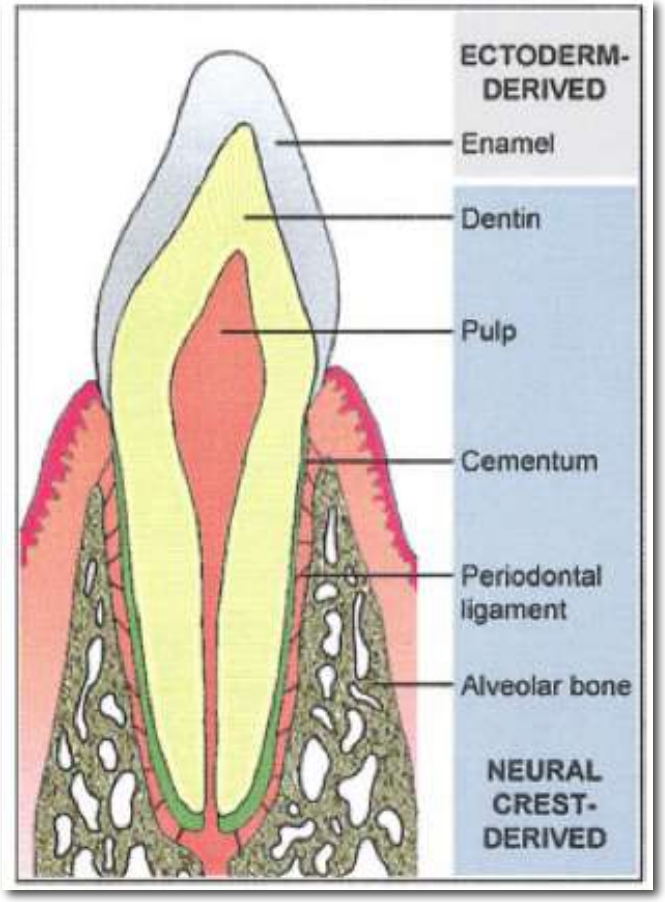
Obecná a srovnávací odontologie

And now something completely different

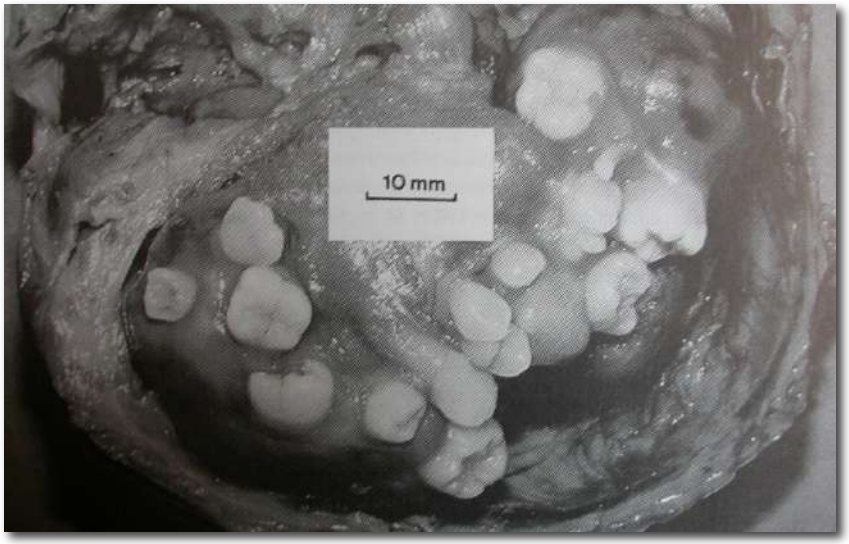
Vývojové souvislosti 4

zubní epitel vs. mesenchym v zubním vývoje i evoluci

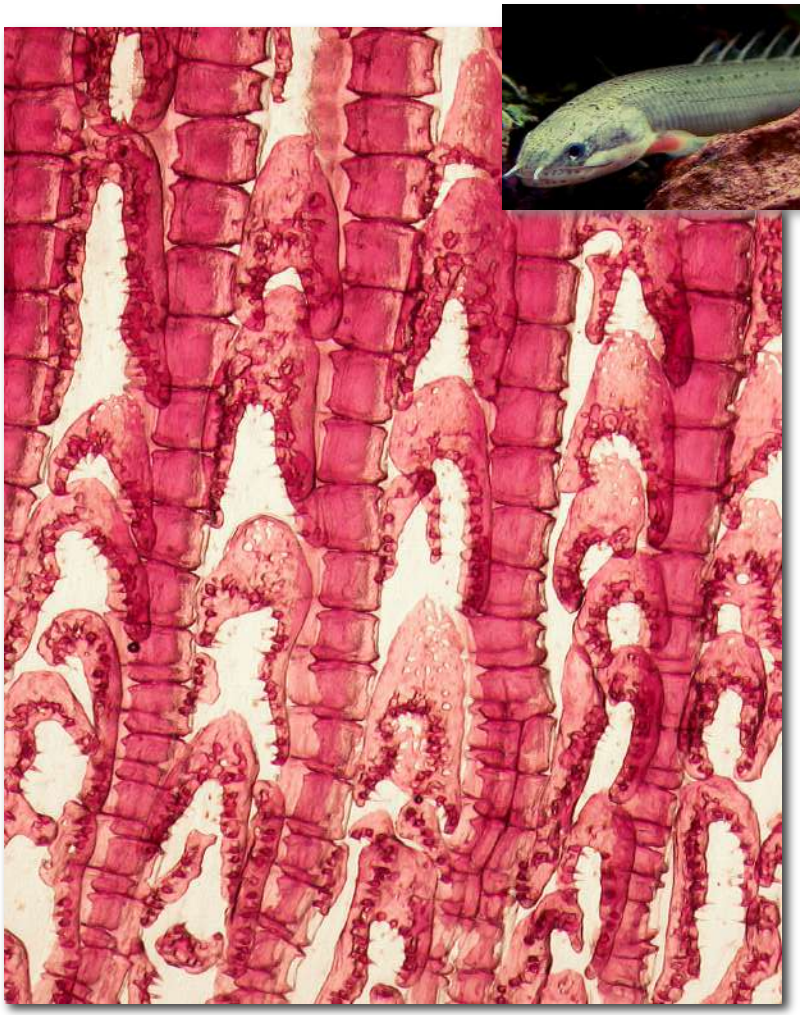
Ontogeneze zubu:
vzájemné a opakující se interakce
zubního mesenchymu a epitelu



Dle současných definic (*myš, člověk* :-) je ontogeneze zubu zakládána interakcemi **orálního ektodermu** a **mesenchymu hlavové neurální lišty**

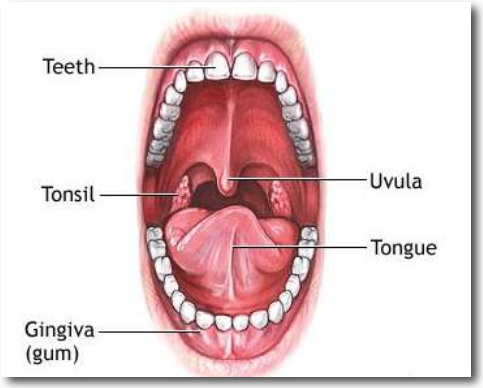


"zuby": lidský teratom z ovaria



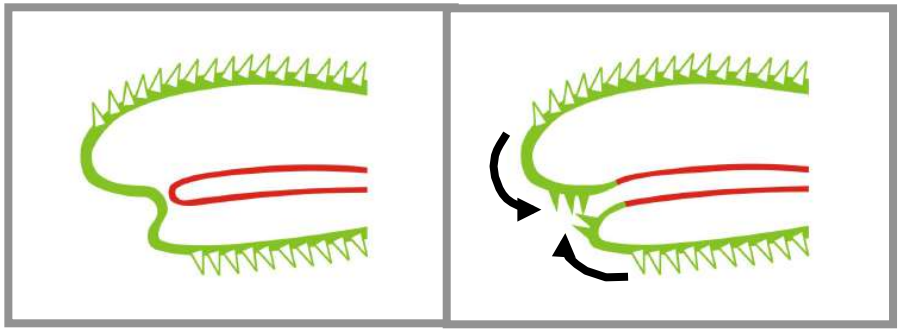
"zuby": struktury v ploutevnich paprscích bichira (Polypterus)

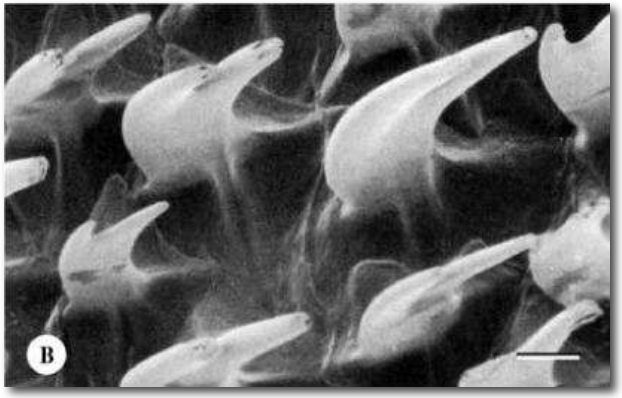
Dle současných definic (*myš, člověk* :-) je ontogeneze zubu zakládána interakcemi **<u>orálního</u> ektodermu** a **mesenchymu <u>hlavové</u> neurální lišty**



Ontogeneze zubu: epitel EKT či ENT původu

Zuby (obecně?) umístěny ve **stomodeu** (EKT epitel)





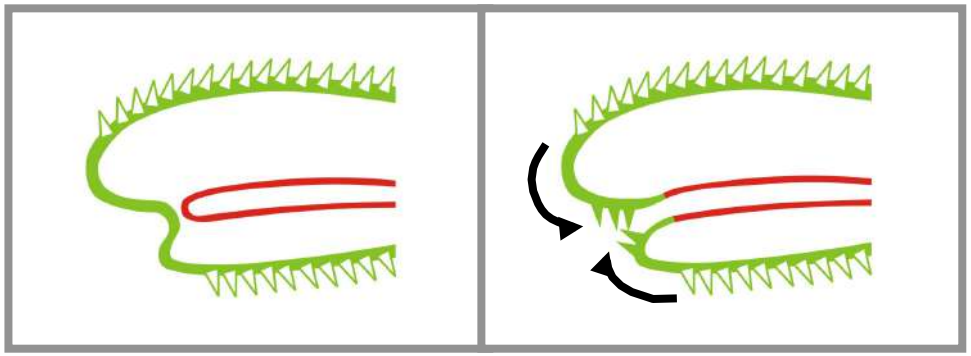
obecná představa:

- povrchové (EKT) šupiny, dentikuly (srv. plakoidní šupiny) vmigrovaly do stomodea, kde se postupně navázaly do čelistí a staly se zuby *s. str.*
- zuby pocházejí z EKT epitelu ontogeneticky i evolučně; <u>založeno na situaci u žraloka</u>
- homologizační předpoklad: gradient šupina - zub

Evoluce zubu:

„OUTSIDE-IN“ theory

Teeth from ECTODERM
(e.g. *sensu* W.E. Reif)



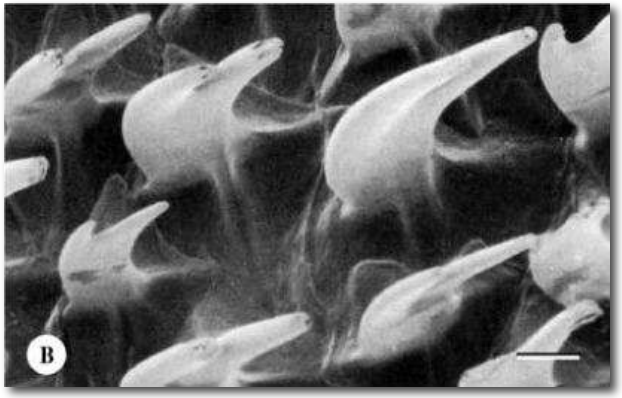
Dermal denticles of ECT origin migrated into the stomodeum, where they became teeth

Tooth =

ECTODERM

+

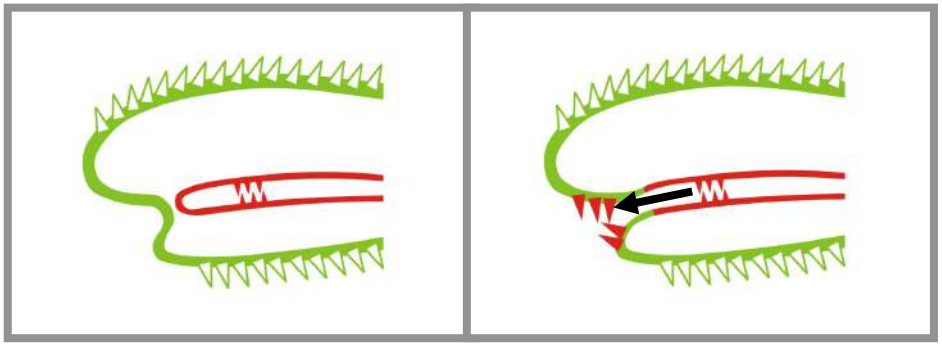
NEURAL CREST



Evoluce zubu:

