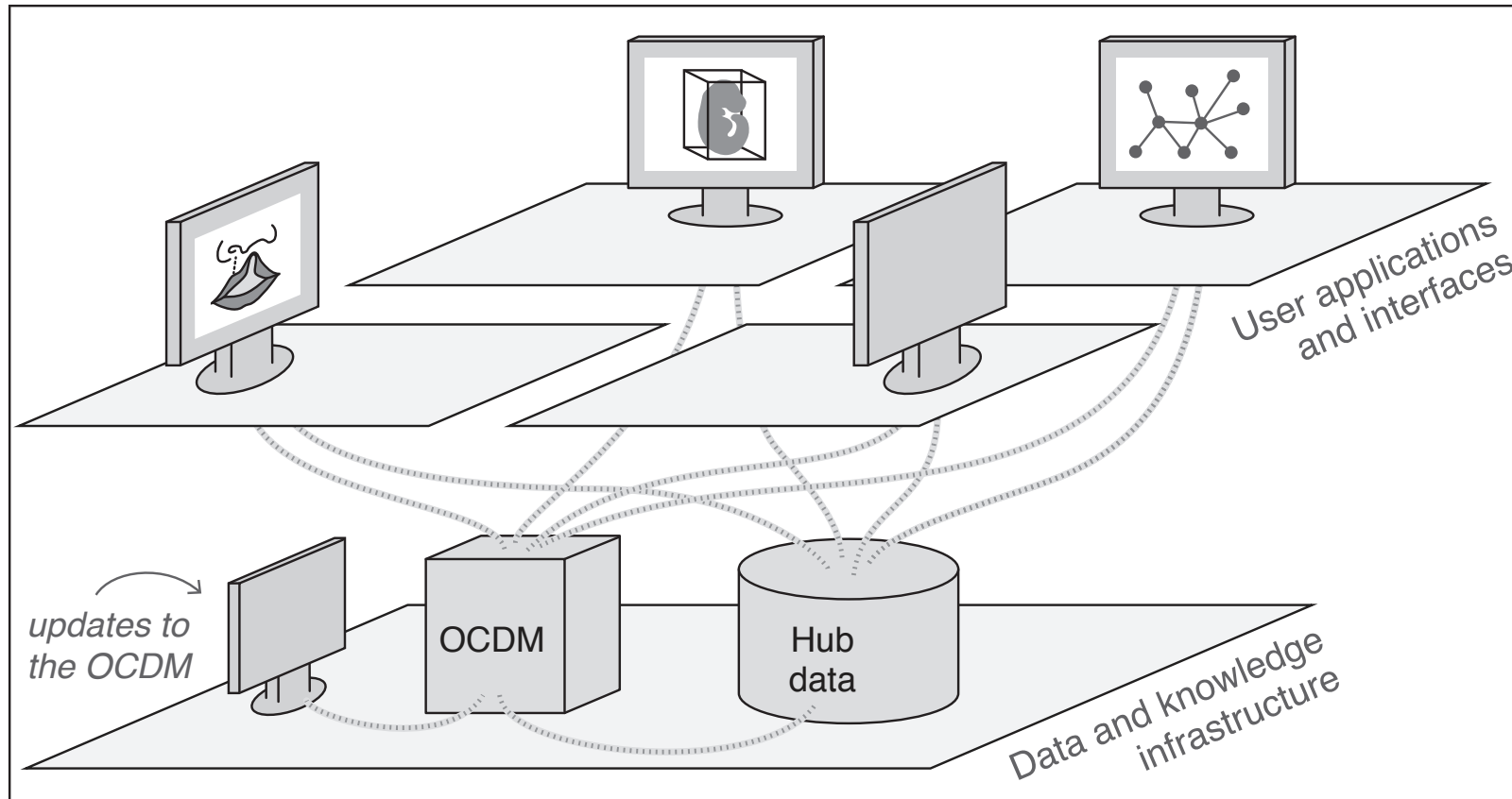
OCDM



Importing Other Ontologies



OCDM as part of the infrastructure



Principles of the OCDDM

- Based on human anatomy and development
 - Foundational Model of Anatomy (FMA)
- Utilize existing ontologies as much as possible
- Modular
- Ontology best practices

FaceBase 1

- Use Case
 - Cleft lip and/or palate
- Species
 - Mouse, human
- Developed an overall framework
- Anatomy
 - Mouth and nose
 - Additional anatomy “for free”

Topics

- Overall Framework
- FaceBase 2 content to-date
- Milestones for future content
- Conversion to OWL 2
- Workflow and access

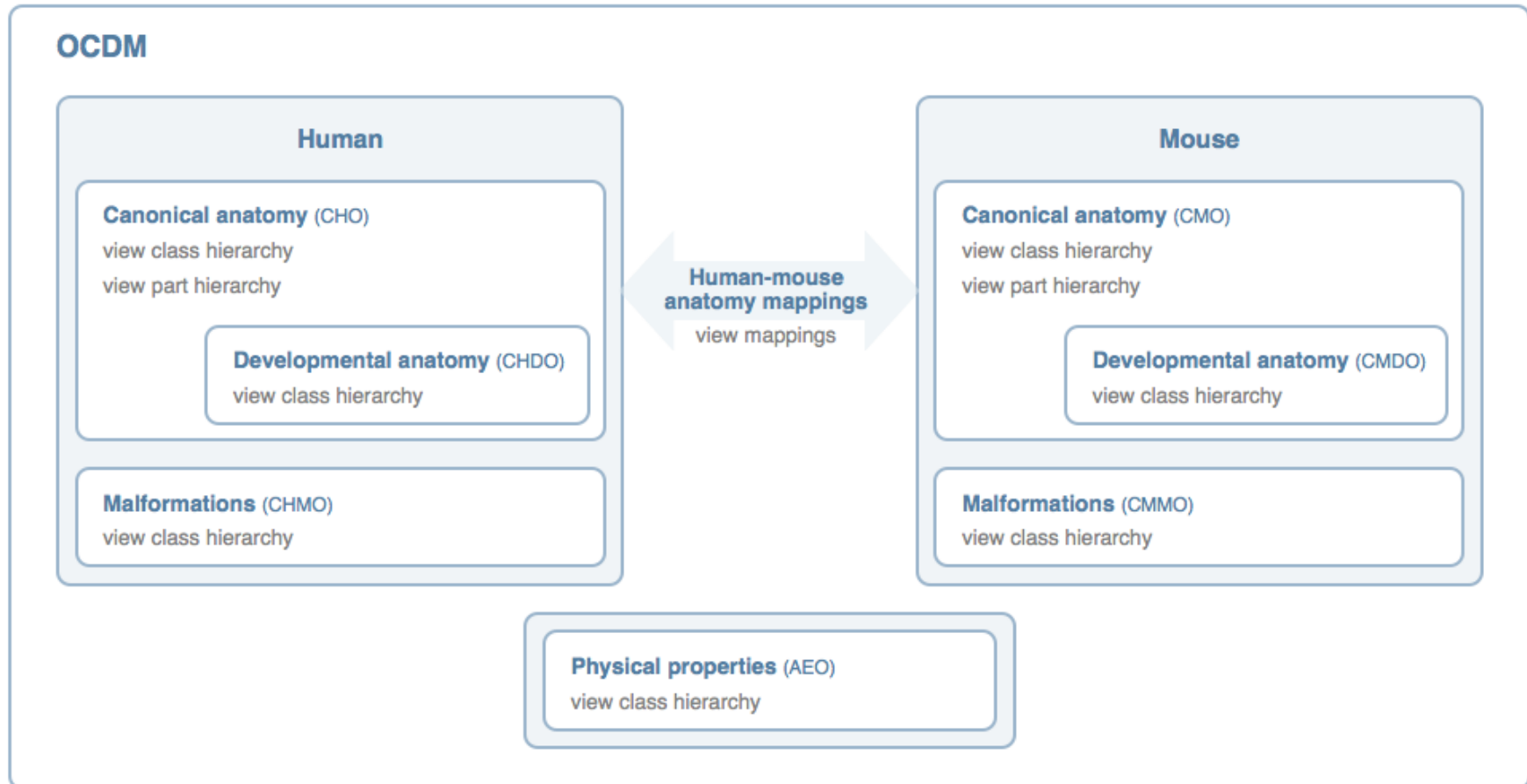
Overall Framework of the OCDM

<http://purl.org/sig/ocdm/viewer>

[About the OCDM](#) | [About ontologies](#) | [FaceBase](#) | [Contact](#)

The Ontology of Craniofacial Development and Malformation (OCDM)

A project of the FaceBase Consortium



FaceBase 2

- Filling in the framework created in FaceBase 1
- Use Cases
 - Craniosynostosis
 - Midface hypoplasia
 - Interactive atlas of normal skull development
 - Mandible development
 - 3-D craniofacial morphometrics
- Species: human, mouse, zebrafish
- Anatomy: Musculoskeletal system of head, additional “for free”

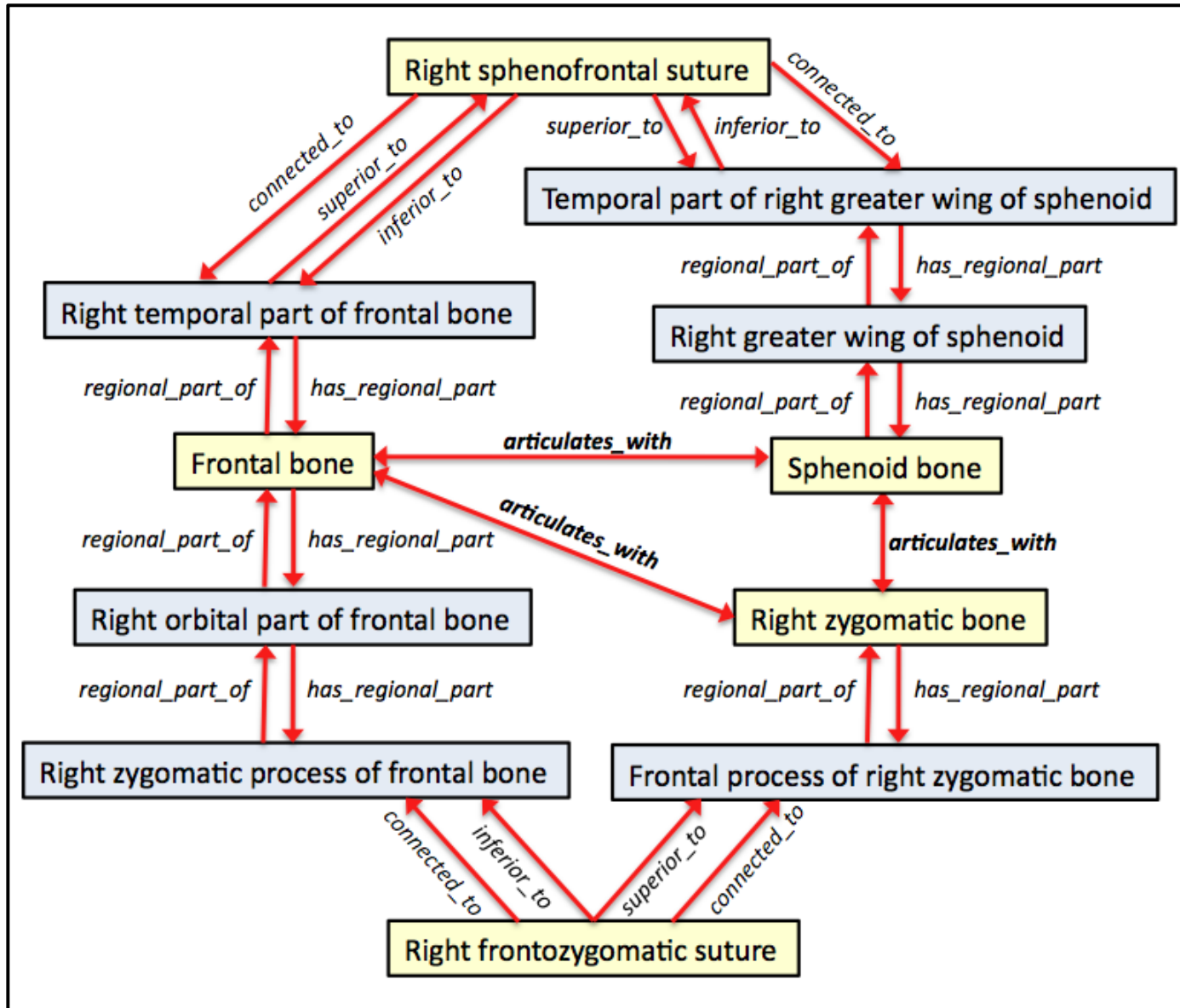
Content enhancement: Musculoskeletal system of head

Foundational Model of Anatomy Ontology (FMA)

The screenshot displays the FMA ontology interface for the 'Frontal bone' entity. The left sidebar shows a hierarchical tree of anatomical concepts, with 'Frontal bone' selected. The main panel shows the following details:

