Mandible development

Skull development

Tooth morphogenesis

Palatogenesis

Wt

Tgfbr2 CKO

Development
Stem cells and craniofacial tissue regeneration

Zhao et al., 2014
Cell Stem Cell
Craniosynostosis

- Incidence 0.04%-0.1%
- Most non-syndromic, single suture
- Neurocognitive effects
- Pressure effects
- Hearing loss
- Developmental deficits

Hypothesis: Failure or premature loss of MSC population within the suture?
Building a biological suture
A novel biological approach for treating CS patients

Zhao et al., 2015 Nature Cell Biology
Cranial neural crest cells
rhombomeres

N. Le Douarin
Neural Crest Cell Fate Analysis using DiI injection
Germ Layer Derivatives

- **Ectoderm**
- **Endoderm**
- **Mesoderm**
A  
1st arch (Meckel) cartilage  
Site of developing internal ear  
2nd arch (Reichert) cartilage

B  
Spine of sphenoid bone  
Anterior ligament of malleus  
Malleus  
Incus  
Stapes  
Styloid process  
Stylohyoid ligament  
Greater cornu (horn) of hyoid bone  
Lesser cornu of hyoid bone  
Sphenomandibular ligament  
Body of hyoid bone  

Color Coding:  
- First arch cartilage  
- Second arch cartilage  
- Third arch cartilage  
- Fourth and sixth arch cartilages
<table>
<thead>
<tr>
<th>ARCH</th>
<th>NERVE</th>
<th>MUSCLES</th>
<th>SKELETAL STRUCTURES</th>
<th>LIGAMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>First (mandibular)</td>
<td>Trigeminal† (CN V)</td>
<td>Muscles of mastication†</td>
<td>Malleus</td>
<td>Anterior ligament of malleus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mylohyoid and anterior belly of digastric</td>
<td>Incus</td>
<td>Sphenomandibular ligament</td>
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<td></td>
<td></td>
<td>Tensor tympani</td>
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<td>Tensor veli palatini</td>
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<tr>
<td>Second (hyoid)</td>
<td>Facial (CN VII)</td>
<td>Muscles of facial expression§</td>
<td>Stapes</td>
<td>Stylohyoid ligament</td>
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<tr>
<td></td>
<td></td>
<td>Stapedius</td>
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<tr>
<td></td>
<td></td>
<td>Stylohyoid</td>
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<td></td>
<td></td>
<td>Posterior belly of digastric</td>
<td></td>
<td></td>
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<tr>
<td>Third</td>
<td>Glossopharyngeal (CN IX)</td>
<td>Stylopharyngeus</td>
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<tr>
<td>Fourth and sixth‡</td>
<td>Superior laryngeal branch of</td>
<td>Cricothyroid</td>
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<tr>
<td></td>
<td>vagus (CN X)</td>
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<tr>
<td></td>
<td>Recurrent laryngeal branch</td>
<td>Levator veli palatini</td>
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<tr>
<td></td>
<td>of vagus (CN X)</td>
<td>Constrictors of pharynx</td>
<td></td>
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<td></td>
<td></td>
<td>Intrinsic muscles of larynx</td>
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<tr>
<td></td>
<td></td>
<td>Striated muscles of esophagus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The derivatives of the aortic arch arteries are described in Chapter 13.*

†The ophthalmic division fifth cranial nerve (CN V) does not supply any pharyngeal arch components.

‡Temporals, masseter, medial, and lateral pterygoids.

§Buccinator, auricularis, frontalis, platysma, orbicularis oris, and orbicularis oculi.

‡The fifth pharyngeal arch is often absent. When present, it is rudimentary and usually has no recognizable cartilage bar. The cartilaginous components of the fourth and sixth arches fuse to form the cartilages of the larynx.
A. Cranial nerves

B. 

C. Nasal cavity
Palate
Tongue
Pharynx
Esophagus
Larynx
Sublingual, parotid, and submandibular glands

1st pharyngeal arch

- V₂ Maxillary division of trigeminal n.
- V₃ Mandibular division of trigeminal n.

2nd pharyngeal arch

- VII Facial n.

3rd pharyngeal arch

- IX Glossopharyngeal n.

4th pharyngeal arch

- X Vagus n.
Migration of cranial neural crest cells and facial development
The anatomy of palatogenesis

6 wks

12 wks
Tooth Development

- **Initiation Stage**: Odontogenic Epithelium, Mesenchyme (ecto), Dental Lamina, Dental Papilla.
- **Bud Stage**: Stratum Intermedium, Permanent Tooth Bud.
- **Cap Stage**: Successional Lamina, Enamel Knot, Stellate Reticulum, Inner Dental Epithelium, Cervical Loop.
- **Crown Formation**: Enamel Organ, Ameloblasts, Enamel, Dentin, Odontoblasts, Pulp.
Molecular Regulation of Tooth Morphogenesis

DENTAL LAMINA

BMP
FGF
SHH
WNT

BMP
FGF
SHH
TGF-β
WNT

BMP
FGF
Msx2
PDGF
LEF1

BMP
FGF
Msx2
SHH
TGF-β
WNT

p21

ACTIVIN
BMP
Barx1
Dlx1
Dlx2
Gli1
Gli2
Gli3
Lhx6
Lhx7
Msx1
Msx2
Pax9

BMP
FGF
Barx1
Cbfa1
Dlx1
Dlx2
Gli1
Gli2
Gli3
Lef1
Lhx6
Lhx7
Msx1
Pax9

BMP
FGF
WNT
Barx1
Cbfa1
Dlx1
Dlx2
Gli1
Gli2
Gli3
Lef1
Lhx6
Lhx7
Msx1
Pax9

ERUPTION

enamel
dentin
pulp
cementum

ds = dental sac
eoe = enamel organ epithelium
iee = inner enamel epithelium
oeo = outer enamel epithelium
sr = stellate reticulum
Arches:
1. Median lingual swelling (tongue bud)
2. Foramen cecum of tongue
3. Copula
4. Hypopharyngeal eminence

Esophagus
Laryngotracheal groove

Migration of third arch mesoderm
Hypopharyngeal eminence
Rima glottis (opening to vocal apparatus)

Oral part of tongue
Circumvallate papillae
Terminal sulcus
Pharyngeal part of tongue
Epiglottis

Arch Derivatives of Tongue
- 1st pharyngeal arch (CN V-mandibular division)
- 2nd pharyngeal arch (CN VII-chorda tympani)
- 3rd pharyngeal arch (CN IX-glossopharyngeal)
- 4th pharyngeal arch (CN X-vagus)
Foramen cecum of tongue

Hyoid bone

Thyroid cartilage

Thyroglossal duct cyst

Thyroid gland

Opening of thyroglossal duct sinus

Lingual thyroglossal duct cyst

Hyoid bone

Cervical thyroglossal duct cyst
Good luck tomorrow...