„INSIDE-OUT “ theory

Teeth from ENDODERM
(*sensu* M.M. Smith)

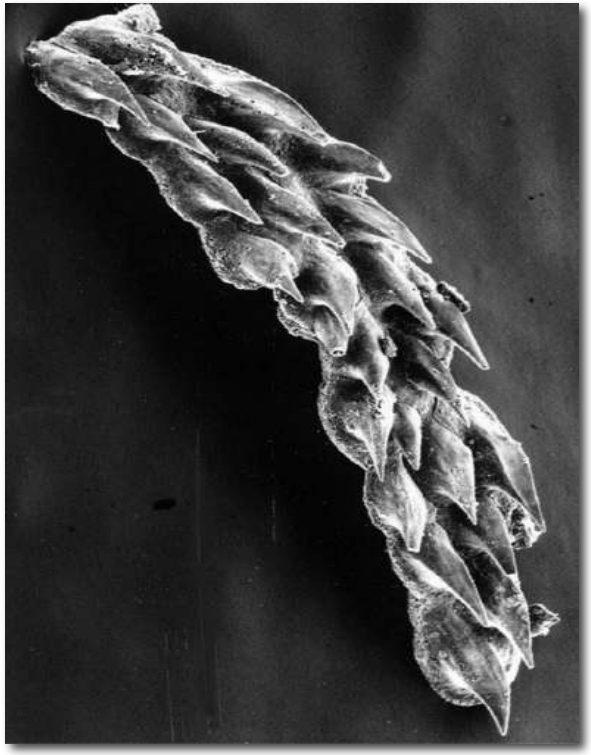


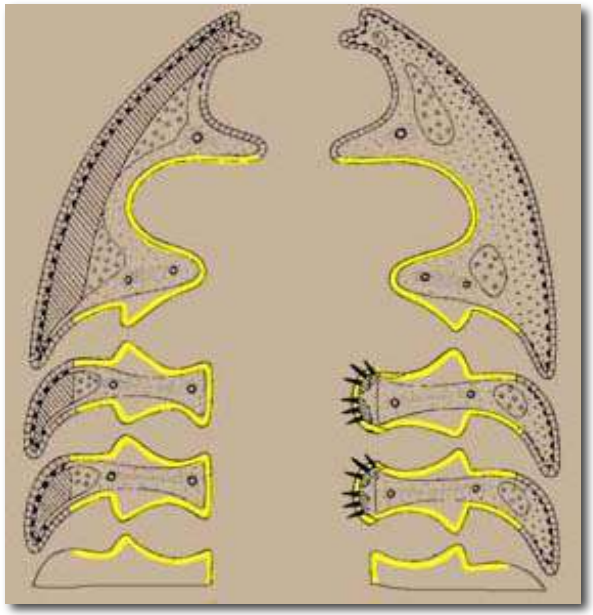
Pharyngeal denticles of END origin were later co-opted for ECT areas

ENDODERM
+
NEURAL CREST

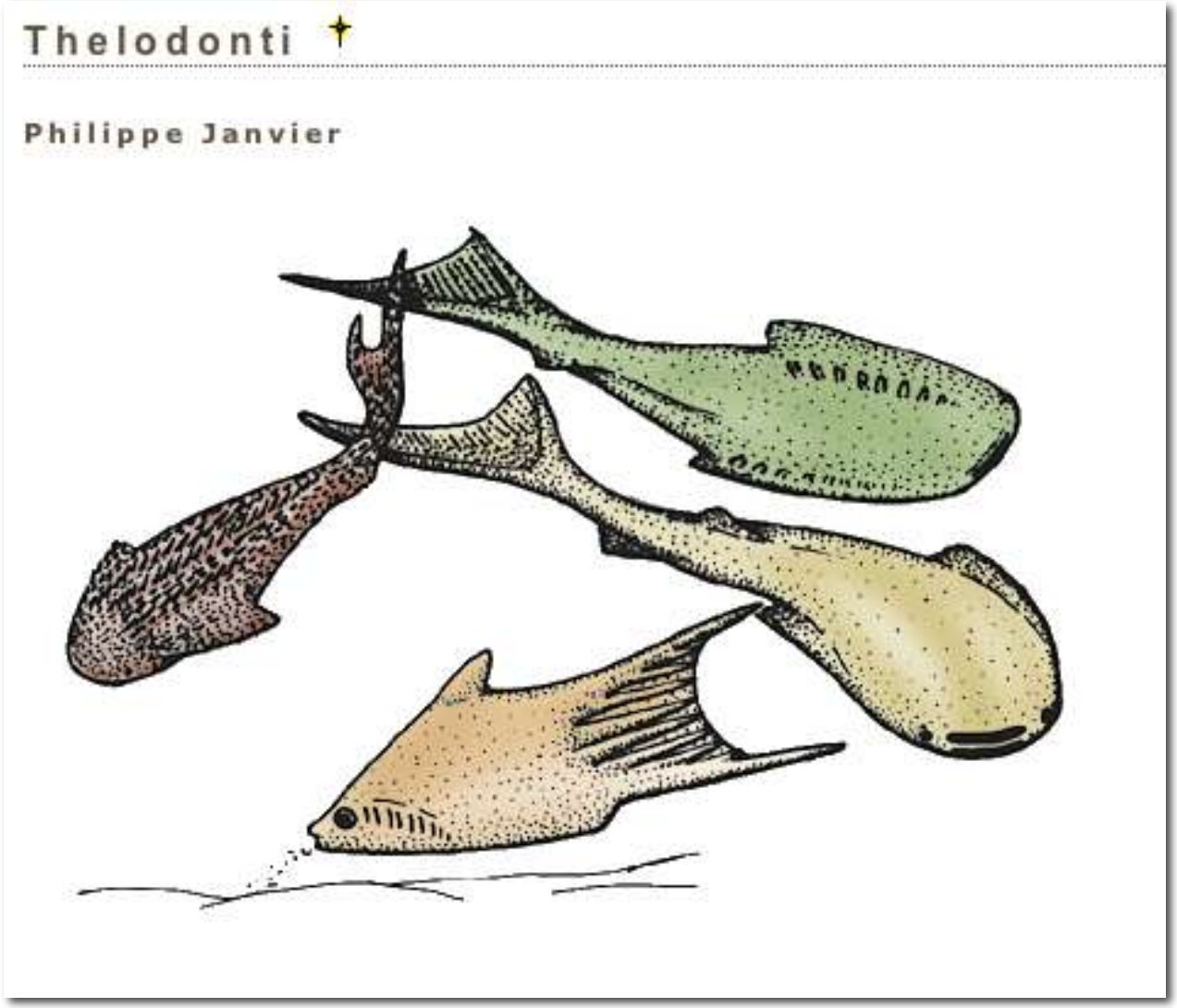
→

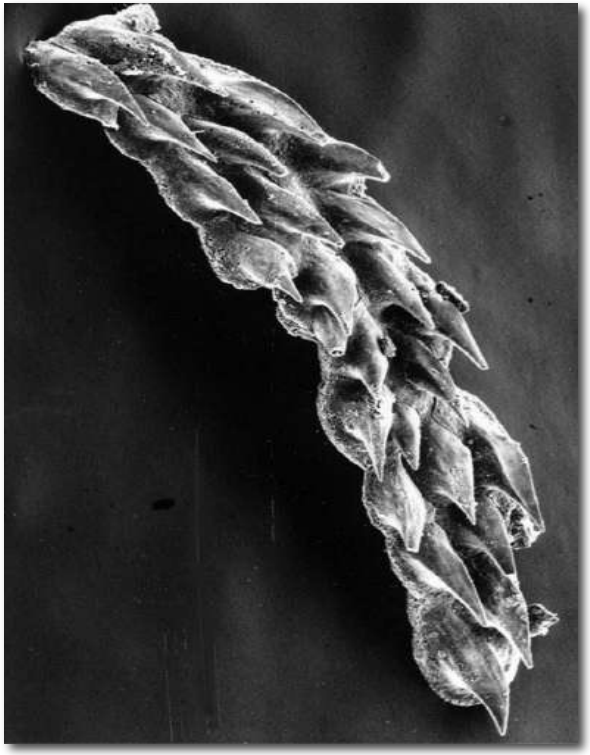
ECTODERM
+
NEURAL CREST

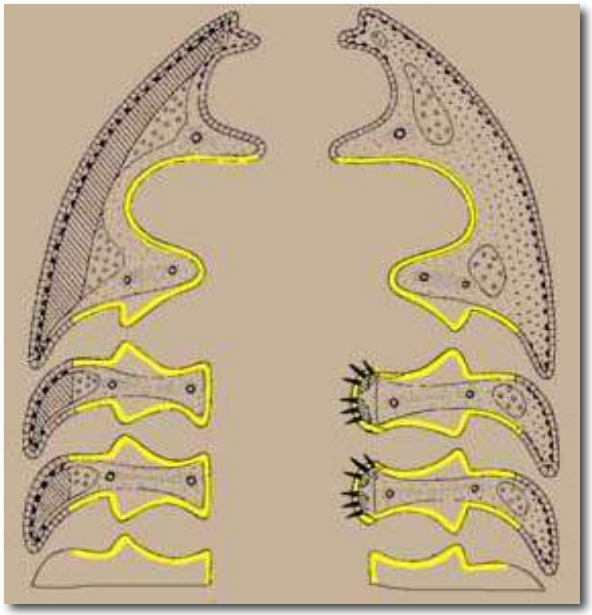




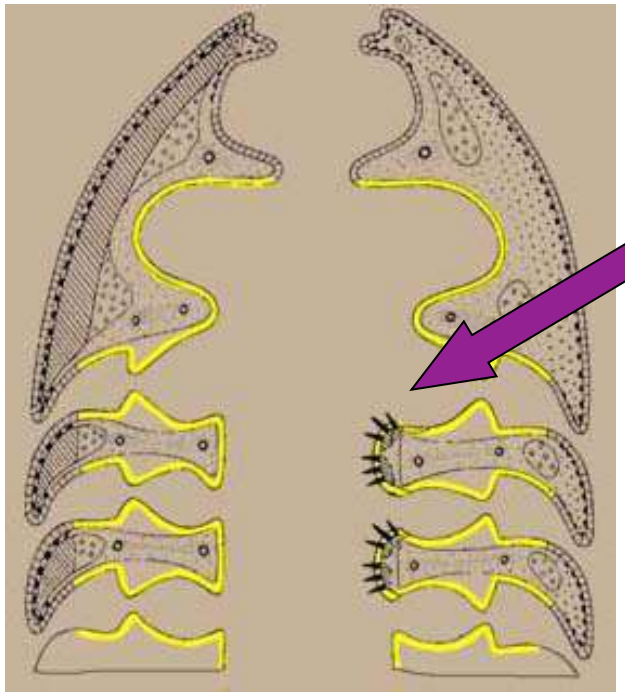
Thelodont (agnathan) pharyngeal denticles

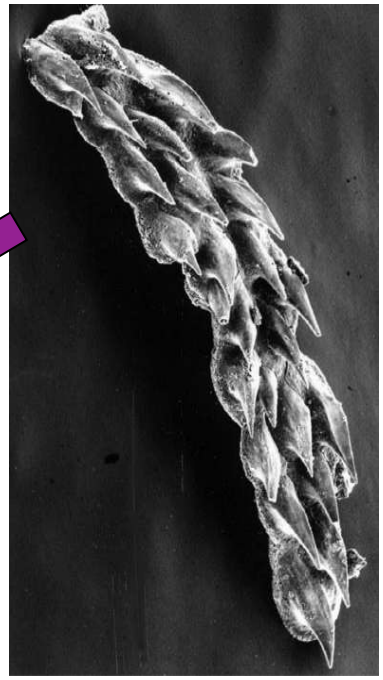


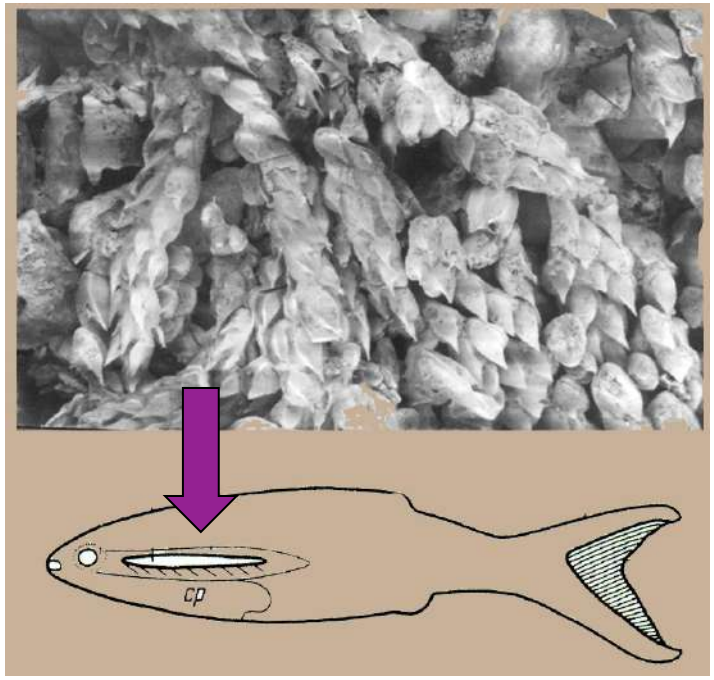


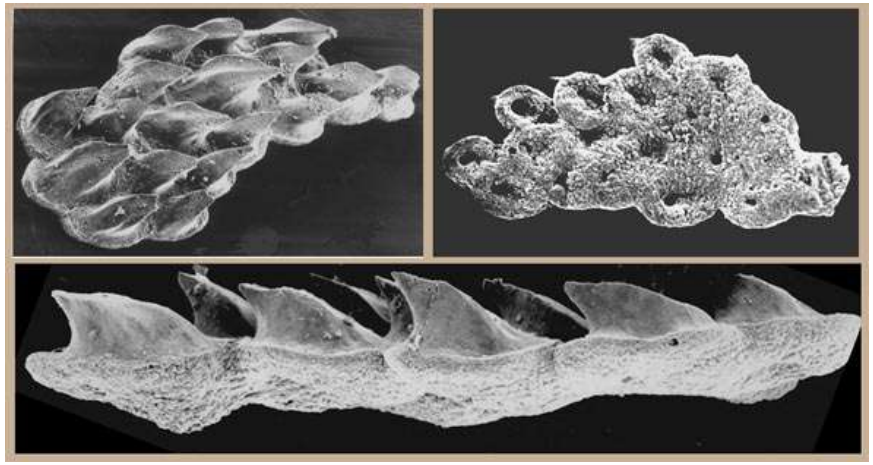


Thelodont (agnathan) pharyngeal denticles (*sensu M.M. Smith*)