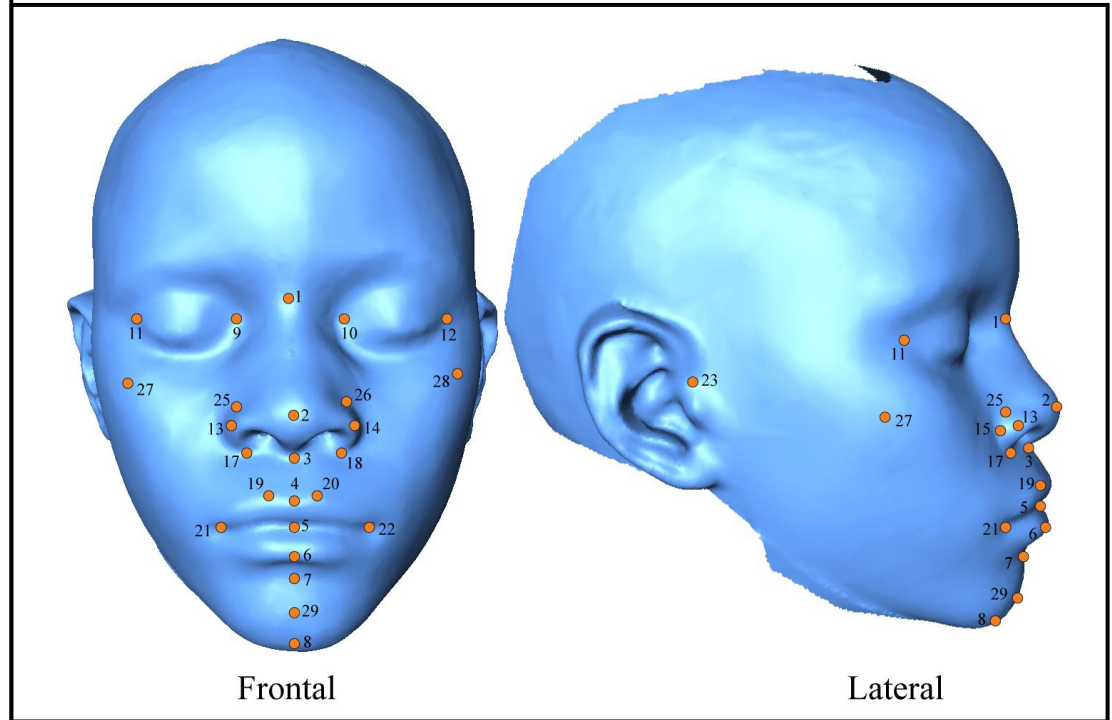
- Entity:** Frontal bone (type=Flat bone)
- Relationships:**
 - Has Dimension:** 3-dimen...
 - Has Boundary:** Solid
 - Has Mass:** (checked)
 - Has Inherent 3-D Shape:** (checked)
 - Has Shape:** (empty field)
 - Bounded By:** Surface of frontal bone
- Part Of:** Neurocranium, Calvarium, Skeleton of head
- Constitutional Part Of:** Neurocranium, Calvarium
- Regional Part:** Squamous part of frontal bone, Nasal part of frontal bone, Left orbital part of frontal bone, Right orbital part of frontal bone
- Constitutional Part:** Bony part of frontal bone, Endosteum of frontal bone, Periosteum of frontal bone, Vasculature of frontal bone, Right frontal sinus, Left frontal sinus, Neural network of frontal bone
- Articulates With:** Left parietal bone, Right parietal bone, Ethmoid, Sphenoid bone, Right zygomatic bone
- Member Of:** Skeleton of head

Enhanced spatio-structural relationships between bones and joints



- 'Physical anatomical entity'
- ▼ ● 'Immaterial anatomical entity'
- ▼ ● 'Anatomical boundary entity'
- ▶ ● 'Anatomical line'
- ▼ ● 'Anatomical point'
- ▶ ● 'Anatomical apex of lung'
- ▼ ● 'Anatomical point of head'
- ▼ ● 'Anatomical point of face'
- ▶ ● 'Alar curvature point'
- ▶ ● Alare
- ▶ ● Chelion
- ▶ ● 'Crista philtri'
- ▶ ● Endocanthion
- ▶ ● Exocanthion
- ▶ ● 'Lateral point of nostril'
- ▶ ● 'Medial point of nostril'
- ▶ ● 'Midline anatomical point of face'
- ▶ ● 'Soft tissue nasion'
- ▶ ● Subalare
- ▶ ● Tragon
- ▼ ● 'Anatomical point of skull'
- ▶ ● Alveolare
- ▶ ● 'Apex of petrous part of temporal bone'
- ▶ ● Asterion
- ▶ ● Auriculare
- ▶ ● 'Condylion laterale'
- ▶ ● 'Condylion mediale'
- ▶ ● 'Condylion superiore'
- ▶ ● Coronale
- ▶ ● Coronion
- ▶ ● 'Cranial apex'
- ▶ ● 'Cranial incision point'
- ▶ ● Dacryon
- ▶ ● Ectoconchion
- ▶ ● Ectomolare
- ▶ ● Endomolare
- ▶ ● Euryon
- ▶ ● 'Frontomolare orbitale'
- ▶ ● 'Frontomolare temporale'
- ▶ ● Frontotemporale
- ▶ ● Gonion
- ▶ ● Hormion
- ▶ ● 'Inferolateral point of nasal bone'
- ▶ ● Infradentale
- ▶ ● Jugale

Craniofacial morphometry

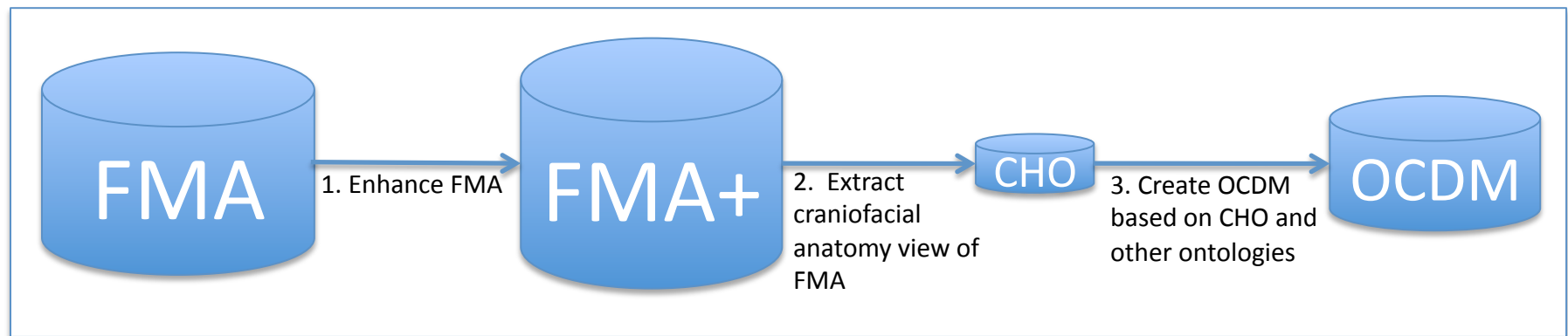


Frontal

Lateral

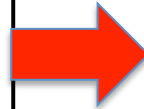
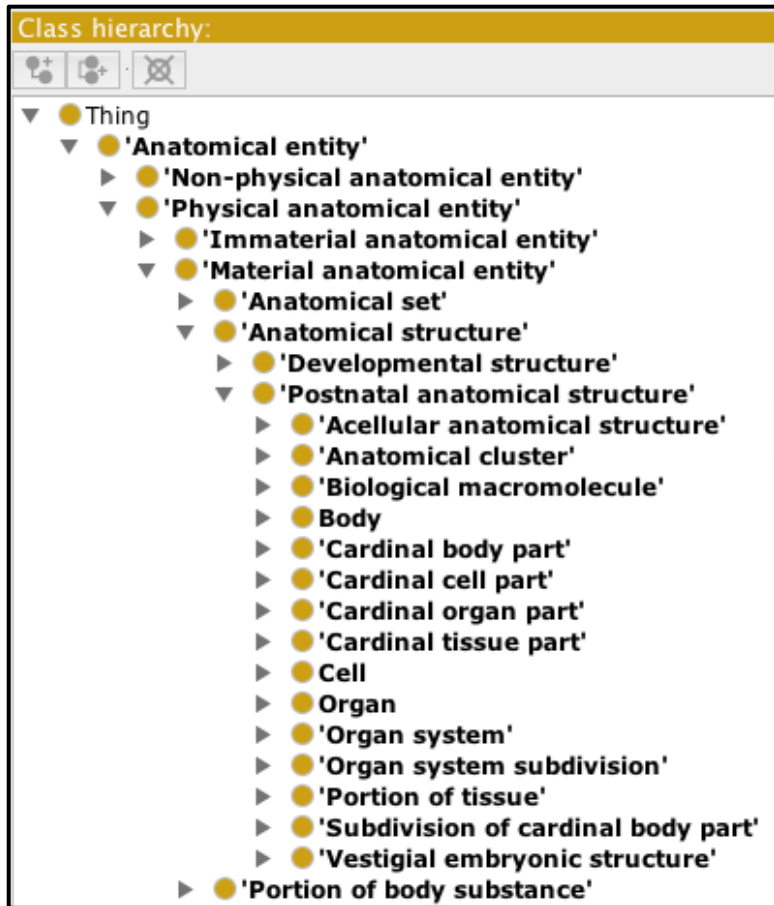
Spritz et. al.

Extract Craniofacial Human Ontology (**CHO**) from the **FMA**

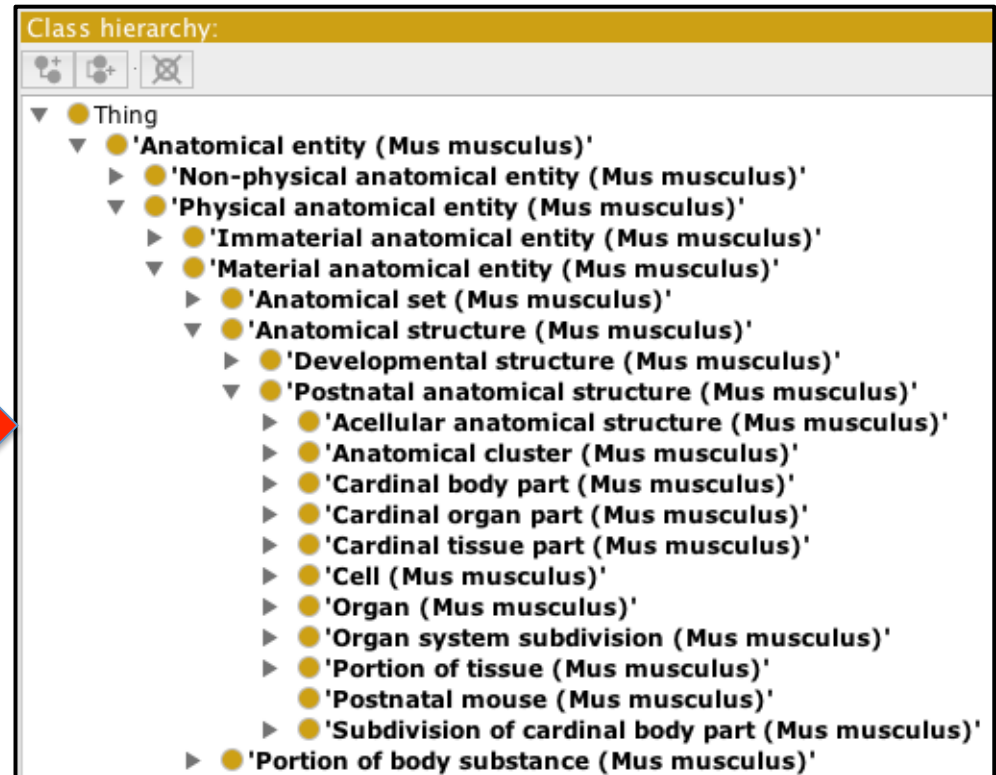


Create CMO from CHO

Human: **CHO**



Mouse: **CMO**

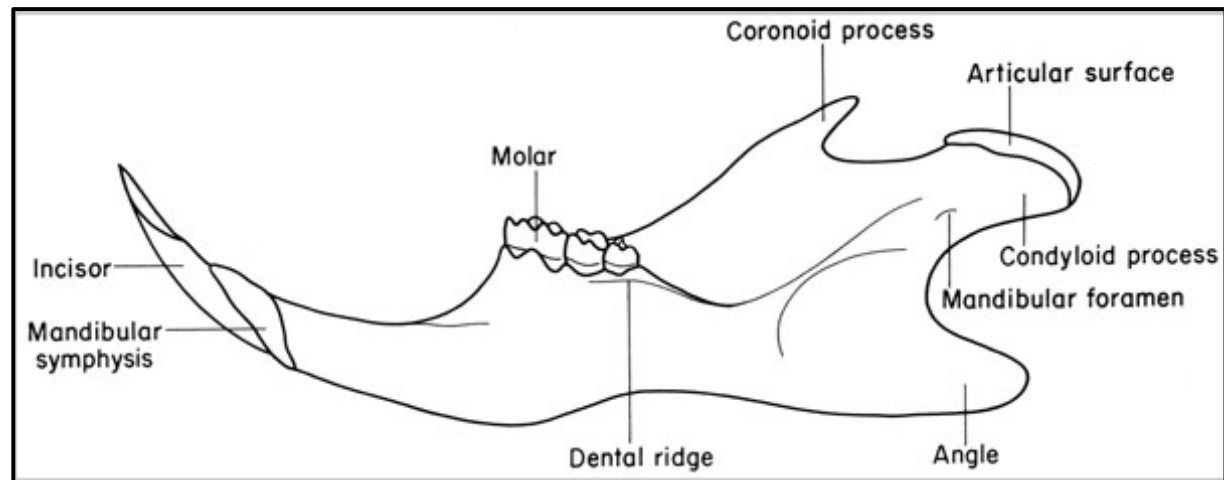
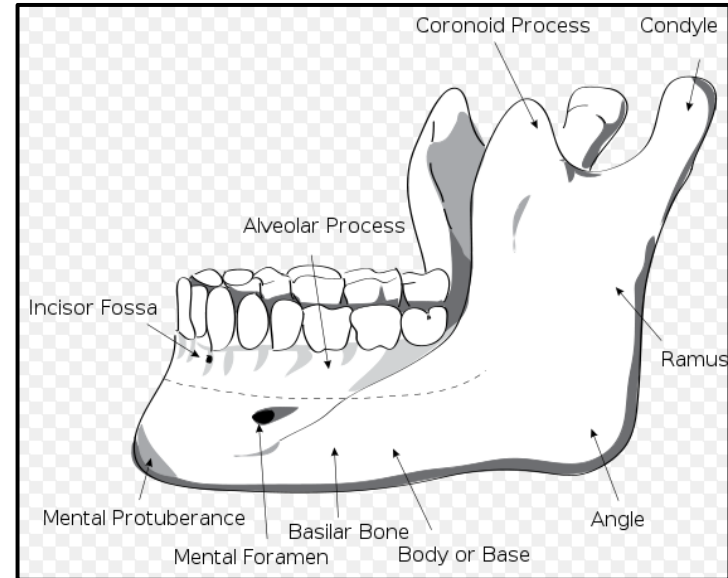