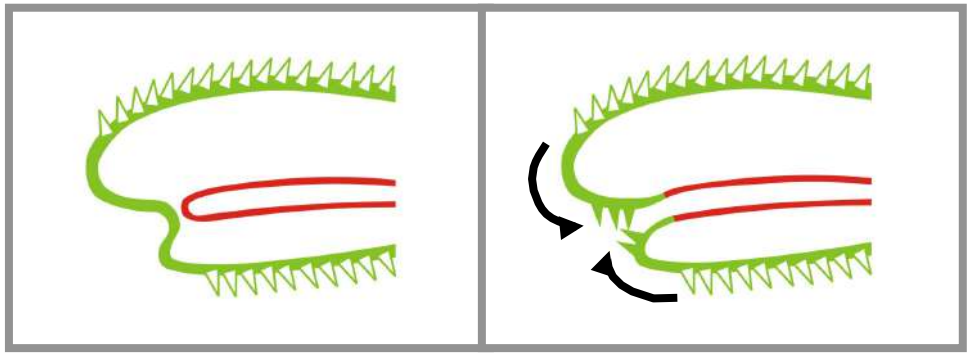




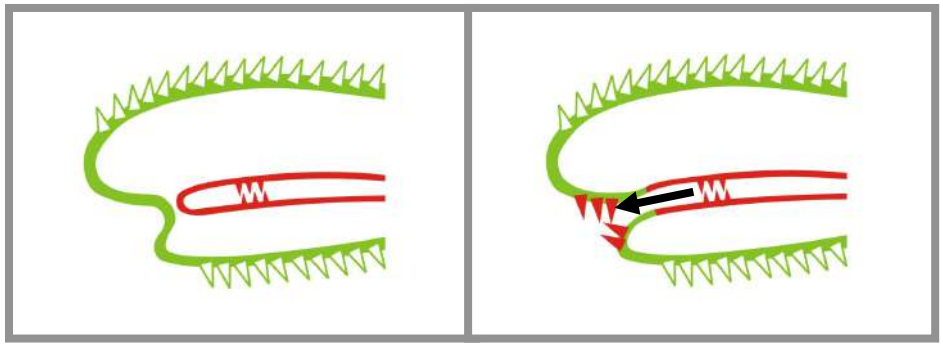
- Internal branchial denticle whorls
- Timed sequential formation
- Thick basal bone joins them
- Different from outer denticles

Evoluce zubů:

OUT-IN vs. IN-OUT (EKT vs. END?)



Dermal denticles of ECT origin migrated into the stomodeum, where they became teeth



Pharyngeal denticles of END origin were later co-opted for ECT areas

Teeth from pharyngeal denticles would mean that genetic and developmental regulatory mechanisms responsible for tooth patterns on jaws were co-opted from the pharyngeal region and not from the skin, as clasically thought

Smith & Johansson, 2003: teeth may have evolved independently (sic!), several times, through a mechanism of convergent evolution.

Evoluce zubů:

OUT-IN vs. IN-OUT (EKT vs. END?)

THE CUTTING-EDGE OF MAMMALIAN DEVELOPMENT; HOW THE EMBRYO MAKES TEETH

Abigail Tucker and Paul Sharpe

A wealth of information has recently become available on the molecular signals that are required to form and pattern the dentition in the mouse, shedding light on how important decisions about tooth shape, tooth number and cusp (cone-shaped prominence) number are generated. This information, which has been gleaned principally from knockout mice and manipulation of organ cultures, has been used to identify the genes and developmental processes that underlie the many human disorders in which tooth development is defective. Mouse models of several of these syndromes have also indicated ways in which such conditions could be treated.

We use them every day, clean them religously and rely on them for eating, communication and physical appearance. We spend millions on educating and training people specifically to maintain them. But, despite all this attention, the importance and uniqueness of teeth in development, disease and evolution is often not appreciated. Each species has an individual and unique set of teeth, known as the dentition. The dentition is as diagnostic of a species as its DNA, and, more significantly, the preservation of teeth in the fossil record means that they tell us far more about vertebrate evolution than do genomes (see BOX 1). Because dentitions are a direct reflection of feeding habits, fossil teeth can provide a vivid picture of the life of extinct species. Indeed, much of the understanding of our own recent evolutionary origins is based on the fossil remains of teeth.

The non-essential function of teeth make them an attractive model to study organogenesis. Mutant mice with abnormal teeth can survive in laboratory conditions, so much of the recent advances in understanding the molecular control of development have, not surprisingly, come from the analysis of mouse mutants. In addition, embryonic tooth primordia are easy to culture as explants, which lend themselves to many kinds of experimental manipulation. A further feature of these explants is that they can be transplanted to ectopic sites in adults, for example, in renal capsules, where they continue development into recognizable, mineralized teeth.

Of the many dental anomalies in humans, hypodontia (selective tooth loss) is the most common, affecting almost 10% of the population. Most cases of hypodontia affect the permanent but not the deciduous dentition (milk teeth). This creates a significant problem when trying to use mouse developmental genetics to identify and study genes that are involved in human hypodontia because mice only have one set of teeth, the development of which is equivalent to that of human deciduous teeth. Nevertheless, an increasing number of genes that cause human hypodontia are being identified, and more careful and sophisticated analysis of mouse dental development is starting to reveal gene functions that are common to all mammalian tooth development.

In this review, we examine the molecular mechanisms that control mouse tooth development, and then look at how this information can be used to understand the developmental genetic processes that underlie the many human syndromes that affect dental pattern. We will also examine how the defining aspects of mammalian dentition, such as tooth position, type and number, are determined as the embryo develops. It is impossible to exhaustively discuss the role of each gene that is expressed in the tooth, and so we have concentrated on the more important ones and those that are involved in human dental disorders.

Department of Craniofacial Development, Dental Institute, Kings College London, Floor 28 Guys Hospital, London Bridge, London SE1 9RT, UK. Correspondence to A.T. e-mail: Abigail.tucker@kcl.ac.uk and P.S. e-mail: paul.sharpe@kcl.ac.uk
doi:10.1038/nrg1380

Tucker & Sharpe, 2004: diversity of dentitions might have been explained by combinatorial derivation of teeth from both external (ECT), as well as internal (END) denticles and teeth.

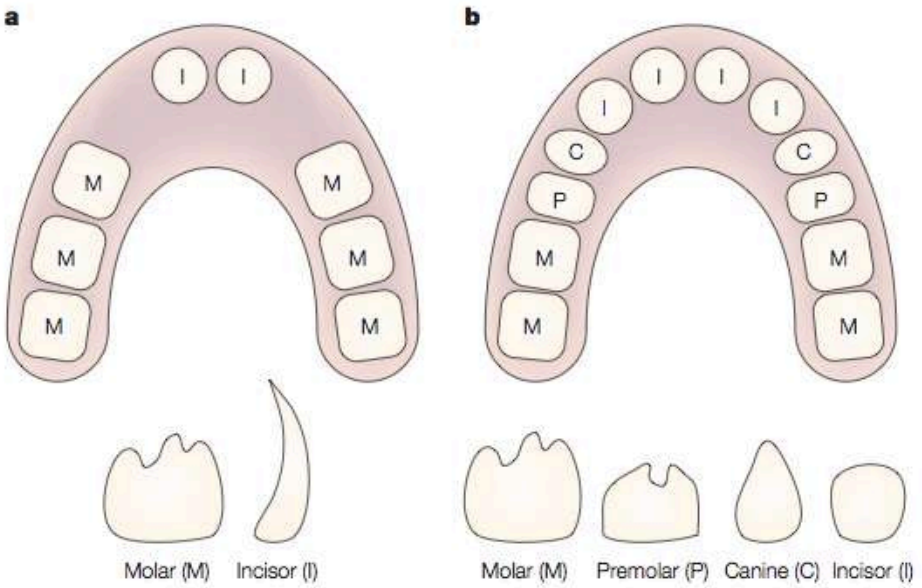
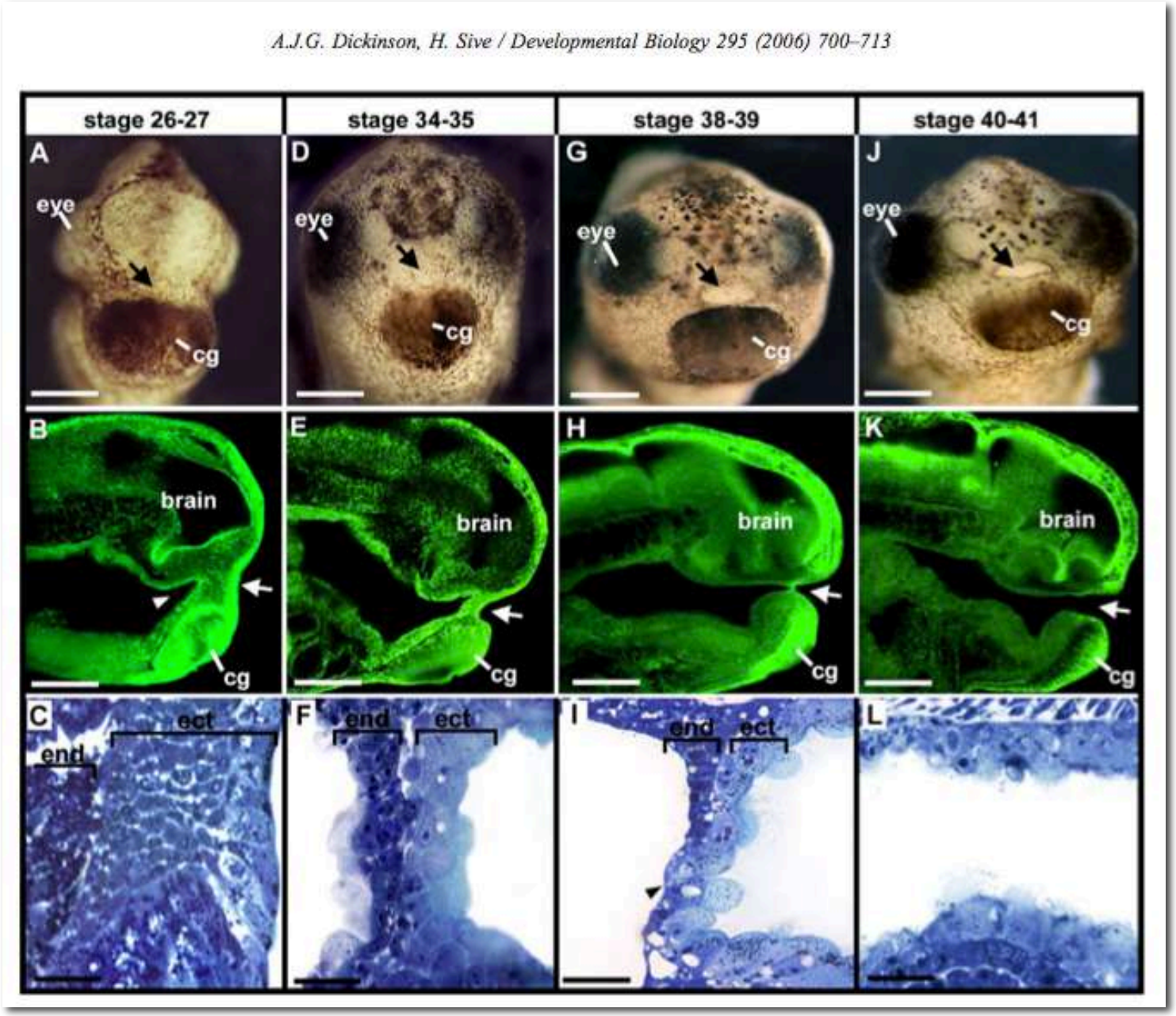
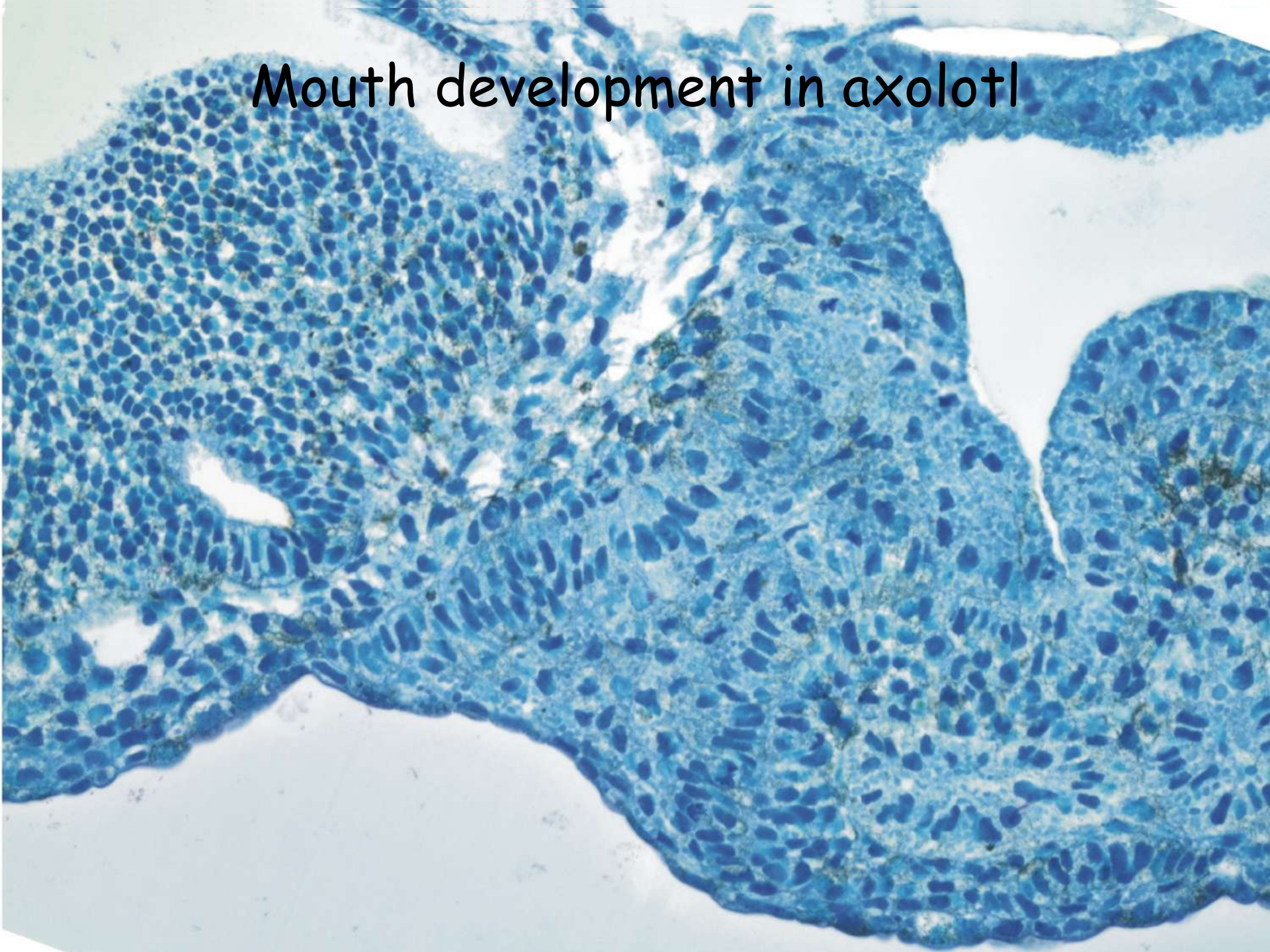