Update CMO content

- remove anatomical entities (classes) not related to the mouse
- add anatomical entities (classes) missing from CHO
- verify existence of mouse anatomical entities
 - map to Mouse Adult Gross Anatomy (MA)
 - PubMed literature
 - domain experts (Cox, Cunningham)

Not in mouse:

canine teeth
premolar teeth
mental protuberance



Examples of classes missing from CHO

Hyoid apparatus

Levator auris longus

Intermolar eminence

Levator nasolabialis

Mandible petrous part

Supraoccipital bone

Squamosal bone

Septal organ of Masera

Septal organ of Gruneberg

CMO-MA mapping

The screenshot displays a software interface with three main panels:

- Class hierarchy: 'Frontal bone (Mus musculus)'**: A tree view showing the classification of the frontal bone. The path is: Organ with cavitated organ parts (Mus musculus) > Bone organ (Mus musculus) > Flat bone (Mus musculus) > Frontal bone (Mus musculus).
- Annotations: 'Frontal bone (Mus musculus)'**: A list of annotations for the selected class. The 'preferred_name' annotation is highlighted in blue and shows the value 'Frontal bone'. Other annotations include 'FMA_reference' (52734), 'non-English_equivalent' (Hueso frontal, Os frontal, Os frontale), 'verified' (true), and 'verified_by' (MA).
- 'Frontal bone (Mus musculus)' preferred_**: A panel showing the 'MA_ID' annotation, which is highlighted with a red box and has the value 'MA:0001466'. Other annotations include 'Date_entered_modified' (May 31 2013 20:13:39 GMT), 'author' (CHO2CMOConverter), and 'authority' (Craniofacial Human Ontology (CHO)).

Total craniofacial mappings = **725**

Verify existence of entity in mouse

Publications

<ul style="list-style-type: none">Faucial pillar (Mus musculus)Hard palate (Mus musculus)Internal nose (Mus musculus)Internal table of calvaria (Mus musculus)Jaw (Mus musculus)	<input checked="" type="checkbox"/> Verified	Verified By http://www.ncbi.nlm.nih.gov/pubmed/?term=%28%22hard+pa
--	--	--

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed ("hard palate" AND (mouse OR mice OR "Mouse"[MeSH]))

RSS Save search Advanced

Show additional filters

Display Settings: Summary, 20 per page, Sorted by Recently Added

Quoted phrase not found.
See the search details.

Results: 1 to 20 of 78

1. [Combined fertility and embryotoxicity study.](#)
Reynaud L, Marsden E.
Methods Mol Biol. 2013;947:125-37. doi: 10.1007/978-1-62703-131-8_11.
PMID: 23138901 [PubMed - indexed for MEDLINE]
[Related citations](#)

2. [Examining the role of nasopharyngeal-associated lymphoreticular tissue \(NALT\) in mouse responses to vaccines.](#)
Cisney ED, Fernandez S, Hall SI, Krietz GA, Ulrich RG.
J Vis Exp. 2012 Aug 1;(66):3960. doi: 10.3791/3960.
PMID: 22871688 [PubMed - indexed for MEDLINE] **Free PMC Article**
[Related citations](#)

3. [The mouse palate and its cellular responses to midpalatal suture expansion forces.](#)
Katebi N, Kolpakova-Hart E, Lin CY, Olsen BR.
Orthod Craniofac Res. 2012 Aug;15(3):148-58. doi: 10.1111/j.1601-6343.2012.01547.x. Epub 2012 Jun 29.
PMID: 22812437 [PubMed - indexed for MEDLINE] **Free PMC Article**
[Related citations](#)

Verify existence of entity in mouse

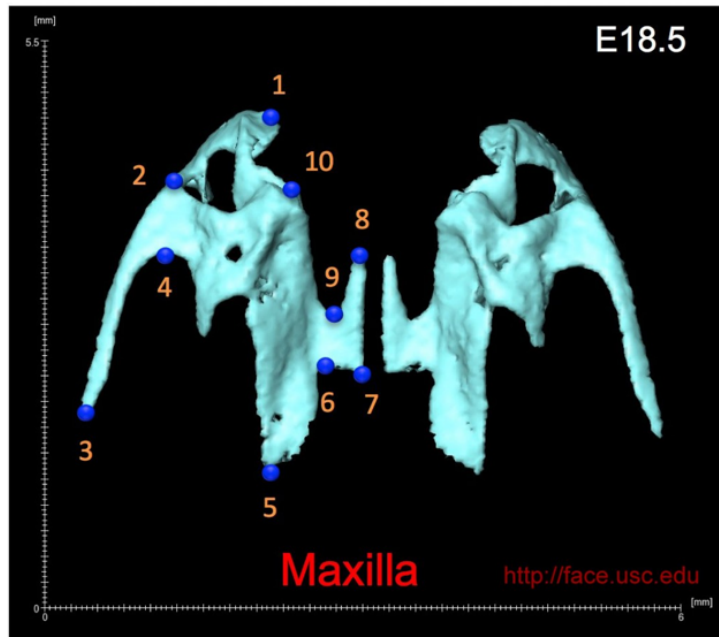
Verified by domain expert

Region of internal nose (Mus musculus)	
Region of soft palate (Mus musculus)	
Anterior part of soft palate (Mus musculus)	
Posterior part of soft palate (Mus musculus)	
Soft palate proper (Mus musculus)	
Uvula (Mus musculus)	
Right side of lower jaw (Mus musculus)	
Right side of nasal septum (Mus musculus)	
Right side of upper jaw (Mus musculus)	

FMA Reference	59852
<input checked="" type="checkbox"/> Verified	Verified By T. Cox

Update CMO with FaceBase terms

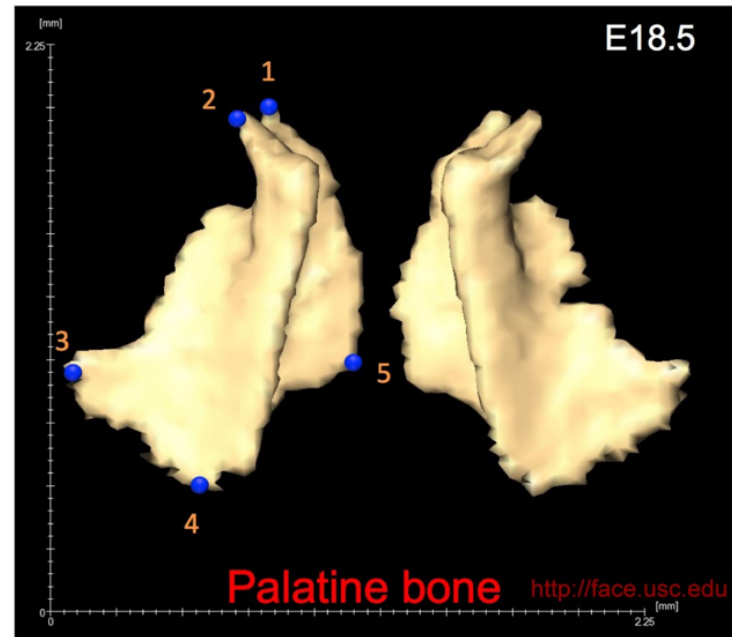
Micro CT: Wildtype maxilla anatomical landmarks



Normal anatomy at E18.5

1. Anterior point of maxilla
2. Lateral point of premaxillary-maxillary suture
3. Tip of zygomatic process of maxilla
4. Anterior-medial point to zygomatic process
5. Posterior point of maxilla
6. Posterior-lateral point of palatal process of maxilla
7. Posterior-medial point of palatal process of maxilla
8. Most anterior-medial point of palatal process of maxilla
9. Anterior-lateral point of palatal process of maxilla
10. Medial point of premaxillary-maxillary suture

Micro CT: Wildtype palatine bone anatomical landmarks



Normal anatomy at E18.5

1. Anterior point of palatine bone
2. Anterior point of ridge of palatine bone
3. Lateral point of pyramidal process of palatine bone
4. Posterior point of pyramidal process of palatine bone
5. Posterior-medial point of horizontal plate of palatine bone

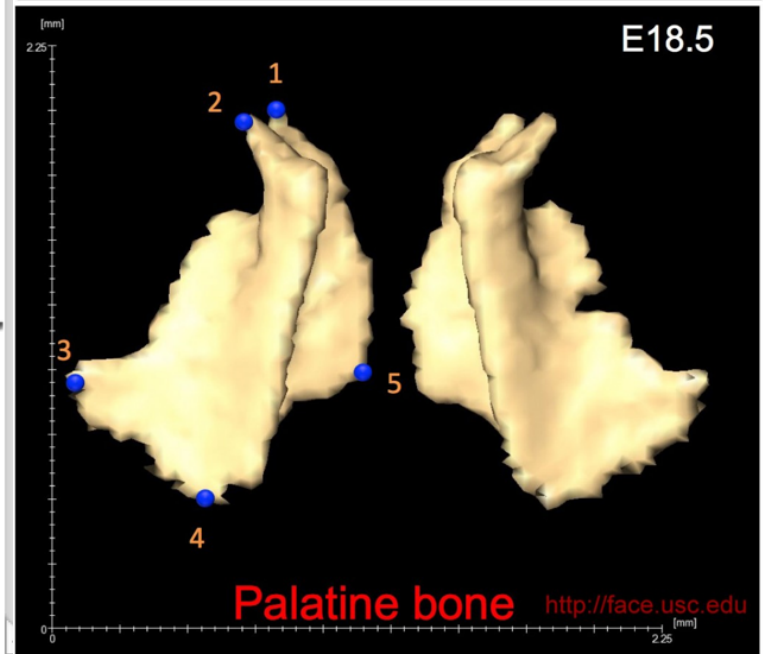
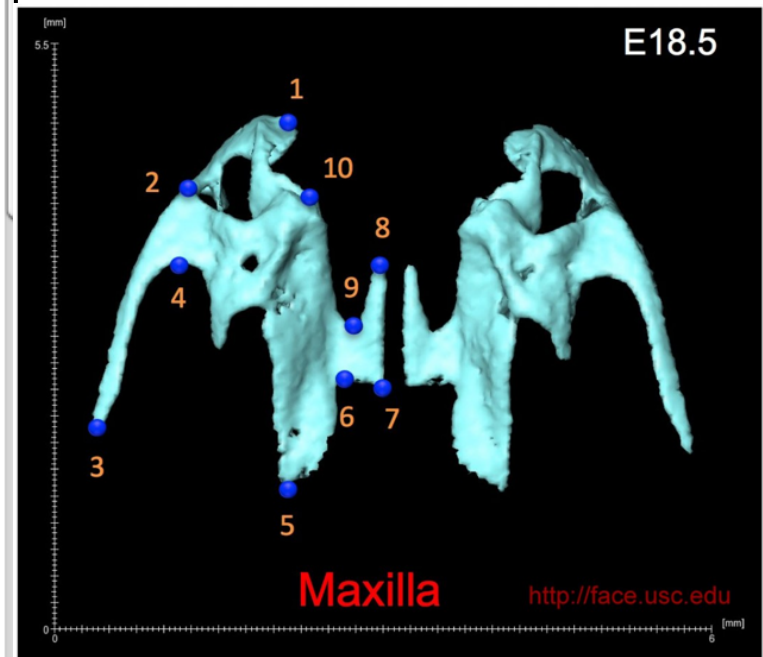
Craniofacial Central