Figure 1 | **Dentition in mice and humans.** A comparison of mouse and human dentition. **a** | Mice have three molars and one incisor in each quadrant that are separated by a toothless diastema. **b** | The human tooth pattern is much more complex. The layout for deciduous teeth is shown, with six teeth developing in each quadrant: two molars, a premolar, a canine and two incisors. The general shape of the teeth is also distinct between the two species.

Development of oral opening: ECT vs. END mouth lining

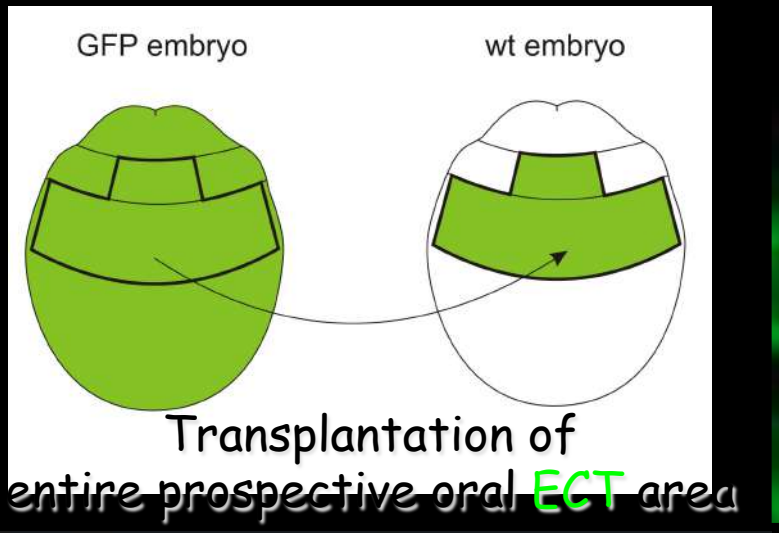


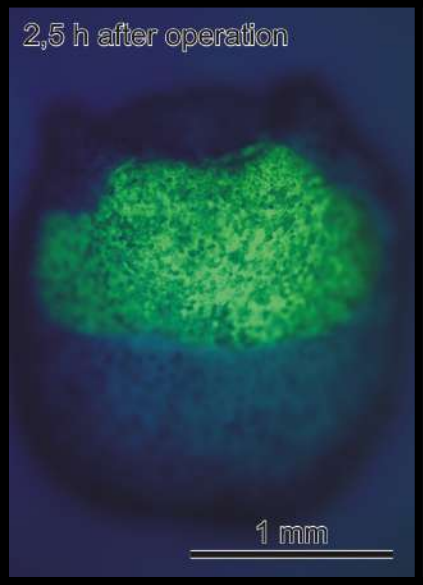
Mouth development in axolotl

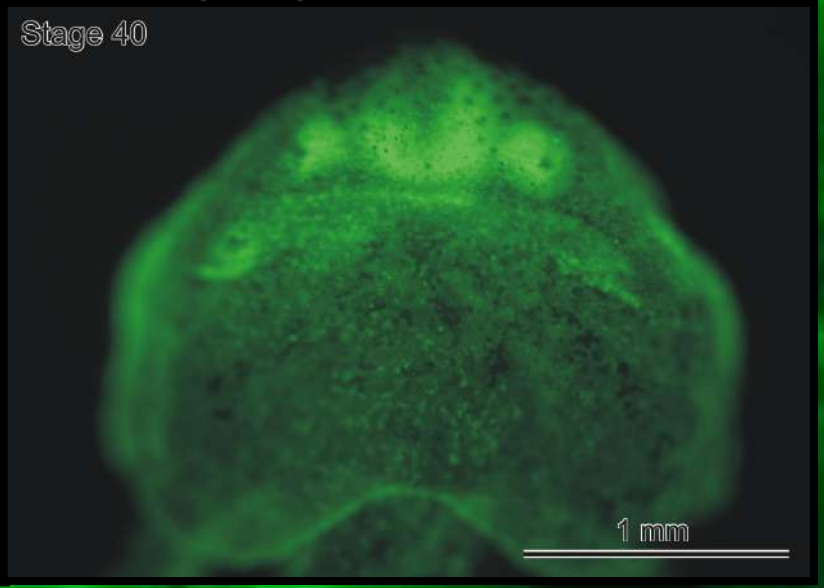


GFP axolotl embryos:

tracing the fate of the oral ECT during mouth and tooth formation

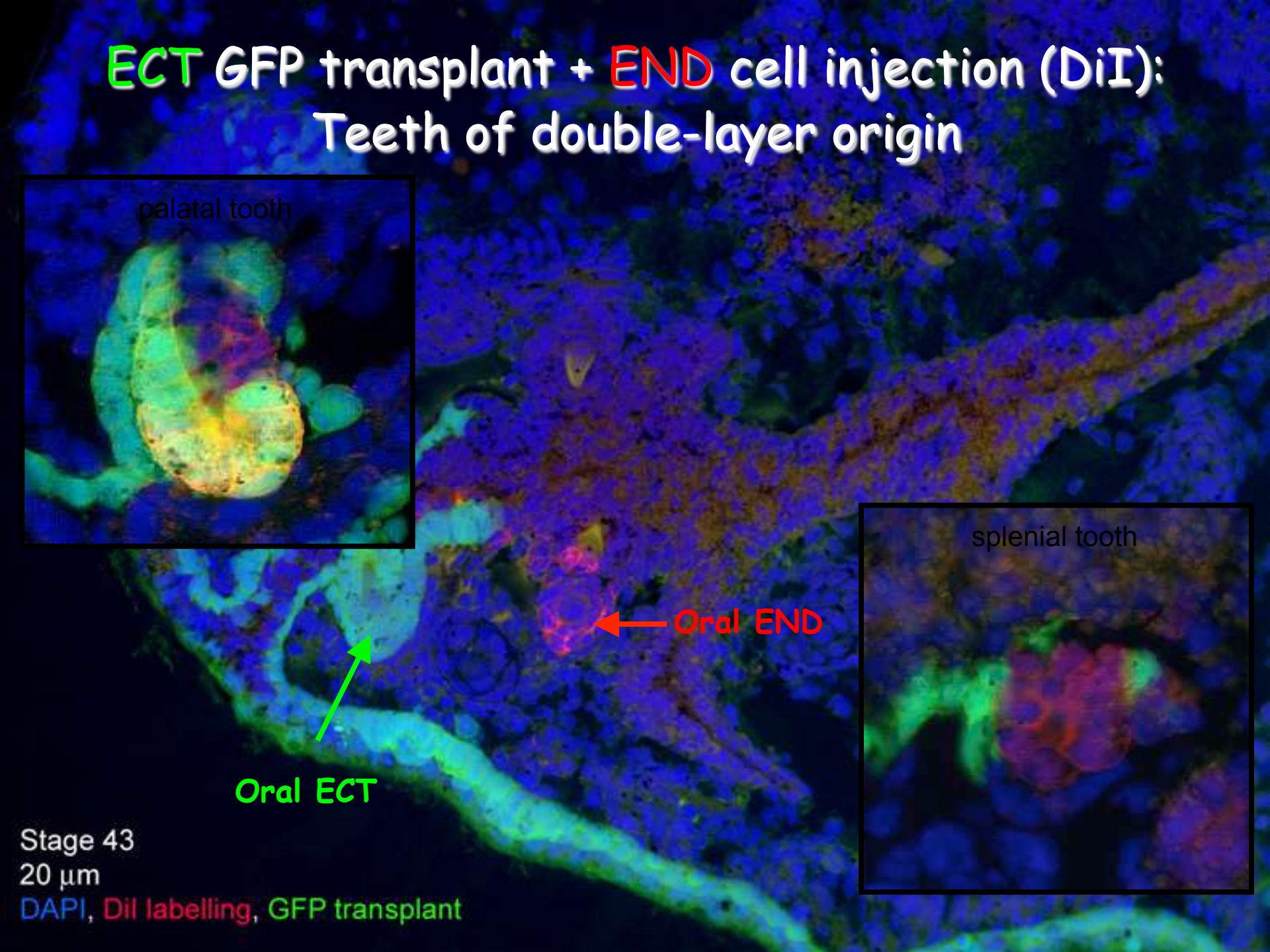




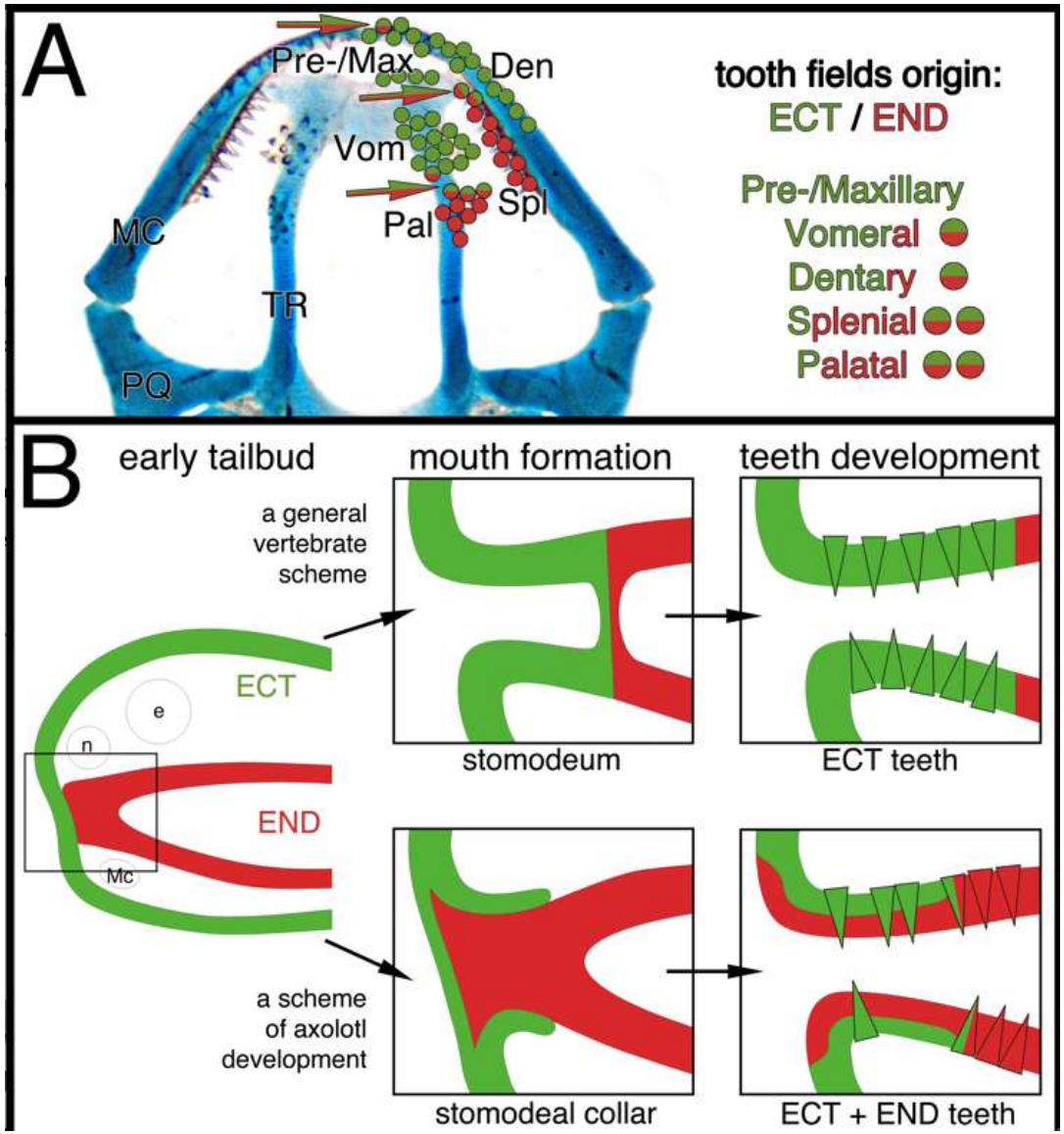


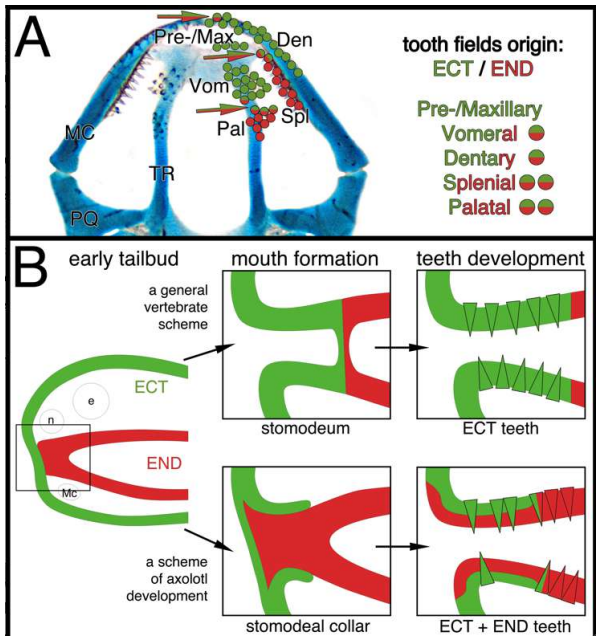
GFP axolotls: developed in **Elly Tanaka lab** (MPI-CBG Dresden; Sobkow et al. DB 290, 2006)

ECT GFP transplant + END cell injection (DiI): Teeth of double-layer origin



Germ layer origin of **tooth enamel epithelia** in the Mexican axolotl *(c) V. Soukup*





The oral cavity of vertebrates is generally thought to arise as an ectodermal invagination[1,2]. Consistent with this, oral teeth are proposed to arise exclusively from ectoderm, contributing to tooth enamel epithelium, and from neural crest derived mesenchyme, contributing to dentin and pulp[3–5]. Yet in many vertebrate groups, teeth are not restricted only to the oral cavity[6–9], but extend posteriorly as pharyngeal teeth that could be derived either directly from the endodermal epithelium, or from the ectodermal epithelium that reached this location through the mouth or through the pharyngeal slits[6]. However, when the oropharyngeal membrane, which forms a sharp ecto/endodermal border[10], is broken, the fate of these cells is poorly known. Here, using transgenic axolotls with a combination of fate-mapping approaches, we present reliable evidence of oral teeth derived from both the ectoderm and endoderm and, moreover, demonstrate teeth with a mixed ecto/endodermal origin. Despite the enamel epithelia having a different embryonic source, oral teeth in the axolotl display striking developmental uniformities and are otherwise identical. This suggests a dominant role for the neural crest mesenchyme over epithelia in tooth initiation and, from an evolutionary point of view, that an essential factor in teeth evolution was the odontogenic capacity of neural crest cells, regardless of possible 'outside-in'[11] or 'inside-out'[12] influx of the epithelium.

doi:10.1038/nature07304

nature

LETTERS

Dual epithelial origin of vertebrate oral teeth

Vladimír Soukup[1], Hans-Henning Epperlein[2], Ivan Horácek[1] & Robert Cerny[1]

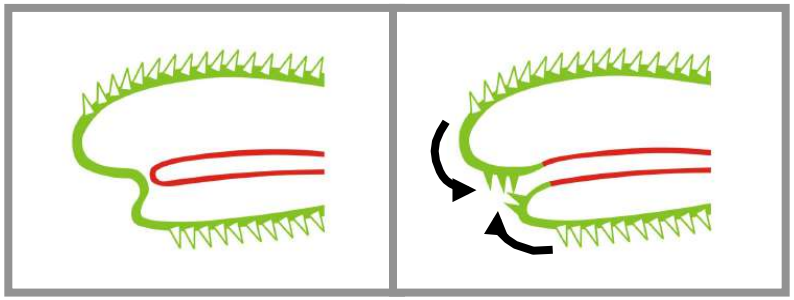
Mixed germ-layer origin of tooth epithelia:

Implications for development and evolution

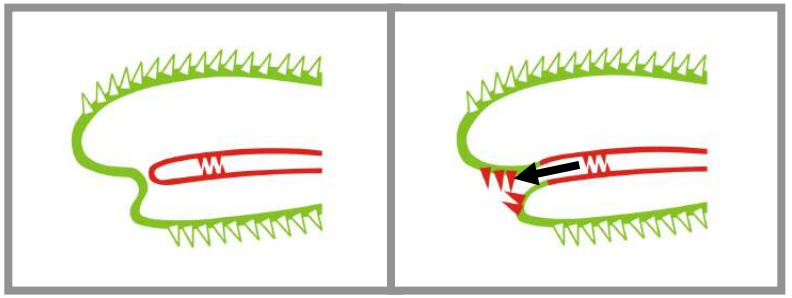
- **The germ-layer origin of epithelium doesn‘t seem to matter at all** - mesenchyme cells can apparently interact both with ECT and END and such teeth look very identical > homology?

- **The key role for NC-mesenchyme in tooth development & evolution** - odontodes/denticles/teeth can form when in the oral or pharyngeal cavity, or even on the skin surface.

Teeth evolution from ECTODERM

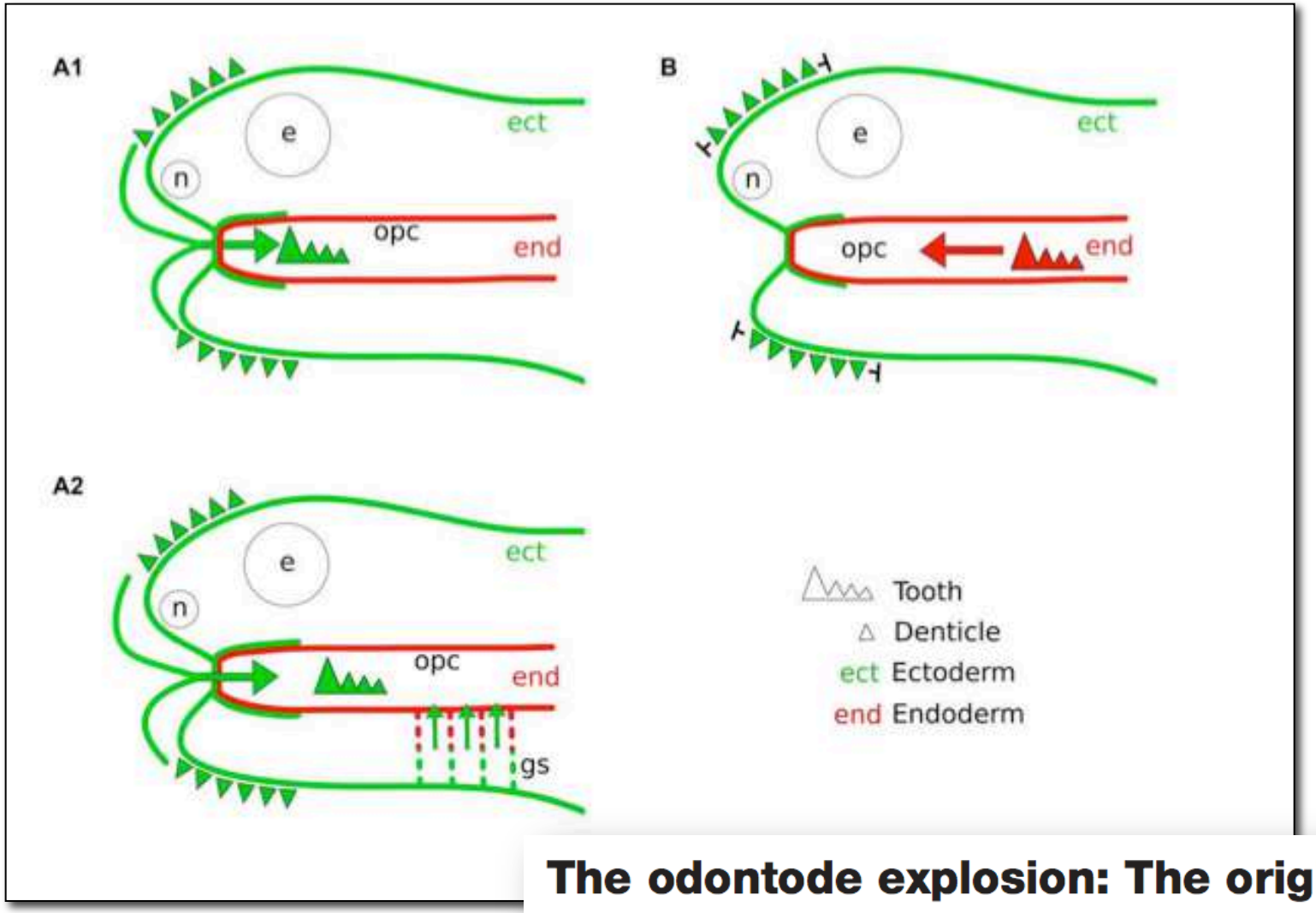


Teeth evolution from ENDODERM



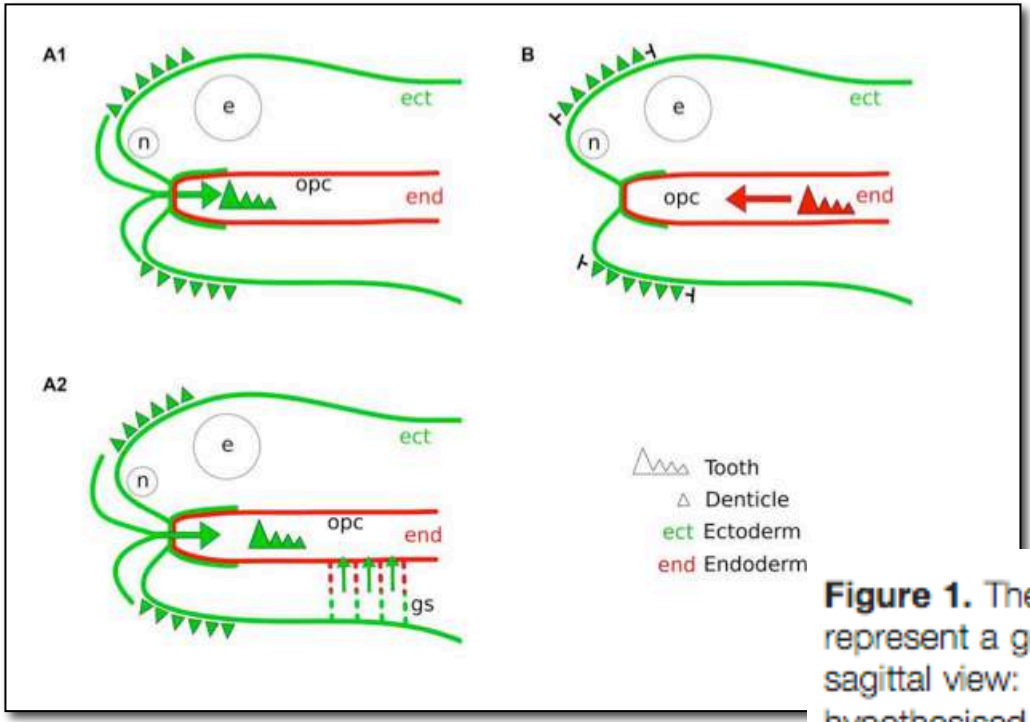
Origin of teeth can be seen in evolution of odontogenic capacity in neural crest-derived mesenchyme