Center for Craniofacial Molecular Biology

CMO

- 'Anatomical point (Mus musculus)'
- ▼ ● 'Anatomical point of head (Mus musculus)'
- ▶ ● 'Anatomical point of face (Mus musculus)'
- ▼ ● 'Anatomical point of skull (Mus musculus)'
- ▼ ● 'Anatomical point of maxilla (Mus musculus)'
- ▼ ● 'Medial point of premaxillary-maxillary suture (Mus musculus)'
- 'Medial point of left premaxillary-maxillary suture (Mus musculus)'
- 'Medial point of right premaxillary-maxillary suture (Mus musculus)'
- ▼ ● 'Anterior-lateral point of palatal process of maxilla (Mus musculus)'
- 'Anterior-lateral point of palatal process of left maxilla (Mus musculus)'
- 'Anterior-lateral point of palatal process of right maxilla (Mus musculus)'
- ▼ ● 'Most anterior-medial point of palatal process of maxilla (Mus musculus)'
- 'Most anterior-medial point of palatal process of left maxilla (Mus musculus)'
- 'Most anterior-medial point of palatal process of right maxilla (Mus musculus)'
- ▼ ● 'Posterior-medial point of palatal process of maxilla (Mus musculus)'
- 'Posterior-medial point of palatal process of left maxilla (Mus musculus)'
- 'Posterior-medial point of palatal process of right maxilla (Mus musculus)'
- ▼ ● 'Posterior-lateral point of palatal process of maxilla (Mus musculus)'
- 'Posterior-lateral point of palatal process of left maxilla (Mus musculus)'
- 'Posterior-lateral point of palatal process of right maxilla (Mus musculus)'
- ▼ ● 'Posterior point of maxilla (Mus msuculus)'
- 'Posterior point of left maxilla (Mus msuculus)'
- 'Posterior point of right maxilla (Mus msuculus)'
- ▼ ● 'Anterior-medial point to zygomatic process (Mus musculus)'
- 'Anterior-medial point to left zygomatic process (Mus musculus)'
- 'Anterior-medial point to right zygomatic process (Mus musculus)'
- ▼ ● 'Tip of zygomatic process of maxilla (Mus musculus)'
- 'Tip of zygomatic process of left maxilla (Mus musculus)'
- 'Tip of zygomatic process of right maxilla (Mus musculus)'
- ▼ ● 'Lateral point of premaxillary-maxillary suture (Mus musculus)'
- 'Lateral point of left premaxillary-maxillary suture (Mus musculus)'
- 'Lateral point of right premaxillary-maxillary suture (Mus musculus)'
- ▼ ● 'Anterior point of maxilla (Mus musculus)'
- 'Anterior point of left maxilla (Mus musculus)'
- 'Anterior point of right maxilla (Mus musculus)'
- ▼ ● 'Anatomical point of palatine bone (Mus musculus)'
- ▼ ● 'Posterior-medial point of horizontal plate of palatine bone (Mus musculus)'
- 'Posterior-medial point of horizontal plate of left palatine bone (Mus musculus)'
- 'Posterior-medial point of horizontal plate of right palatine bone (Mus musculus)'
- ▼ ● 'Posterior point of pyramidal process of palatine bone (Mus msuculus)'
- 'Posterior point of pyramidal process of left palatine bone (Mus msuculus)'
- 'Posterior point of pyramidal process of right palatine bone (Mus msuculus)'
- ▼ ● 'Lateral point of pyramidal process of palatine bone (Mus musculus)'
- 'Lateral point of pyramidal process of left palatine bone (Mus musculus)'
- 'Lateral point of pyramidal process of right palatine bone (Mus musculus)'
- ▼ ● 'Anterior point of of ridge of palatine bone (Mus musculus)'
- 'Anterior point of of ridge of left palatine bone (Mus musculus)'
- 'Anterior point of of ridge of right palatine bone (Mus musculus)'
- ▼ ● 'Anterior point of palatine bone (Mus musculus)'
- 'Anterior point of left palatine bone (Mus musculus)'
- 'Anterior point of right palatine bone (Mus musculus)'

Anatomical landmarks



Correlate different sources

Currently Viewing E 18.5 C 57BL/6

Craniofacial Central

Center for Craniofacial Molecular Biology

Reset

Exclude all bones

- Frontal bone
- Interparietal bone
- Mandible
- Maxilla
- Nasal bone
- Occipital bone
- Palatine
- Parietal
- Premaxilla
- Skull outline

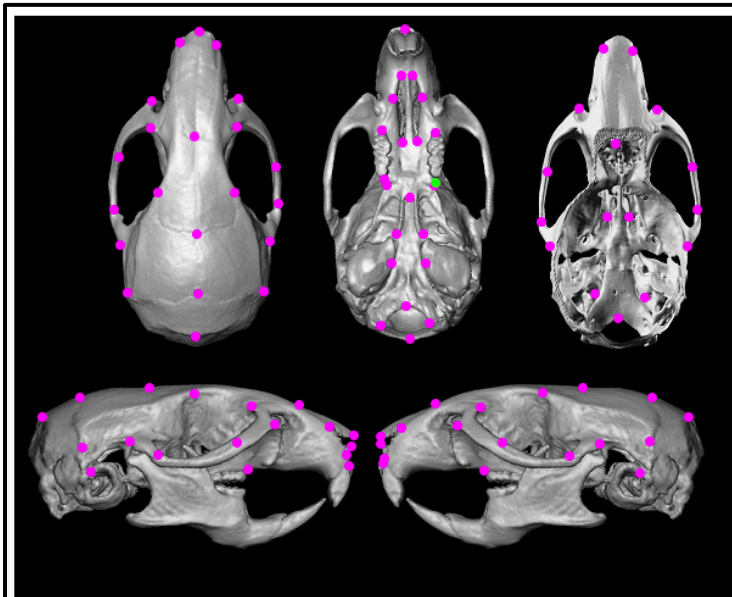
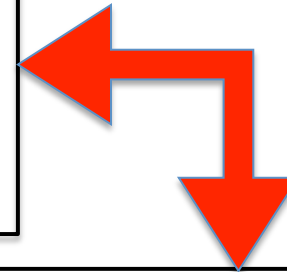
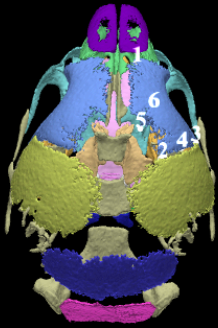
Landmark

Frontal bone

- 1. Most anterior-superior point of frontal bone
- 2. Most posterior-superior point of frontal bone
- 3. Most posterior-lateral intersection of the frontal bone and parietal bone
- 4. Most posterior-inferior point of frontal bone
- 5. Most anterior-inferior point of frontal bone
- 6. Most posterior point of orbitocranial canal

Calculate the distance between and

Calculate



PENNSTATE



Richtsmeier Lab

- 1. laalf - Most anterior point of the anterior palatine foramen, left side
- 2. raalf - Most anterior point of the anterior palatine foramen, right side
- 3. lflac - Intersection of frontal process of maxilla with frontal and lacrimal bones, left side
- 4. rflac - Intersection of frontal process of maxilla with frontal and lacrimal bones, right side
- 5. lfsq - Frontal-squamosal intersection at temporal crest, left side
- 6. rfsq - Frontal-squamosal intersection at temporal crest, right side
- 7. lmax - Center of alveolar ridge over maxillary incisor, left side
- 8. rmax - Center of alveolar ridge over maxillary incisor, right side
- 9. lmxph - Lateral intersection of maxilla and palatine bone posterior to the third molar, left side
- 10. rmxph - Lateral intersection of maxilla and palatine bone posterior to the third molar, right side
- 11. lorb - Anterior notch on frontal process lateral to infraorbital fissure, left side
- 12. rorb - Anterior notch on frontal process lateral to infraorbital fissure, right side
- 13. lpalf - Most posterior point of the anterior palatine foramen, left side
- 14. rpalf - Most posterior point of the anterior palatine foramen, right side
- 15. lmaxna - Anterior-most point at intersection of premaxillae and nasal bones, left side
- 16. rmaxna - Anterior-most point at intersection of premaxillae and nasal bones, right side
- 17. lpmx - Most infero lateral point on premaxilla-maxilla suture, left side
- 18. rpmx - Most infero lateral point on premaxilla-maxilla suture, right side
- 19. lpto - Intersection of parietal, temporal and interparietal bones, left side
- 20. rpto - Intersection of parietal, temporal and interparietal bones, right side

Correlate different sources

The screenshot displays a software interface with three main panels:

- Left Panel (Class hierarchy):** Shows a tree view of anatomical classes for *Mus musculus*. The class **'Inferior point of mandibular body (Mus musculus)'** is selected and highlighted in blue. Other visible classes include 'Anatomical point of mandible (Mus musculus)', 'Anterior point of condylar process (Mus musculus)', 'Midpoint of external oblique ridge (Mus musculus)', and 'Apex of petrous part of temporal bone (Mus musculus)'.
- Middle Panel (Annotations):** Displays the annotations for the selected class. It includes:
 - label [language: en]:** Inferior point of mandibular body (Mus musculus)
 - preferred_name:** Inferior point of mandibular body
 - synonym:** Inferior point on mandibular symphysis
- Right Panel (Annotations for AnnotationAssertion):** Shows a list of annotations for the selected class, including:
 - 'Inferior point of mandibular body (Mus musculus)' synonym "Inferior point on mandibular symphysis"
 - 'reference source': Willmore, KE, CC Roseman, J Rogers, JM Cheverud, JT Richtsmeier. 2009. Comparison of mandibular phenotypic and genetic integration between baboon and mouse. *Evolutionary Biology*, 36: 19-36.

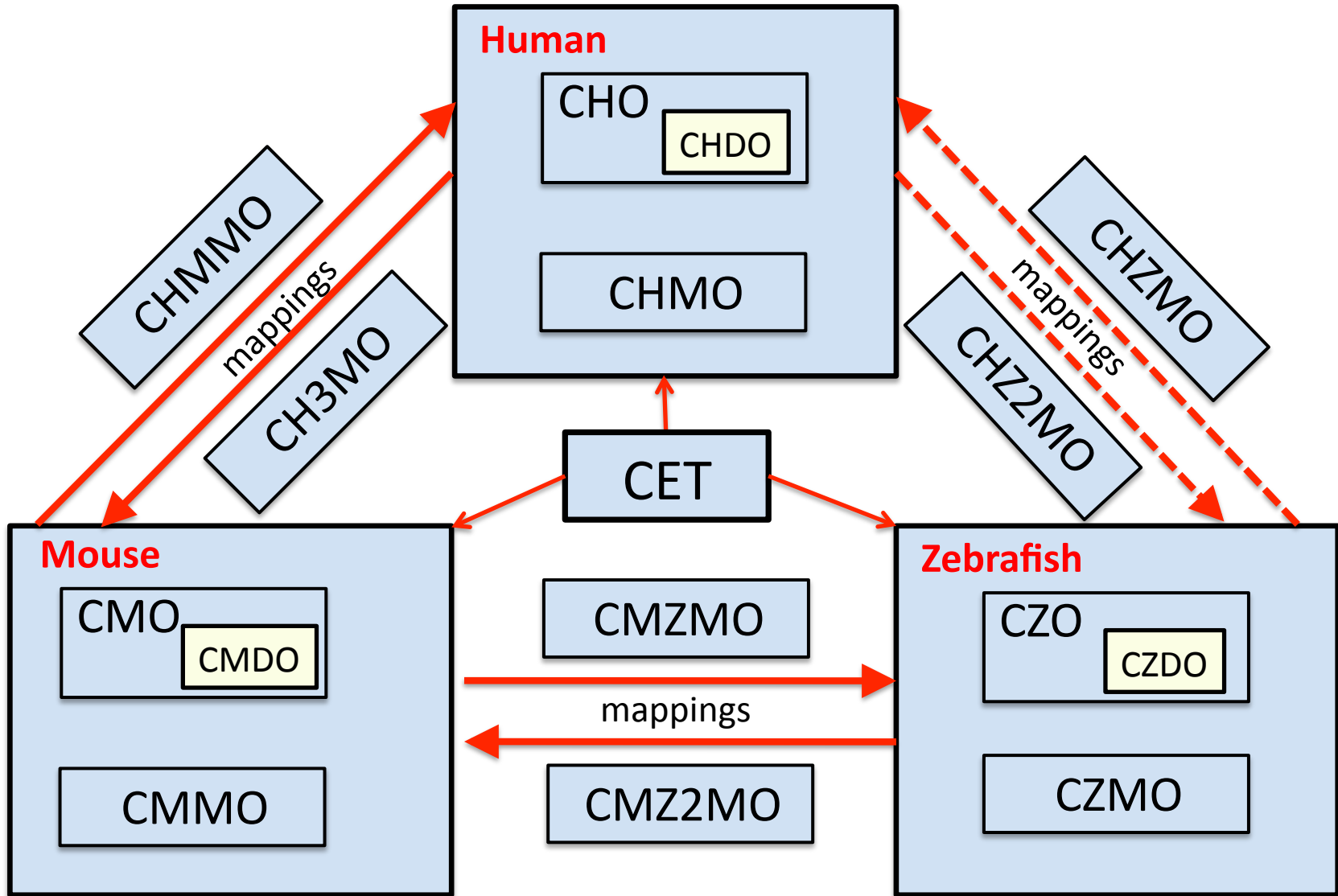
Content Milestones

Task	Date
Canonical musculoskeletal system (MS) of head	
a. CHO (Human)	May 1, 2014 – Aug. 31, 2014
b. CMO (Mouse)	Sept 1, 2014 – Dec, 31, 2014
c. CZO (Zebrafish)	Jan 1, 2015 – March 31, 2015
Embryonic development of MS of head	
a. CHDO (Human)	April 1, 2015 – July 31, 2015
b. CMDO (Mouse)	Aug 1, 2015 – Nov. 30, 2015
c. CZDO (Zebrafish)	Dec. 1, 2015 – March 30, 2016
Anatomy mappings	
a. CHO with CMO	April 1, 2016 – Sept 30, 2016
b. CMO with CZO	Oct. 1, 2016 – Jan. 31, 2017
Craniofacial malformation (facial and cranial vault dysmorphology)	
a. CHMO (Human)	Feb 1, 2017 – June 30, 2017
b. CMMO (Mouse)	July 1, 2017 – Nov. 30, 2017
c. CZMO (Zebrafish)	Dec. 1, 2017 – March 30, 2018

Content Milestones

Task	Date
Malformation mappings	
a. CHMO with CMMO	April 1, 2018 – August 30, 2018
b. CHMO with CZMO	Sept 1, 2018 – Dec 31. 2018
Connect all species structure to molecular level	Jan 1, 2019 – April 30, 2019

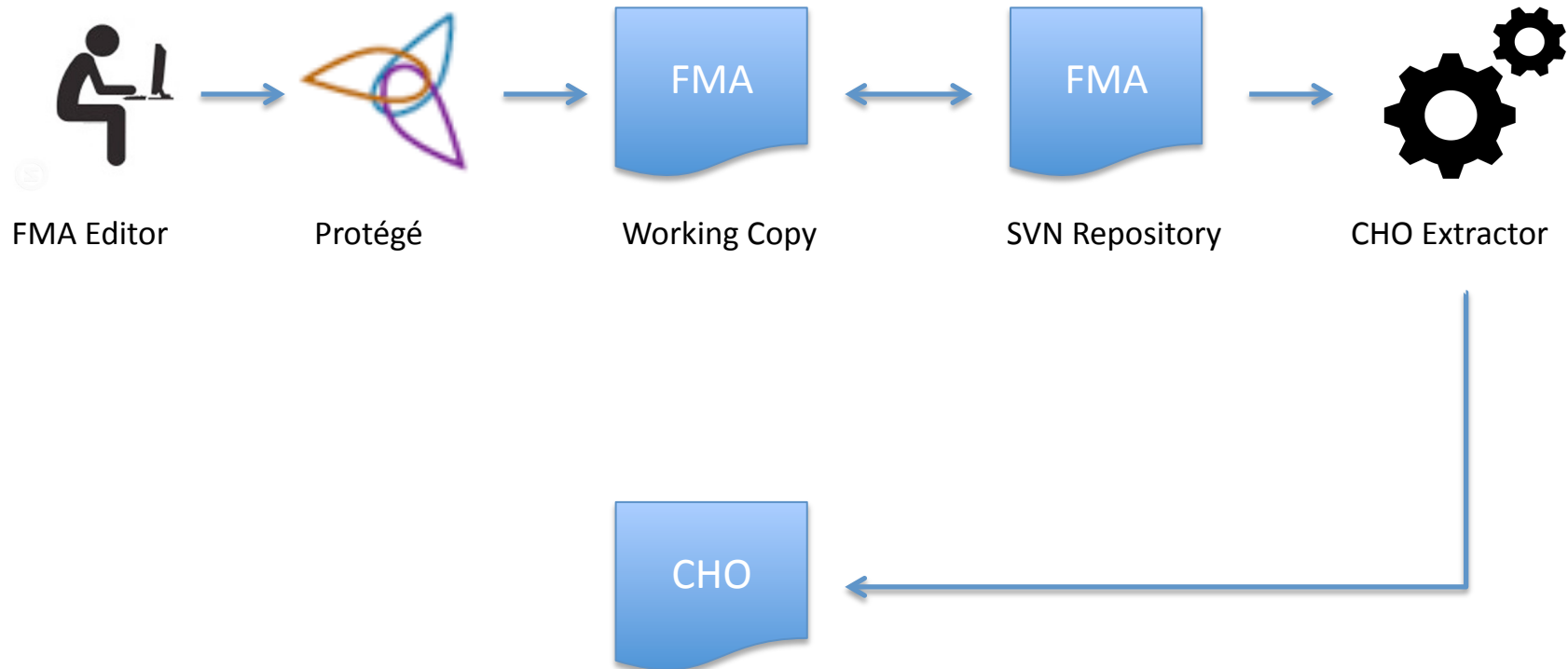
OCDM



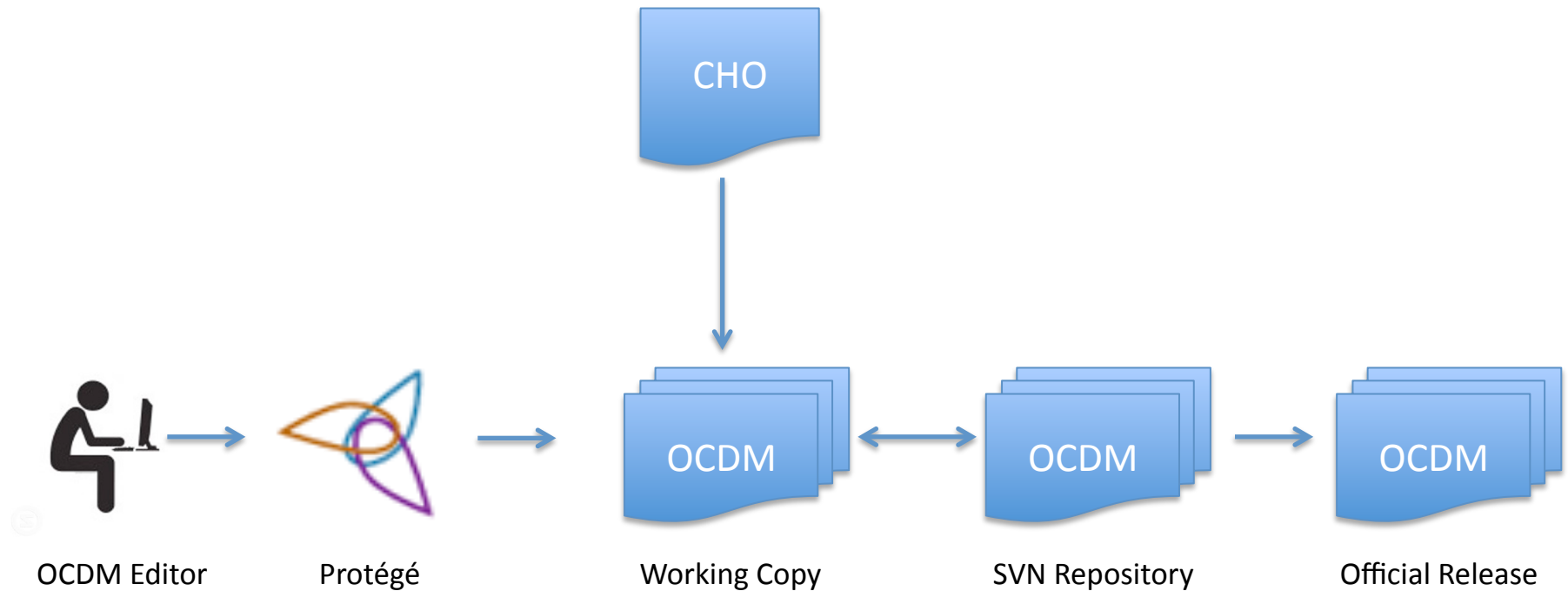
Conversion to OWL 2

- FMA and OCDDM originally in Protégé Frames
- Most ontology development now in OWL2
- Converted both FMA and OCDDM to OWL2
 - Custom program using configuration files
 - Potential use for any Frame-based ontology
- Now all development is in OWL2

Workflow 1: FMA to CHO



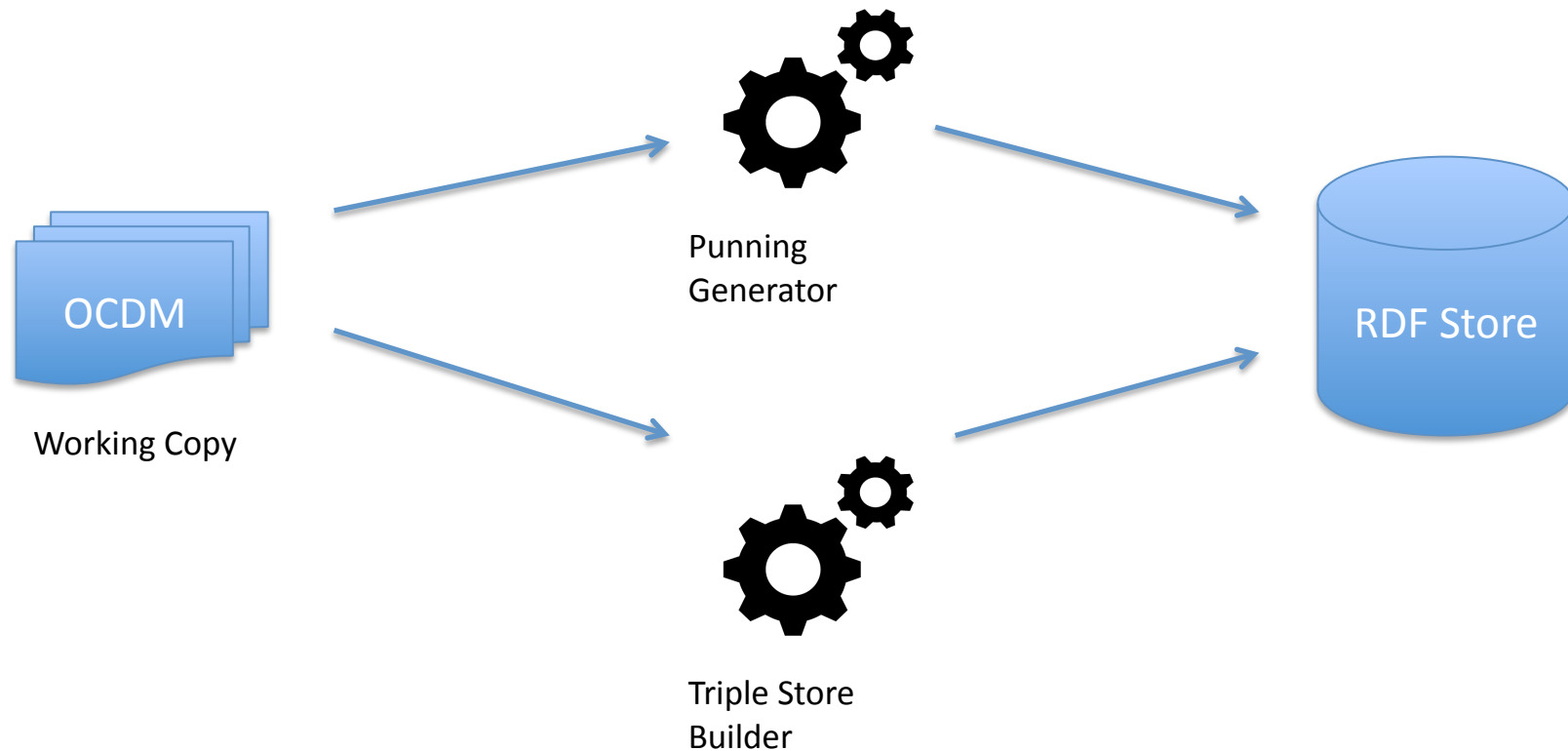
Workflow 2: CHO to OCDM



[https://www.facebase.org/
content/ocdm](https://www.facebase.org/content/ocdm)

<http://purl.org/sig/ont/ocdm>

Workflow 3: OCDM to Queryable Resource



Personnel

- Onard Mejino
- Todd Detwiler
- Tim Cox
- Michael Cunningham
- Linda Shapiro
- Trond Nilsen
- Melissa Clarkson

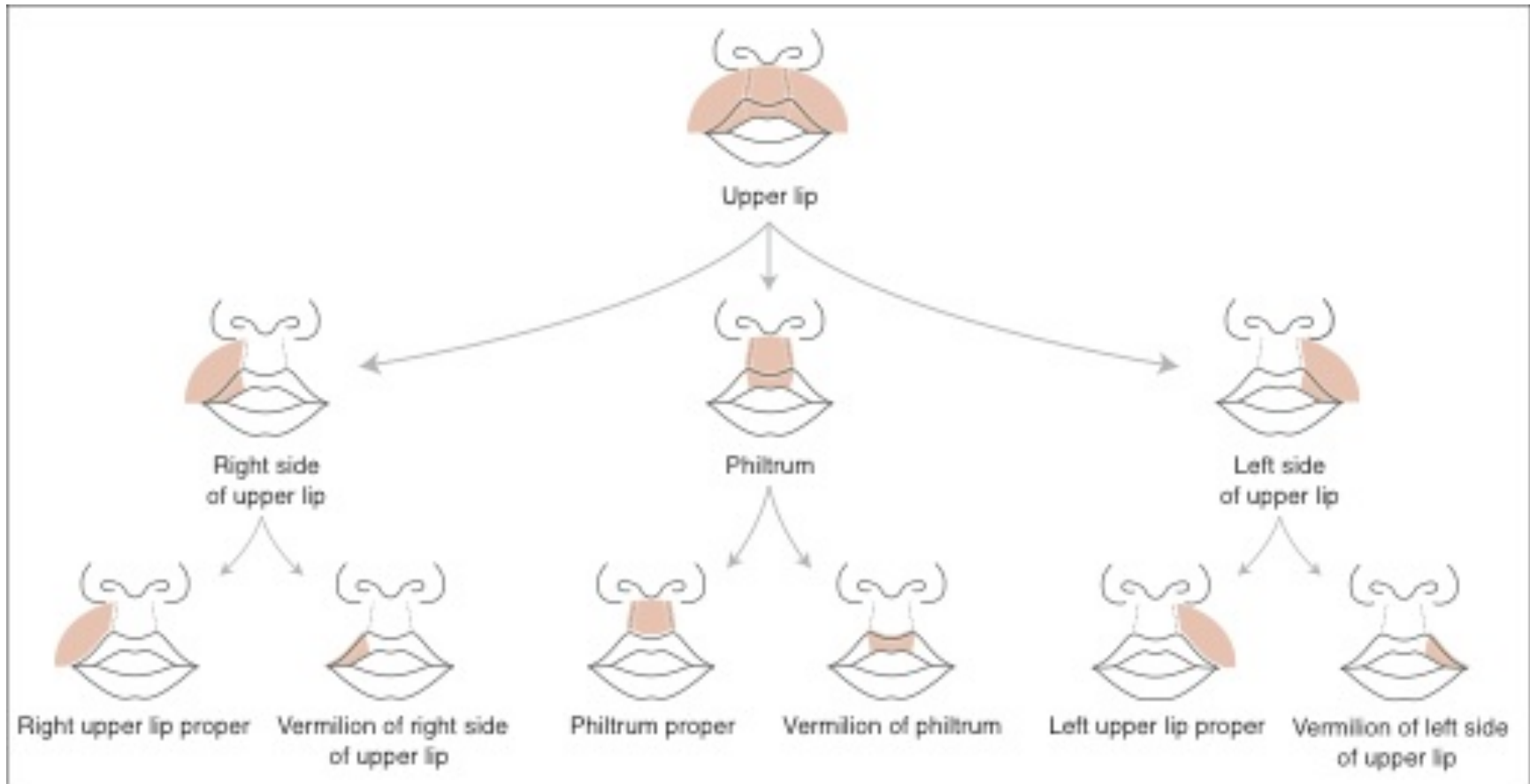
References

- Overview of OCDM
 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4041627/>
- OCDM Viewer
 - <http://purl.org/sig/ocdm/viewer>
- Foundational Model Browser
 - <http://xiphoid.biostr.washington.edu/fma/index.html>