Evoluční původ zubu: EKT vs. ENT



The odontode explosion: The origin of tooth-like structures in vertebrates

Gareth J. Fraser[1)], Robert Cerny[2)], Vladimir Soukup[2)], Marianne Bronner-Fraser[3)] and J. Todd Streelman[4)*]*



A1: **OUT-IN**

A2: **Modified OUT-IN**
(=nezbytný kontakt EKT+ENT :-)

B: **IN-OUT**

Figure 1. Theories of odontode evolution. Schematic diagrams represent a generalised (hypothetical) early vertebrate/fish in lateral/sagittal view: **A1**: Outside-in theory; ectodermal tissue is hypothesised to have integrated (green arrow) into the oro-pharyngeal cavity (opc), leading to the evolution of oral odontodes and subsequently oral and pharyngeal teeth. **A2**: Modified outside-in theory; ectodermal tissue integrated (green arrow) into the endodermal oral cavity *via* the mouth opening (the anterior boundary of the endoderm and ectoderm) and the gill slits (gs) in early vertebrates to initiate/transfer dental competence (arrow) to the endoderm of the oro-pharyngeal cavity. The point is made that ectoderm must be in regional contact with endoderm for teeth to form. **B**: Inside-out theory; skin denticles and teeth are structures forming independently from ectoderm and endoderm, respectively. This theory states that teeth originated in the posterior pharyngeal endoderm of jawless vertebrates; a dental competence that was co-opted anteriorly (red arrow) in concert with the evolution of oral jaws. This theory states that skin denticles did not grade into teeth. e, eye; n, nasal placode; opc, oro-pharyngeal cavity.

A new perspective:
collaborative interactions of epithelial & NC-GRN's

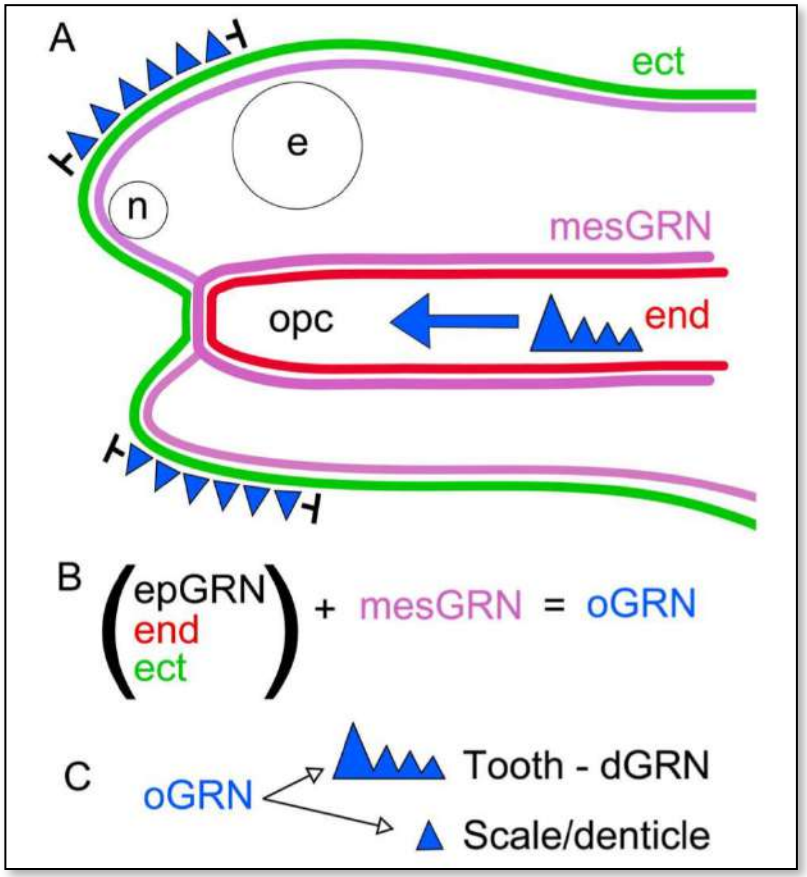
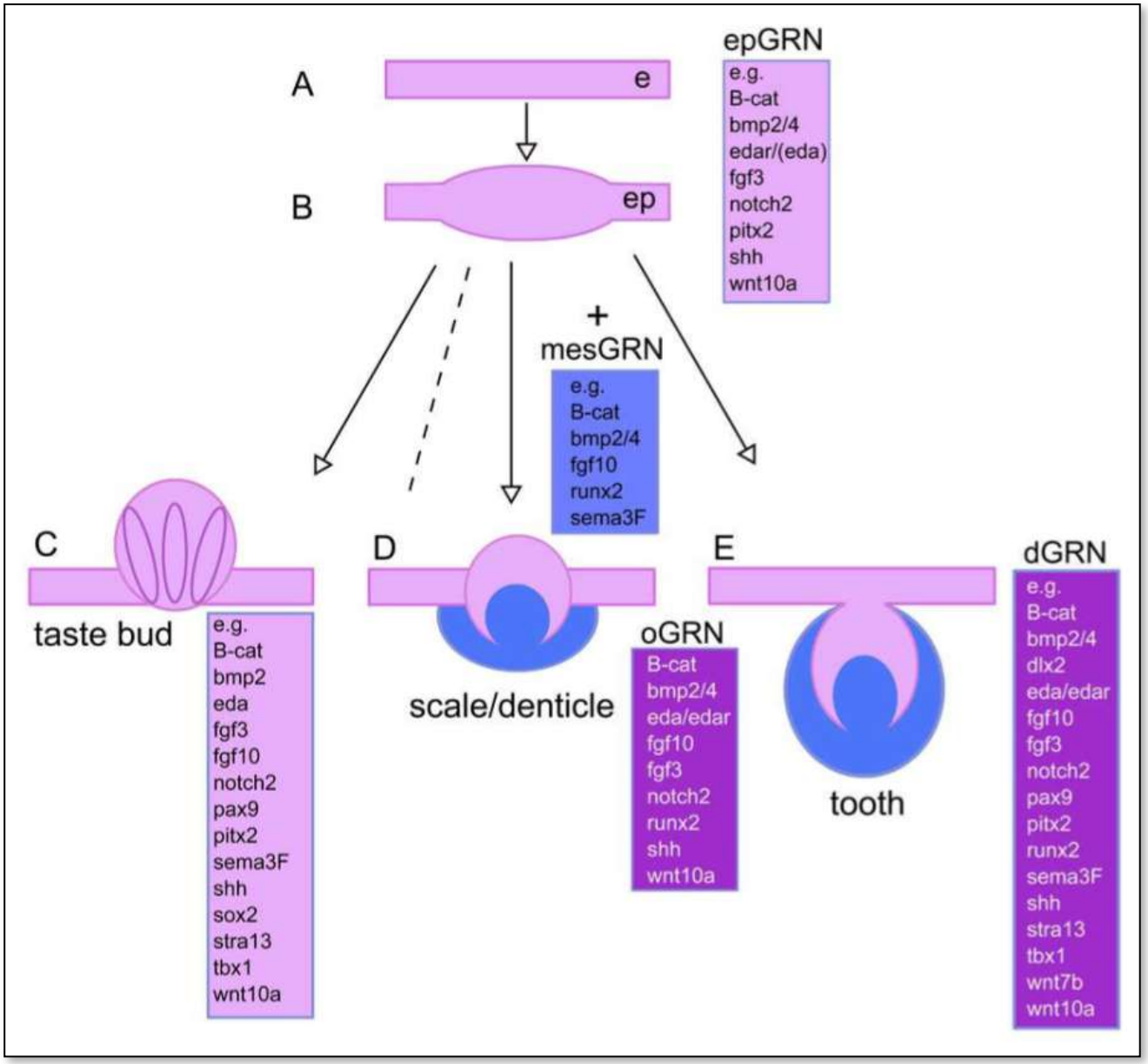


Figure 2. The inside and out gene regulatory hypothesis for odontode evolution. **A**: Schematic diagram represents a generalised early vertebrate/fish in lateral/sagittal view: we propose that regardless of tissue origin (endoderm or ectoderm), the ingredients for odontode evolution, instigated by the appearance of the putative odontode gene regulatory network (oGRN), involved the collaboration of two pre-existing gene co-expression groups: (i) the neural crest-derived ectomesenchymal co-expression group (mesCEG) and (ii) the epithelial co-expression group (epCEG), which operates within both the endoderm and ectoderm (**B**). **C**: The evolution of both skin denticles and teeth were separate operations of the combination of epCEG and mesCEG in alternative locations, the epidermis and the oro-pharyngeal cavity (opc). Within the opc, co-option of the oGRN potential was transferred to the oral jaws during the transition from jawless (agnathans) to jawed vertebrates (gnathostomes). Each CEG (mesCEG and epCEG) must have acted as part of larger yet currently unknown GRN (mesGRN and epGRN).

A new perspective:
collaborative interactions of epithelial & NC-GRN's



A new perspective: collaborative interactions of epithelial & NC-GRN's

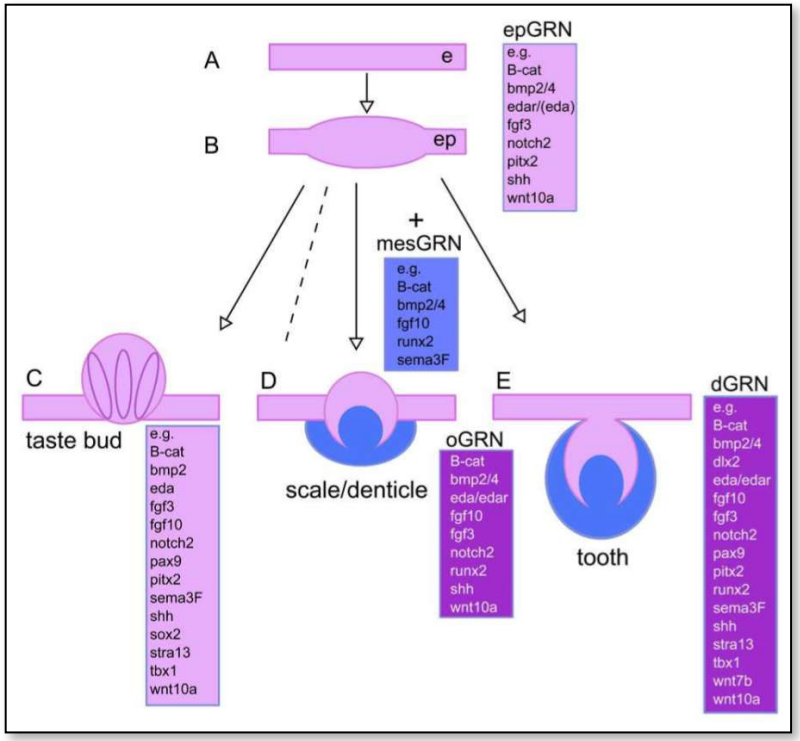
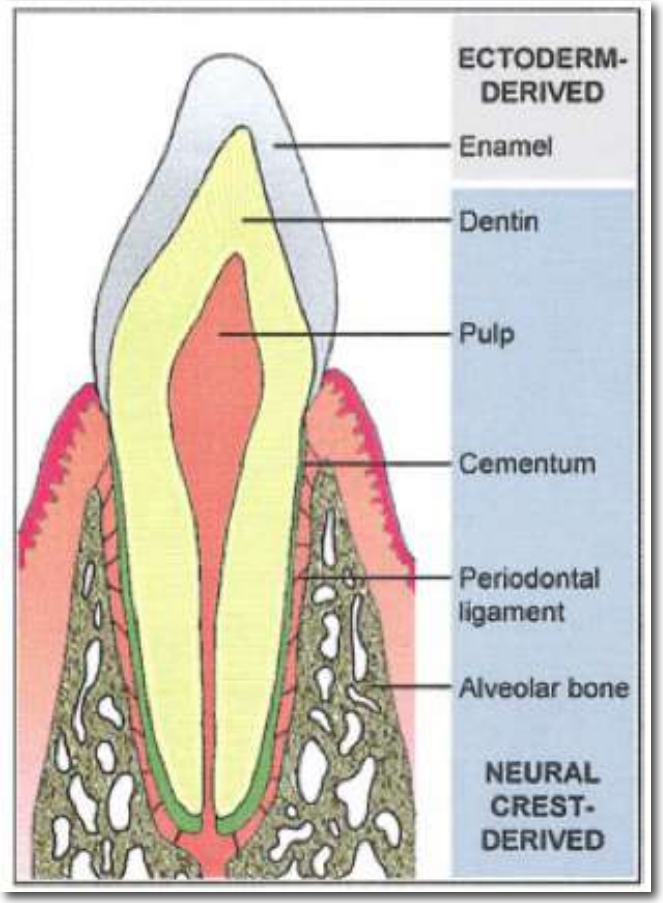
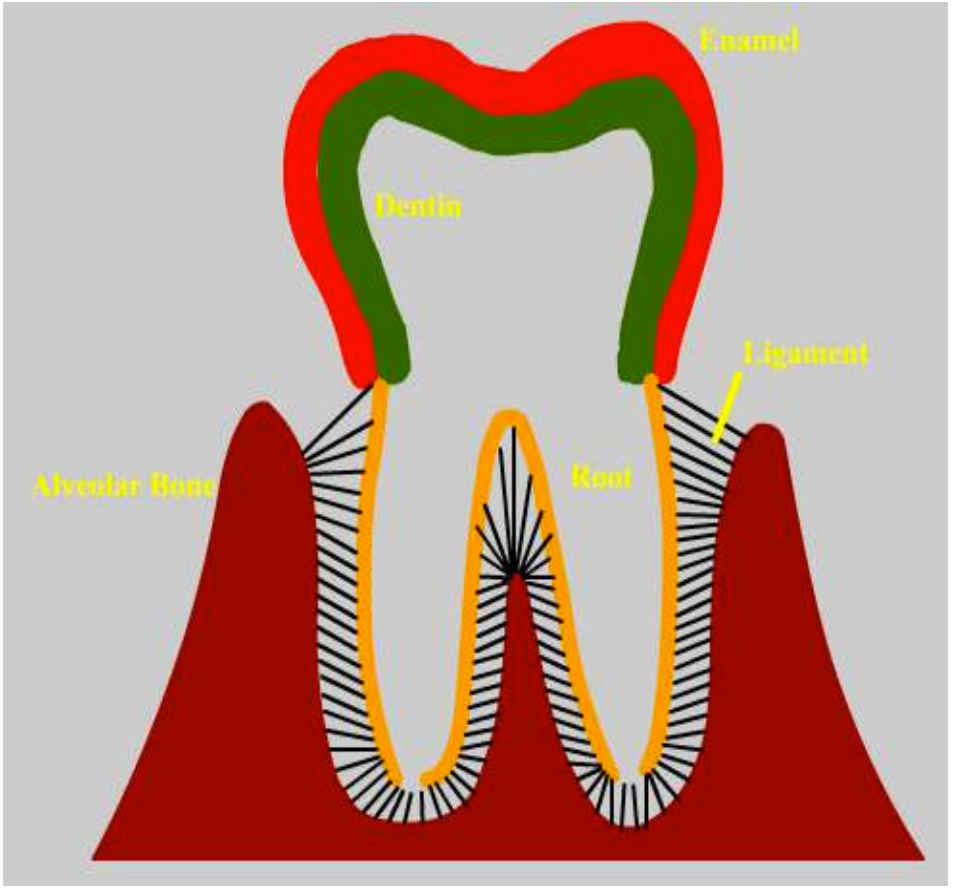


Figure 3. Epithelial transitions and innovative network consolidation. **A**: A generalised epithelium from which a thickened epithelial placode initiates. **B**: The genes expressed within this thickening can be described as the epithelial co-expression group (epCEG). From this thickened epithelial placode the epithelium can transition into a number of structures: (**C**) a taste bud, a similar sensory unit, is a superficial epithelial element posing a unique epithelial gene expression signature (tbCEG); (**D**) a denticle and (**E**) a tooth recruit the underlying mesenchyme that contains the neural crest-derived cell population and the set of genes associated with the neural crest-derived ectomesenchyme (mesCEG). Note that this collection of genes is related to and influenced by the ncGRN. For a more complete list of genes that interact in the ncGRN, embryo-wide, see Refs. [68, 69]. We propose the mesCEG collaborated with the epCEG to provide the ingredients for the oGRN (see also Fig. 2). Skin denticles and teeth are born from the odontode GRN as they are both odontodes by definition. The tooth itself houses a unique subset of genes (collectively the dental GRN). This coordinated gene network contains genes that are not shared with scales and thus we assume dermal denticles, highlighting their evolutionary and developmental separation. The divergence between members of the oGRN and dGRN reflects those genes only expressed in the dentition *versus* those expressed across odontodes determined from expression during teleost scale development; it remains to be tested whether these expression trends hold for denticles of extant sharks and rays.

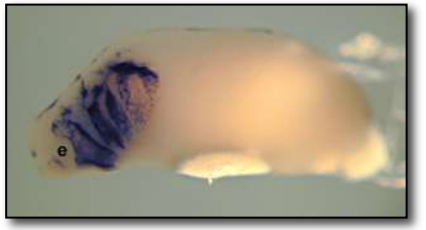
Ontogeneze zubu:
vzájemné a opakující se interakce
zubního mesenchymu a epitelu

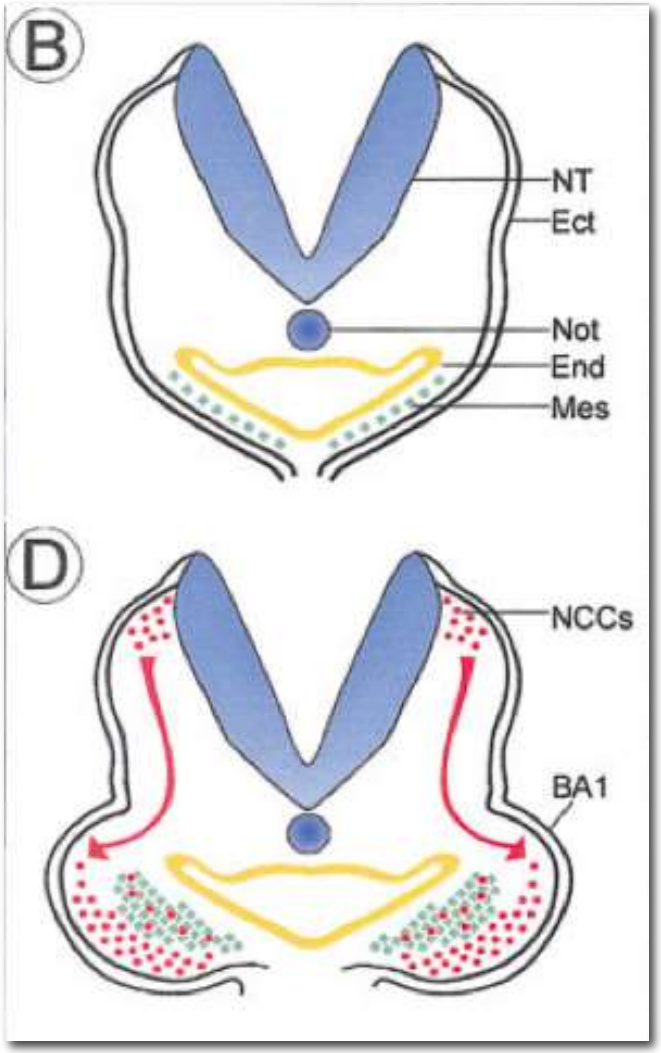




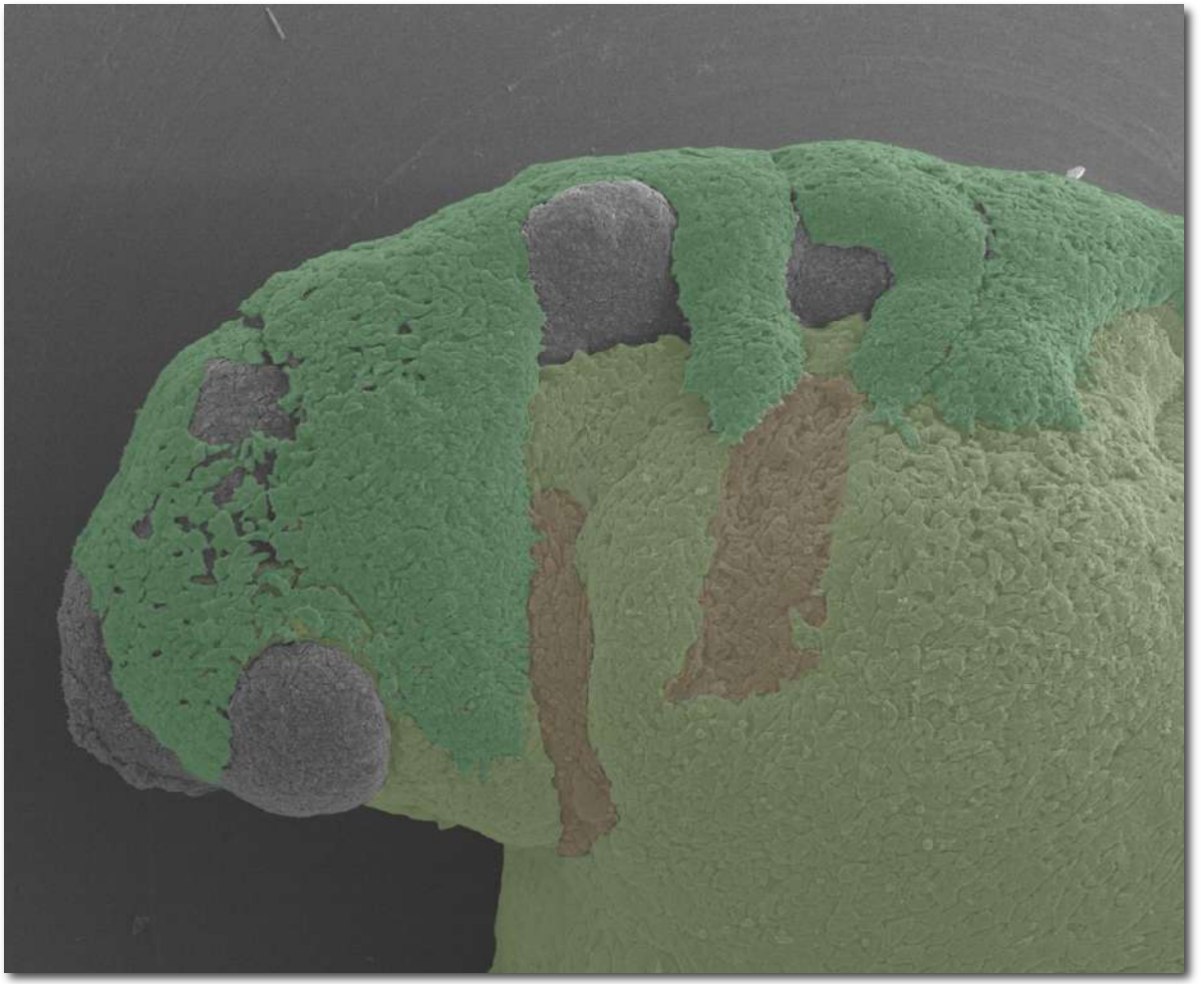
Dle současných definic (*myš, člověk* :-) je ontogeneze zubu zakládána interakcemi **orálního ektodermu** a **mesenchymu hlavové neurální lišty**

Ontogeneze zubu:
mesenchym původu neurální lišty
(vs. MES mesenchym!)