Ontology metrics:

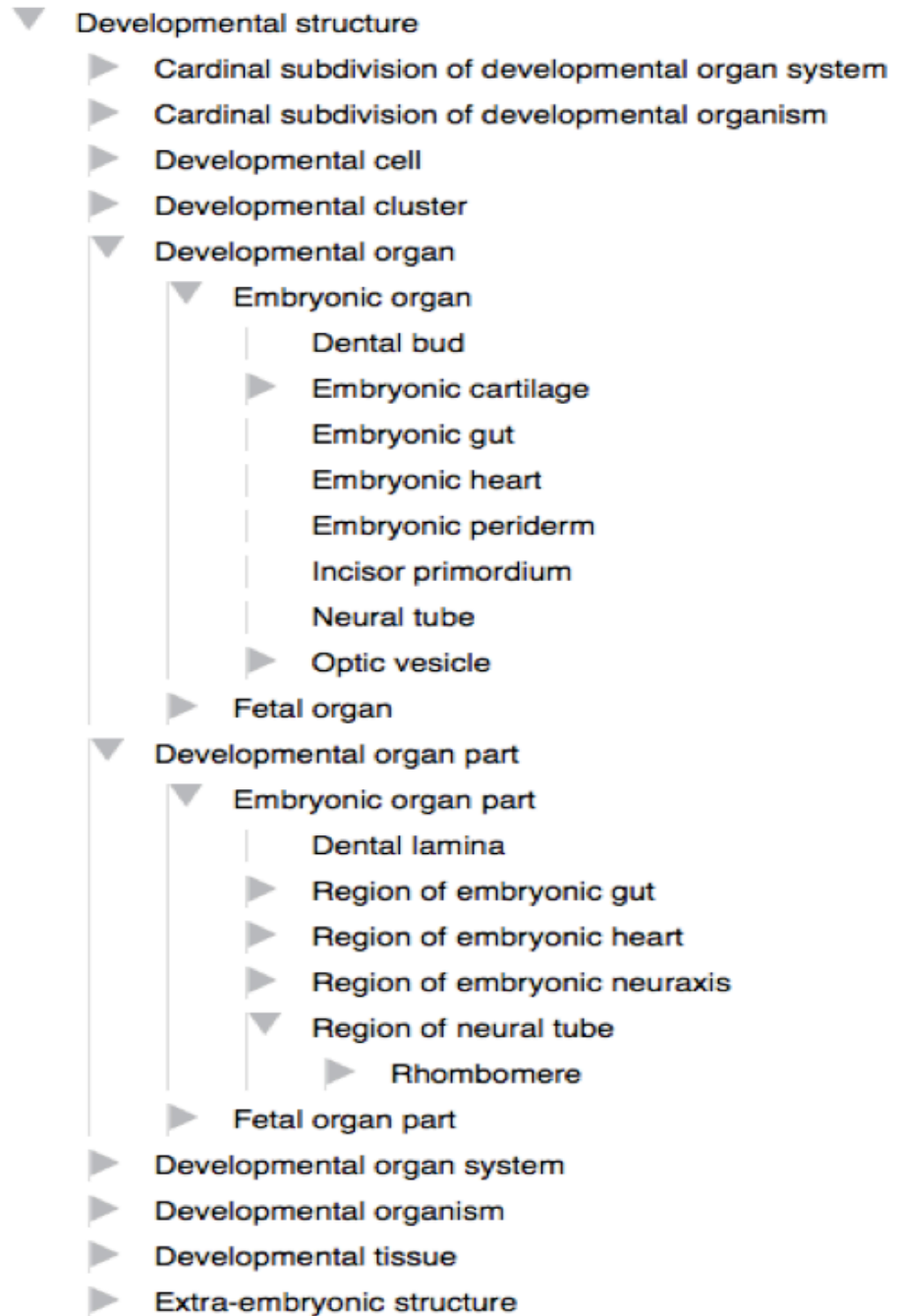
	No of classes	No. of properties	No. of spatio-structural relationships
CHO	14911	169	38857
CMO	12672	161	30657

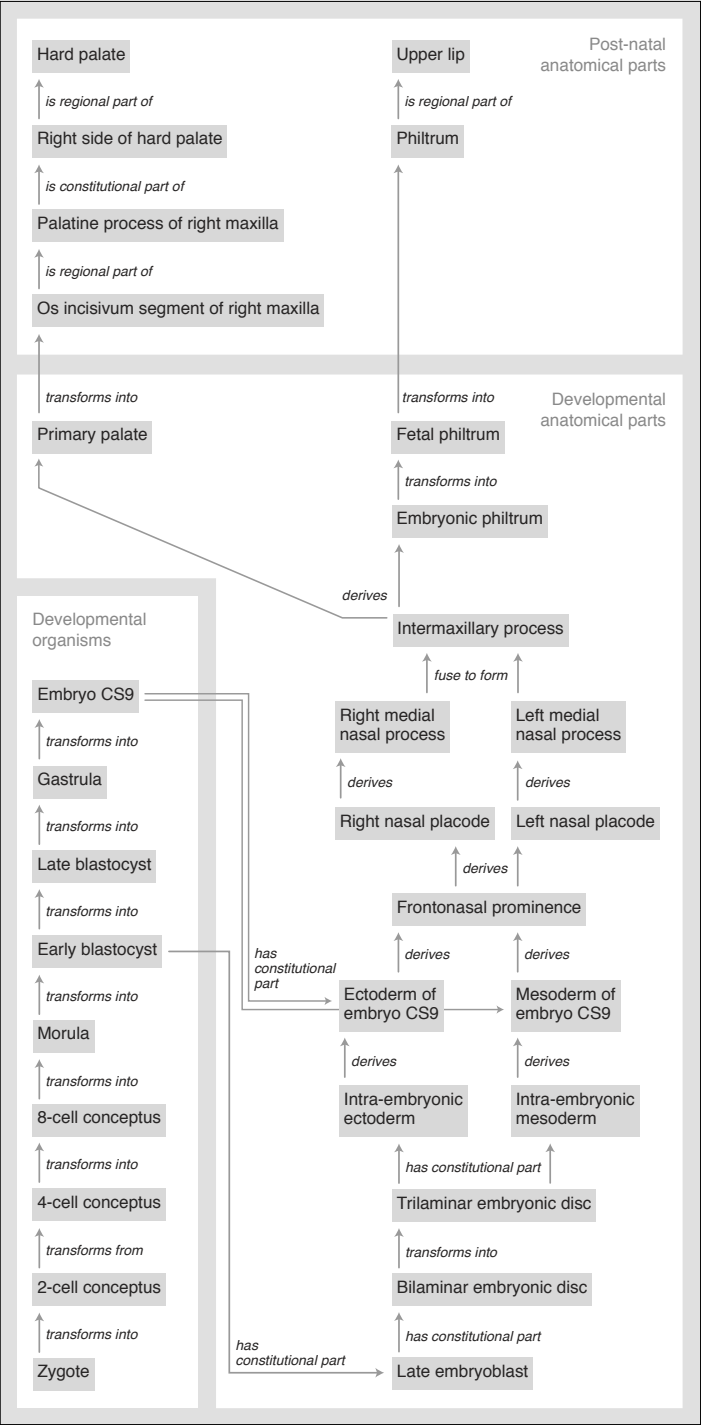
Craniofacial Human Ontology (CHO)



- ▼ **R** Upper lip
 - ▼ **R** Left side of upper lip
 - ▶ **R** Left upper lip proper
 - | **R** Vermilion of left side of upper lip
 - ▼ **R** Philtrum
 - ▶ **R** Philtrum proper
 - ▶ **R** Vermilion of philtrum
 - ▶ **C** Integument of philtrum
 - ▶ **C** Mucosa of philtrum
 - | **C** Philtral part of orbicularis oris
 - ▼ **R** Right side of upper lip
 - ▶ **R** Right upper lip proper
 - | **R** Vermilion of right side of upper lip

Craniofacial Human Developmental Ontology (CHDO)





Craniofacial Mouse Ontology (CMO)

Mouse canonical anatomy

Part hierarchy

[close all]

- ▼ Head (Mus musculus)
 - ▼ R Face (Mus musculus)
 - ▶ R Left eye (Mus musculus)
 - ▶ R Left pharyngotympanic tube (Mus musculus)
 - ▶ R Left temple (Mus musculus)
 - ▼ R Mouth (Mus musculus)
 - ▼ R External part of mouth (Mus musculus)
 - ▶ R External mandibular part of mouth (Mus musculus)
 - ▼ R Labial part of mouth (Mus musculus)
 - ▶ R Lower lip (Mus musculus)
 - ▼ R Upper lip (Mus musculus)
 - ▶ R Left side of upper lip (Mus musculus)
 - ▶ R Philtrum (Mus musculus)
 - ▶ R Right side of upper lip (Mus musculus)
 - ▶ C Integument of upper lip (Mus musculus)
 - ▶ C Mucosa of upper lip (Mus musculus)
 - ▶ C Superior zone of orbicularis oris (Mus musculus)
 - ▶ C Integument of labial part of mouth (Mus musculus)
 - ▶ C Mucosa of labial part of mouth (Mus musculus)
 - ▶ C Orbicularis oris (Mus musculus)

Upper lip (Mus musculus)

is regional part of:

Labial part of mouth Mus musculus

has regional part:

Left side of upper lip Mus musculus

Philtrum Mus musculus

Right side of upper lip Mus musculus

is constitutional part of:

has constitutional part:

Superior zone of orbicularis oris Mus musculus

Integument of upper lip Mus musculus

Mucosa of upper lip Mus musculus

Craniofacial Human Mouse Mappings Ontology (CHMMO)

Craniofacial Human-Mouse Mappings Ontology (CHMMO)
Human-mouse mappings

Human	Mappings	Mouse
<p>Search</p> <p>[close all]</p> <ul style="list-style-type: none"> ▶ Eye ▶ Eyelid Left side of face Midface Mouth Nose Right side of face ▶ Subdivision of external nose ▼ Subdivision of mouth <ul style="list-style-type: none"> Angle of mouth Anterior part of floor of mouth ▶ Cheek Chin External mandibular part of mouth External part of mouth Floor of mouth Glosso-epiglottic region of mouth Internal part of mouth Labial part of mouth Left side of chin Left side of maxillary alveolodental arch Mandibular part of mouth ▶ Mandibular part proper of mouth Posterior part of floor of mouth ▼ Region of labial part of mouth <ul style="list-style-type: none"> ▼ Lip <ul style="list-style-type: none"> Lower lip Upper lip ▶ Lip proper ▶ Region of lower lip ▶ Region of upper lip ▶ Region of vermillion 	<p>[clear]</p> <p><i>mapped from:</i> Upper lip</p> <hr/> <p><i>mapped to:</i> Upper lip (Mus musculus)</p> <hr/> <p><i>confidence:</i> high</p> <hr/> <p><i>reviewer:</i> Tim Cox</p>	<p>Search</p> <p>[clear]</p> <ul style="list-style-type: none"> External nose (Mus musculus) ▶ Eye (Mus musculus) ▶ Eyelid (Mus musculus) Left side of face (Mus musculus) Midface (Mus musculus) Mouth (Mus musculus) Nose (Mus musculus) Right side of face (Mus musculus) Snout (Mus musculus) ▶ Subdivision of external nose (Mus musculus) ▼ Subdivision of mouth (Mus musculus) <ul style="list-style-type: none"> Angle of mouth (Mus musculus) Anterior part of floor of mouth (Mus musculus) ▶ Cheek (Mus musculus) Chin (Mus musculus) External mandibular part of mouth (Mus musculus) External part of mouth (Mus musculus) Floor of mouth (Mus musculus) Glosso-epiglottic region of mouth (Mus musculus) Internal part of mouth (Mus musculus) Labial part of mouth (Mus musculus) Left side of chin (Mus musculus) Left side of maxillary alveolodental arch (Mus musculus) Mandibular part of mouth (Mus musculus) ▶ Mandibular part proper of mouth (Mus musculus) Mouth proper (Mus musculus) Posterior part of floor of mouth (Mus musculus) ▼ Region of labial part of mouth (Mus musculus) <ul style="list-style-type: none"> ▼ Lip (Mus musculus) <ul style="list-style-type: none"> Lower lip (Mus musculus) Upper lip (Mus musculus) ▶ Lip proper (Mus musculus)



Craniofacial Mouse Developmental Ontology (CMDO)

- ▼ ●●● Region of embryonic palatal epithelium (Mus musculus)
 - ▶ ●●● Embryonic nasal palatal epithelium (Mus musculus)
 - ▶ ●●● Embryonic oral palatal epithelium (Mus musculus)
 - ▶ ●●● Epithelium of embryonic hard palate (Mus musculus)
 - ▶ ●●● Epithelium of embryonic secondary palate (Mus musculus)
 - Epithelium of embryonic soft palate (Mus musculus)
 - ▼ ●●● Epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● TS19 epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● TS20 epithelium of palatal shelf (Mus musculus)
 - TS21 epithelium of palatal shelf (Mus musculus)
 - TS22 epithelium of palatal shelf (Mus musculus)
 - TS23 epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● Medial edge epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● Region of epithelium of palatal shelf (Mus musculus)

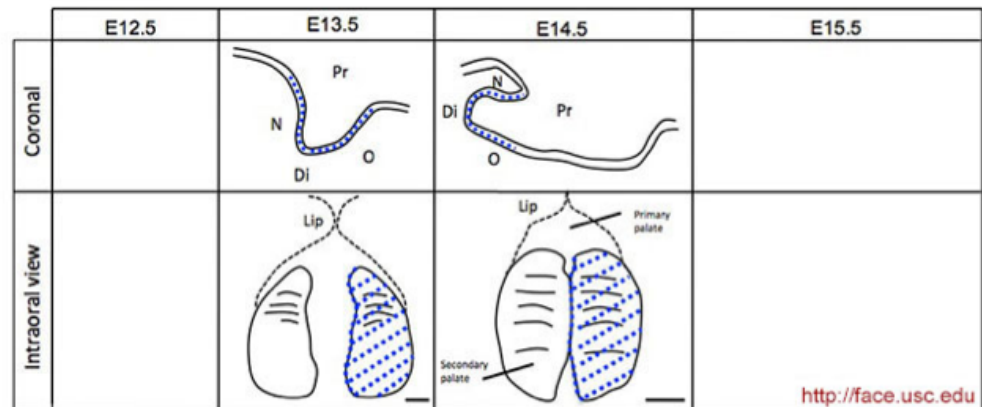
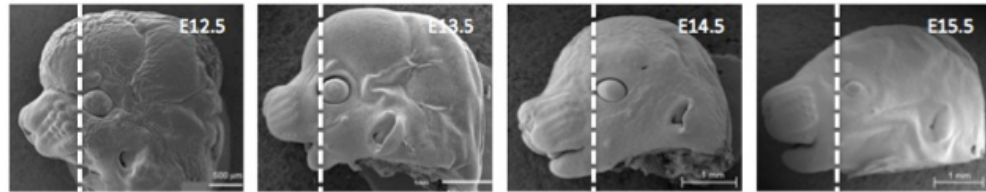
Craniofacial Central

Center for Craniofacial Molecular Biology

- ▶ Home page
- ▶ Cleft of the secondary palate
- ▶ Gene expressions
 - ▶ Molecules
 - ▶ Growth factors
 - ▶ Receptors
 - ▶ Signaling molecules
 - ▶ Transcription factors
 - ▶ Intracellular molecules
 - ▶ Extracellular molecules
 - ▶ Plasma membrane molecules
 - ▶ miRNA
 - ▶ Enhancers
 - ▶ Tissues
 - ▶ Epithelium
 - ▶ Oral epithelium
 - ▶ Nasal epithelium
 - ▶ Midline epithelium
 - ▶ Basal epithelium
 - ▶ Peridermal cells
 - ▶ Mesenchyme
 - ▶ Nasal region
 - ▶ Oral region
 - ▶ Anterior region
 - ▶ Posterior region
 - ▶ Osteogenic mesenchyme
 - ▶ Palatal bone primordium
 - ▶ Muscles of the soft palate

Beta-catenin gene expression

Beta-catenin – MGI gene detail



Description: *Beta-catenin* is expressed in the palatal epithelium along the AP axis throughout development, including the oral and nasal epithelia and in the MEE at E14.5.

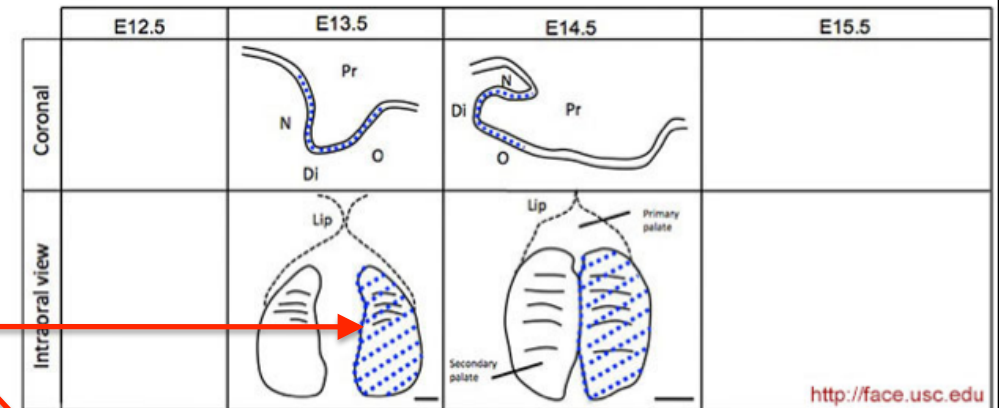
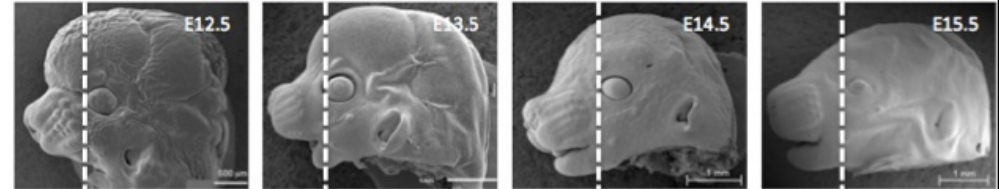
Source: He et al. (2011) Epithelial Wnt/ β -catenin signaling regulates palatal shelf fusion through regulation of Tgf β 3 expression. *Dev. Biol.* 350(2): 511-9.

CMDO

USC CC

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- ▼ ●●● Region of embryonic palatal epithelium (Mus musculus)
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 - ▶ ●●● Embryonic oral palatal epithelium (Mus musculus)
 - ▶ ●●● Epithelium of embryonic hard palate (Mus musculus)
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 - ▶ ●●● TS22 epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● TS23 epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● Medial edge epithelium of palatal shelf (Mus musculus)
 - ▶ ●●● Region of epithelium of palatal shelf (Mus musculus)

USC Craniofacial Central:

Beta-catenin expression in E14.5 palatal epithelium

OCDM CMDO

- Epithelium of embryonic hard palate (Mus musculus)
- Epithelium of embryonic secondary palate (Mus musculus)
- Epithelium of embryonic soft palate (Mus musculus)
- Epithelium of palatal shelf (Mus musculus)
 - TS19 epithelium of palatal shelf (Mus musculus)
 - TS20 epithelium of palatal shelf (Mus musculus)
 - TS21 epithelium of palatal shelf (Mus musculus)
 - TS22 epithelium of palatal shelf (Mus musculus)
 - TS23 epithelium of palatal shelf (Mus musculus)
- Medial edge epithelium of palatal shelf (Mus musculus)
- Region of epithelium of palatal shelf (Mus musculus)

Has Theiler Stage

● TS23 (Mus musculus)

Has Embryonic Day

● E14.5 (Mus musculus)

EMAP ID

EMAP:8172

Name

TS23,epithelium,palatal shelf

€ma

Mouse Anatomy Atlas

€mage

Mouse Gene Expression Spatial Database

Genes detected in
palatal shelf epithelium, TS23

Example: Krt 16

Symbol	Krt16	Vertebrate homology	HomoloGene:21145 Vertebrate Homology Class 1 human; 1 mouse; 1 rat; 1 chimpanzee; 1 rhesus macaque; 1 cattle; 1 dog Gene Tree: Krt16
Name ID	keratin 16 MGI:96690	Human homologs	Human Homolog KRT16, keratin 16 NCBI Gene ID 3868 neXtProt AC NX_P08779
Synonyms	K16, Krt1-16		Human Synonyms CK16, FNEPPK, K16, K1CP, KRT16A, NEPPK, PC1
Feature Type	protein coding gene		Human Chr (Location) 17q21.2; chr17:41609778-41612827 (-) <i>GRCh38</i>
Genetic Map	Chromosome 11 63.44 cM Detailed Genetic Map ± 1 cM		Disease Associations (2) Diseases Associated with Human KRT16

Craniofacial Human Malformations Ontology (CHMO)

A



Unilateral Left CL

Bilateral CL

B



Unilateral Left CL

Bilateral CL

C



Unilateral Left CL

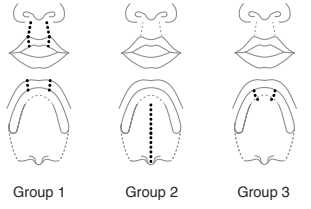
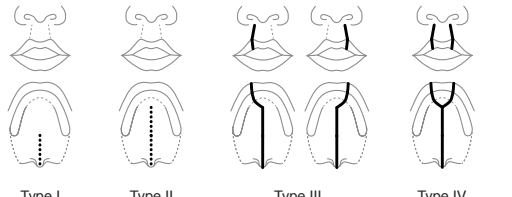
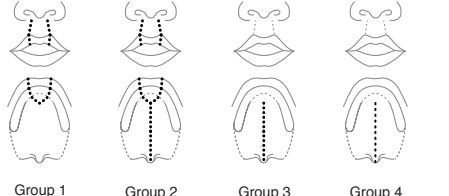
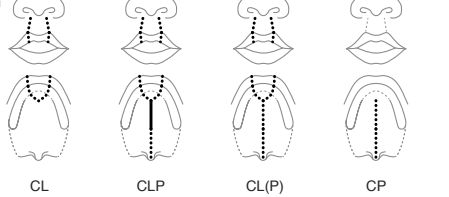
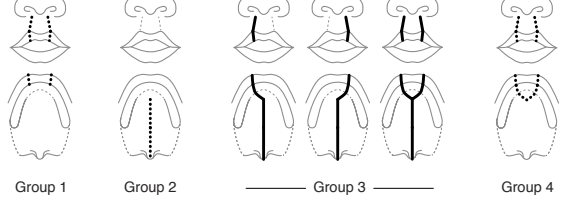
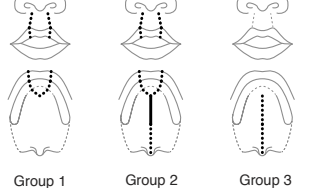
Bilateral CL

ICD-10:
LAHSN:
LAPAL:
Smith:

CL
Subtotal
< 1/2 CL
1/3 CL

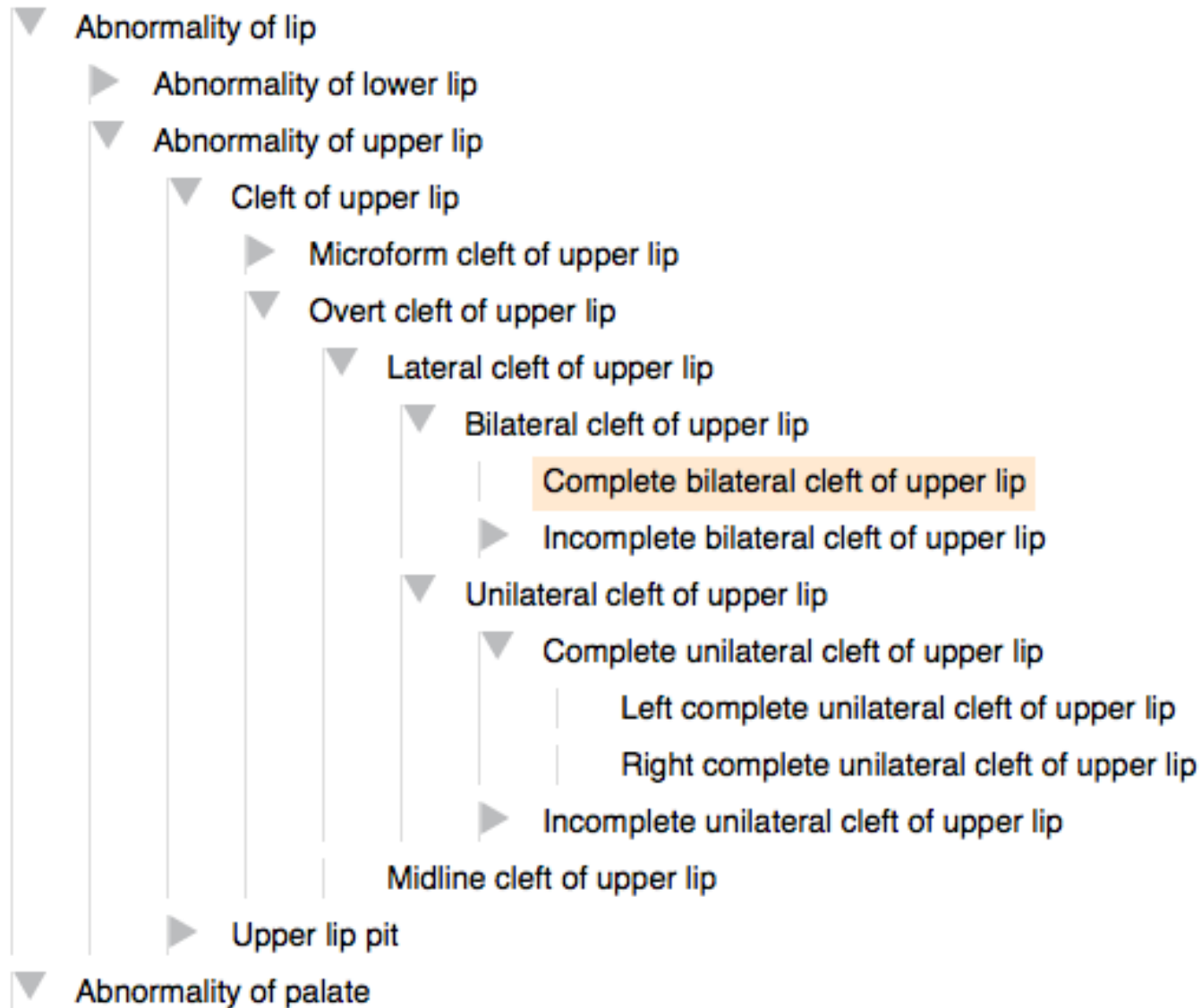
CL
Subtotal
> 1/2 CL
2/3 CL

CL
Total
Complete CL
3/3 CL

Davis and Ritchie	 <p>Group 1 Group 2 Group 3</p>	<p>Group 1 Clefts of the lip: (a) unilateral (incomplete and complete), (b) bilateral (incomplete and complete) <i>cleft of the palate may be associated with this group</i></p> <p>Group 2 Clefts of the palate: (a) soft palate, (b) hard palate <i>cleft of the lip may be associated with this group</i></p> <p>Group 3 Clefts of the alveolus: (a) unilateral (incomplete and complete), (b) bilateral (incomplete and complete) <i>clefts of the lip and palate are usually associated with this group</i></p>	<p>Key</p> <p>———— cleft must be present</p> <p>..... cleft present at some location</p>
Veau*	 <p>Type I Type II Type III Type IV</p>	<p>Type I Clefts of the soft palate</p> <p>Type II Clefts of the soft and hard palate, posterior to the incisive foramen</p> <p>Type III Complete unilateral cleft alveolus and cleft palate</p> <p>Type IV Complete bilateral cleft with complete isolation of the median tubercle</p>	
Pruzansky	 <p>Group 1 Group 2 Group 3 Group 4</p>	<p>Group 1 Clefts of the lip (and alveolus)</p> <p>Group 2 Clefts of the lip and palate</p> <p>Group 3 Clefts of the palate (includes clefts of the soft palate, clefts of both the soft palate and hard palate, but not the hard palate alone)</p> <p>Group 4 Congenital insufficiency of the palate (includes submucous clefts and deficient palatal development)</p>	
Ross and Johnston	 <p>CL CLP CL(P) CP</p>	<p><i>Primary palatal defects</i></p> <p>CL Clefts involving the lip (and alveolus)</p> <p>CLP Clefts involving the lip and palate</p> <p>CL(P) Clefts involving the lip with or without cleft palate</p> <p><i>Secondary palatal defects</i></p> <p>CP Clefts involving the hard and soft palate only</p>	
Iowa system	 <p>Group 1 Group 2 Group 3 Group 4 Group 5</p>	<p>Group 1 Cleft of the lip only</p> <p>Group 2 Secondary palatal clefts</p> <p>Group 3 Clefts of the lip, alveolus, and palate (complete cleft lip and palate)</p> <p>Group 4 Primary cleft palate and lip</p> <p>Group 5 Miscellaneous</p>	
ICPR	 <p>Group 1 Group 2 Group 3</p>	<p>Group 1 Clefts of the primary palate: (a) lip, (b) alveolus</p> <p>Group 2 Clefts of the primary and secondary palate: (a) lip, (b) alveolus, (c) hard palate</p> <p>Group 3 Clefts of the secondary palate: (a) hard palate, (b) soft palate</p>	

* Interpretation of this system was based on secondary descriptions (Mooney 2008)

Phenotypic Abnormality (part of CHMO)

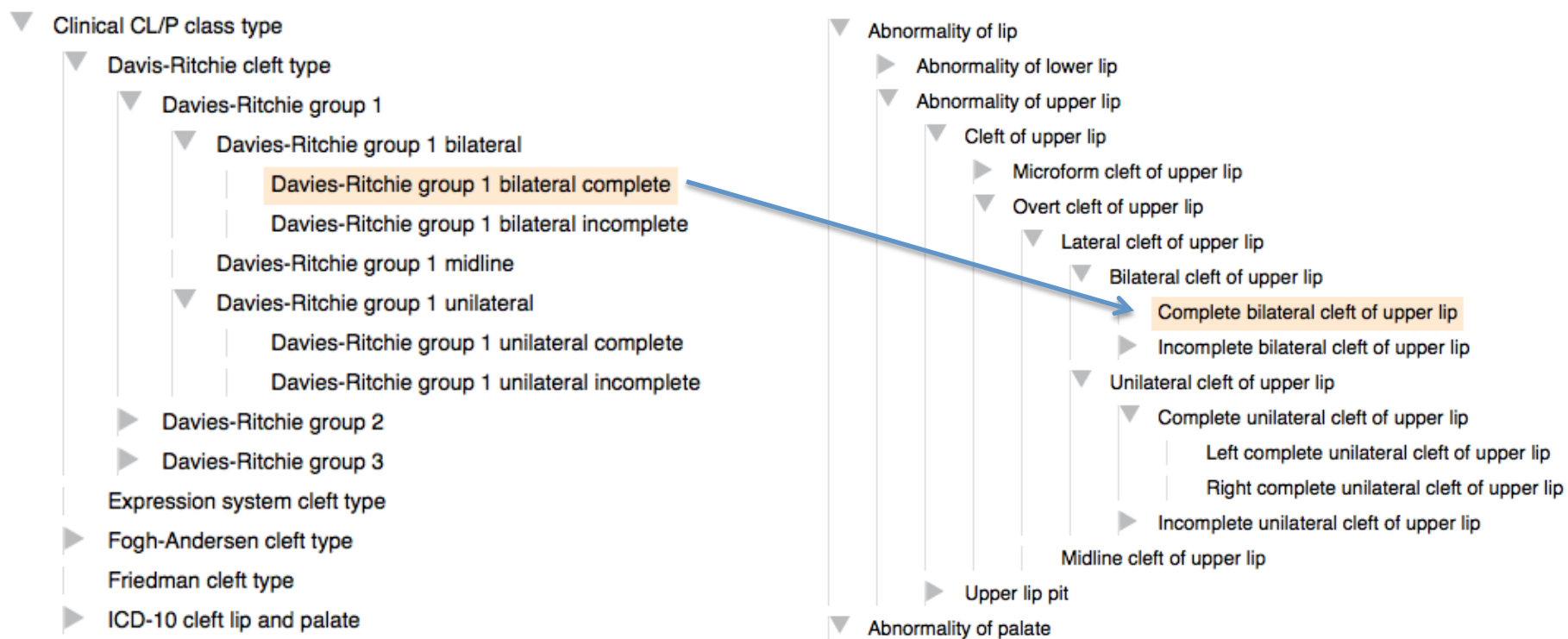


Clinical Classification (part of CHMO)

- ▼ Clinical CL/P class type
 - ▼ Davis-Ritchie cleft type
 - ▼ Davies-Ritchie group 1
 - ▼ Davies-Ritchie group 1 bilateral
 - ▼ Davies-Ritchie group 1 bilateral complete
 - ▼ Davies-Ritchie group 1 bilateral incomplete
 - ▼ Davies-Ritchie group 1 midline
 - ▼ Davies-Ritchie group 1 unilateral
 - ▼ Davies-Ritchie group 1 unilateral complete
 - ▼ Davies-Ritchie group 1 unilateral incomplete
 - ▶ Davies-Ritchie group 2
 - ▶ Davies-Ritchie group 3
 - ▶ Expression system cleft type
 - ▶ Fogh-Andersen cleft type
 - ▶ Friedman cleft type
 - ▶ ICD-10 cleft lip and palate

Clinical Classification

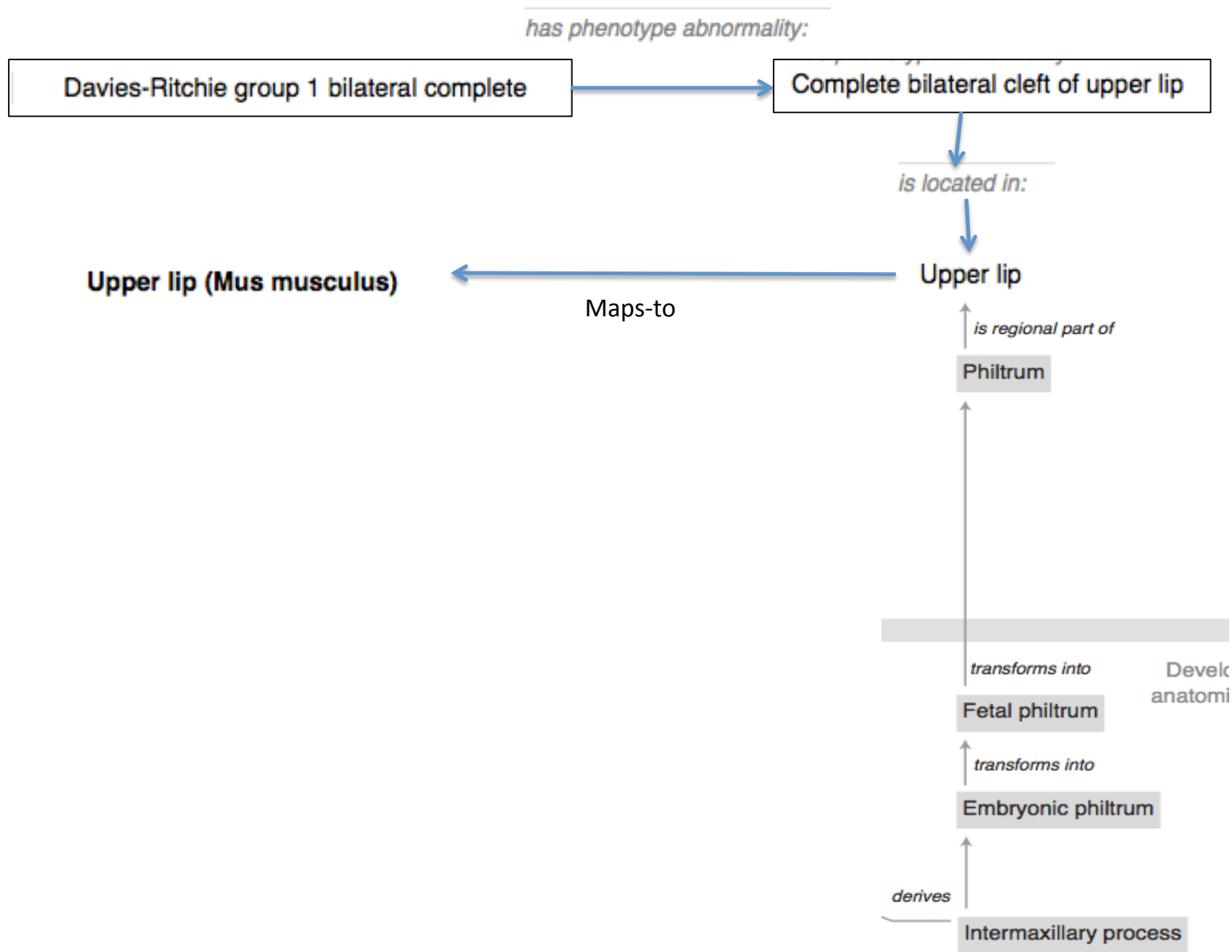
Phenotypic Abnormality



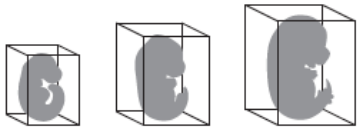
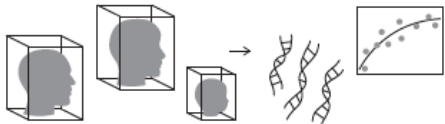
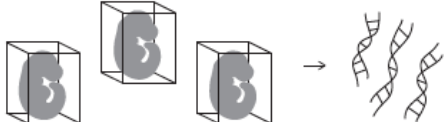

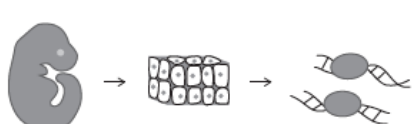
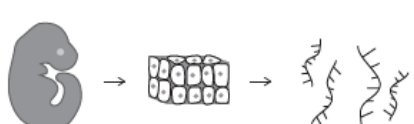
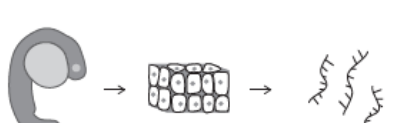
has phenotype abnormality:

Davies-Ritchie group 1 bilateral complete

Complete bilateral cleft of upper lip



Types of anatomical entities needed to be represented in the OCDM based on abstracts

Data and techniques		Anatomical and developmental entities
	<p>Volumetric images of tissues of mouse embryos</p>	<ul style="list-style-type: none"> • Tissue and cell types • Craniofacial regions • Developmental stages
	<p>Volumetric images of adult and child heads, plus genetic analysis</p>	<ul style="list-style-type: none"> • Craniofacial landmarks
	<p>Volumetric images of tissues of mouse strains with different craniofacial morphologies, plus genetic analysis</p>	<ul style="list-style-type: none"> • Craniofacial regions • Craniofacial landmarks • Malformation phenotypes • Developmental stages
	<p>Data on human malformation phenotypes and environmental exposure, plus genetic analysis</p>	<ul style="list-style-type: none"> • Craniofacial landmarks • Malformation phenotypes
	<p>Regions of craniofacial tissue dissected from mouse embryos for analysis by ChIP-seq</p>	<ul style="list-style-type: none"> • Tissue types • Craniofacial regions • Developmental stages
	<p>Regions of craniofacial tissue dissected from mouse embryos for gene expression analysis</p>	<ul style="list-style-type: none"> • Tissue types • Craniofacial regions • Developmental stages
	<p>Regions of craniofacial tissue dissected from zebrafish or mouse embryos for miRNA analysis</p>	<ul style="list-style-type: none"> • Tissue types • Craniofacial regions • Developmental stages

Content extension:

- zebrafish ontology (primary source – Zfin)
- anatomical representation of musculoskeletal system of head
- development of skeletal system of head
- anatomical landmarks
- abnormalities of the musculoskeletal system of head
- cross-species correlation