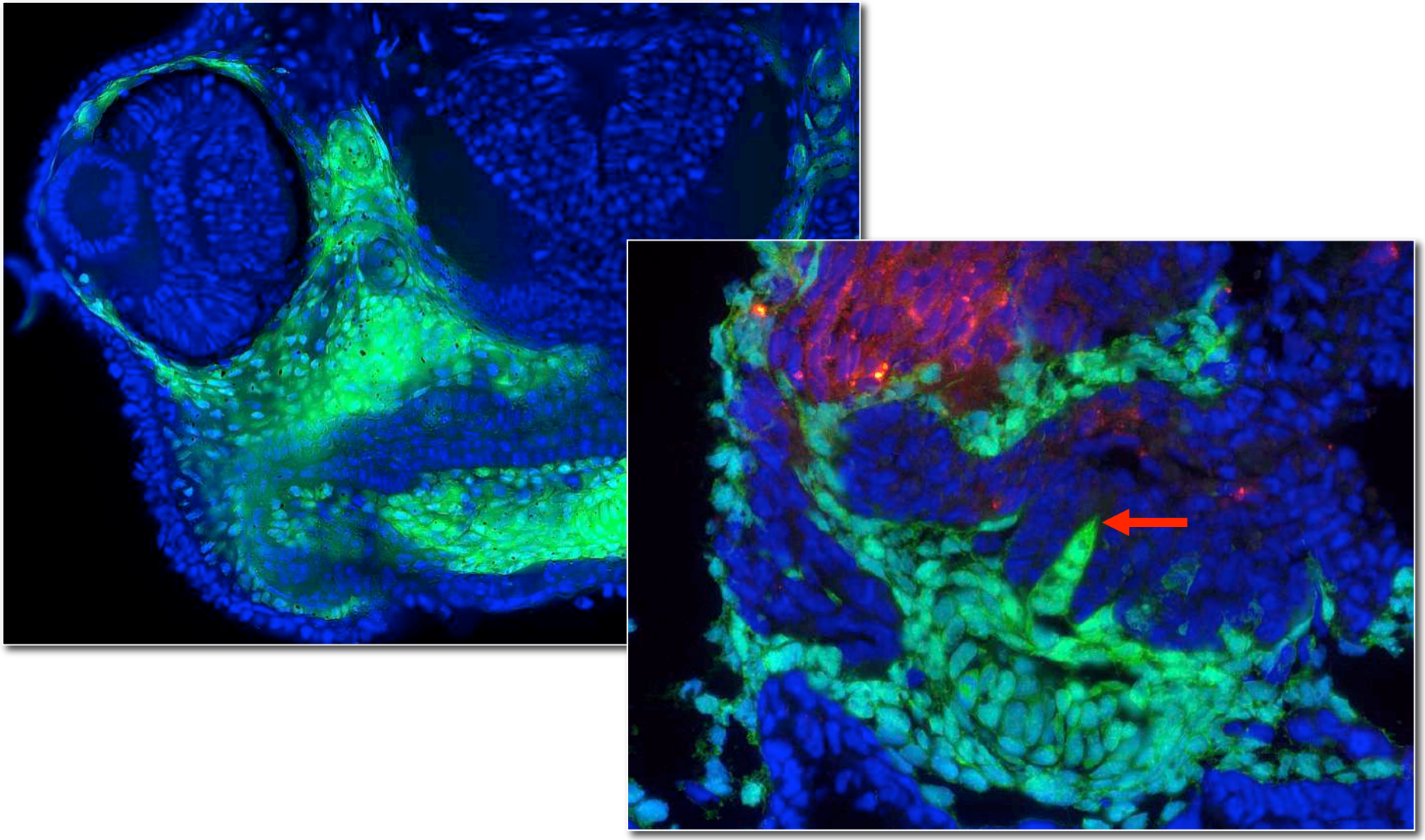


myš: NCC=neural crest cells



embryo axolotla: epidermis odstraněn; migrující mesenchym neurální lišty zeleně; MES žlutě; END růžově

Skeletální elementy vznikají kondenzací mesenchymu



Embryo axolotla: hlavový mesenchym značený zeleně (GFP)
vyplňuje celý prostor (srv. *dermis - škára*) a kondenzuje do čelistních chrupavek a zubů, mj.

Buňky neurální lišty a jejich deriváty

produkují většinu typů buněk, kterými se my obratlovci lišíme od ostatních živočichů; zdroj celkovostní regulace a tkáňové versatility obratlovců

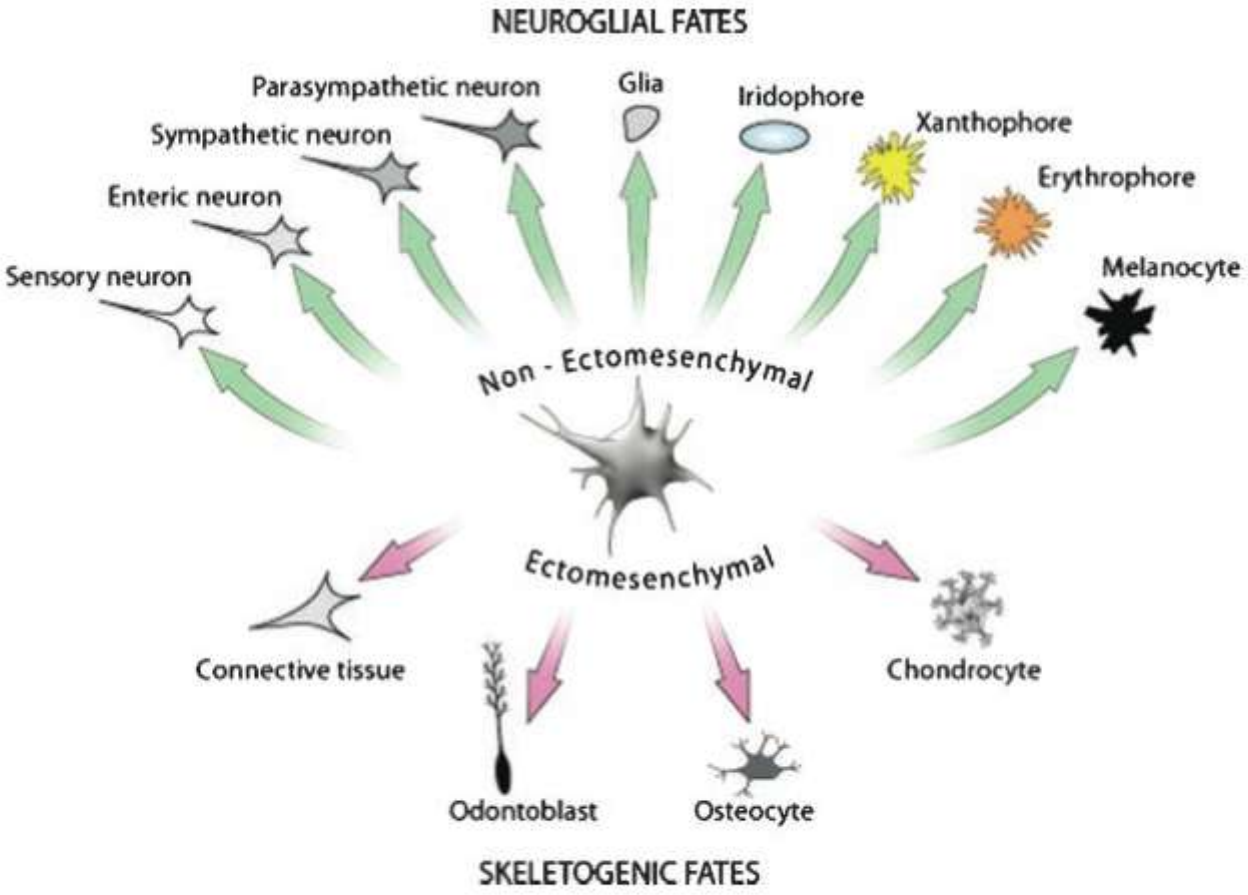


Figure 2. The principal derivative cell types of neural crest. The major derivatives of neural crest cells are schematically illustrated here, grouped according to whether they are classified as ectomesenchymal or non-ectomesenchymal.

Mesenchym původu neurální lišty

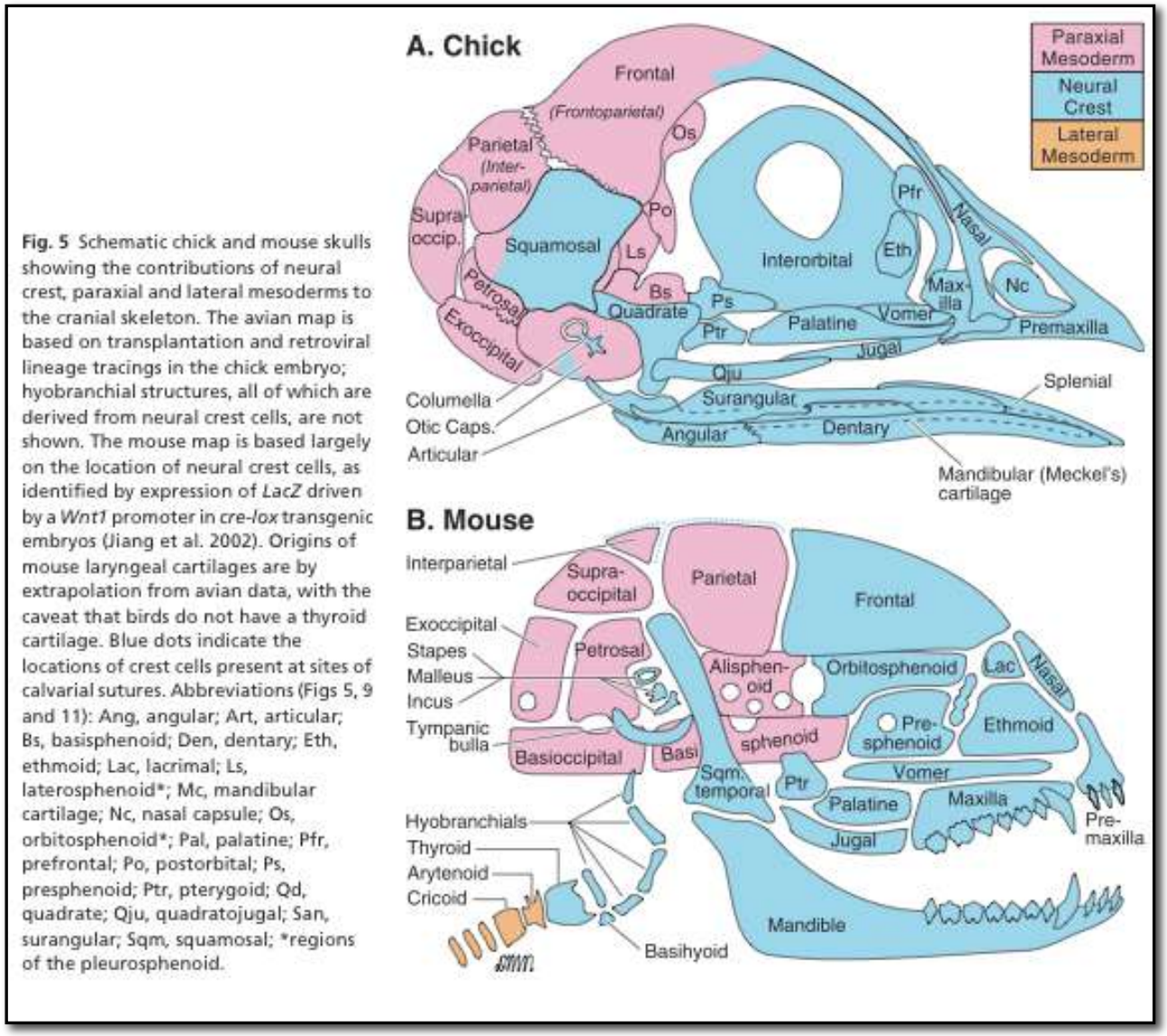
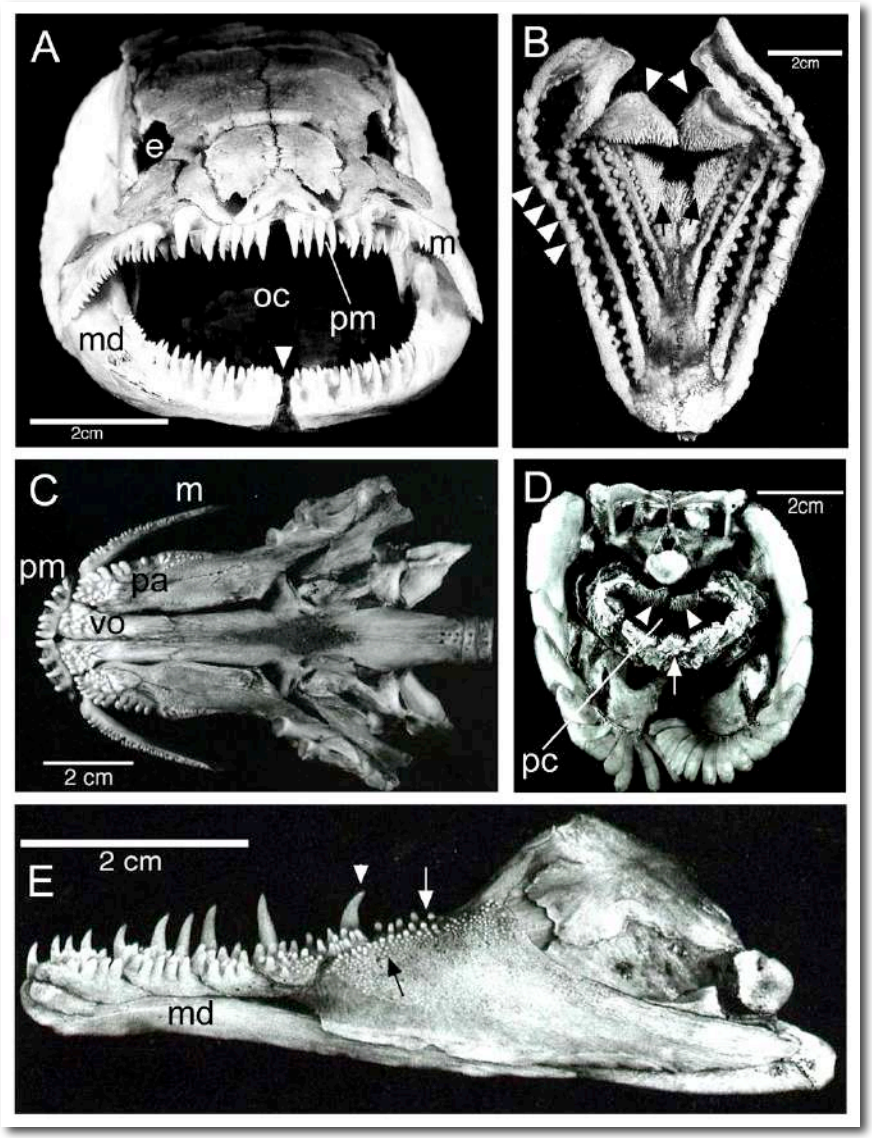


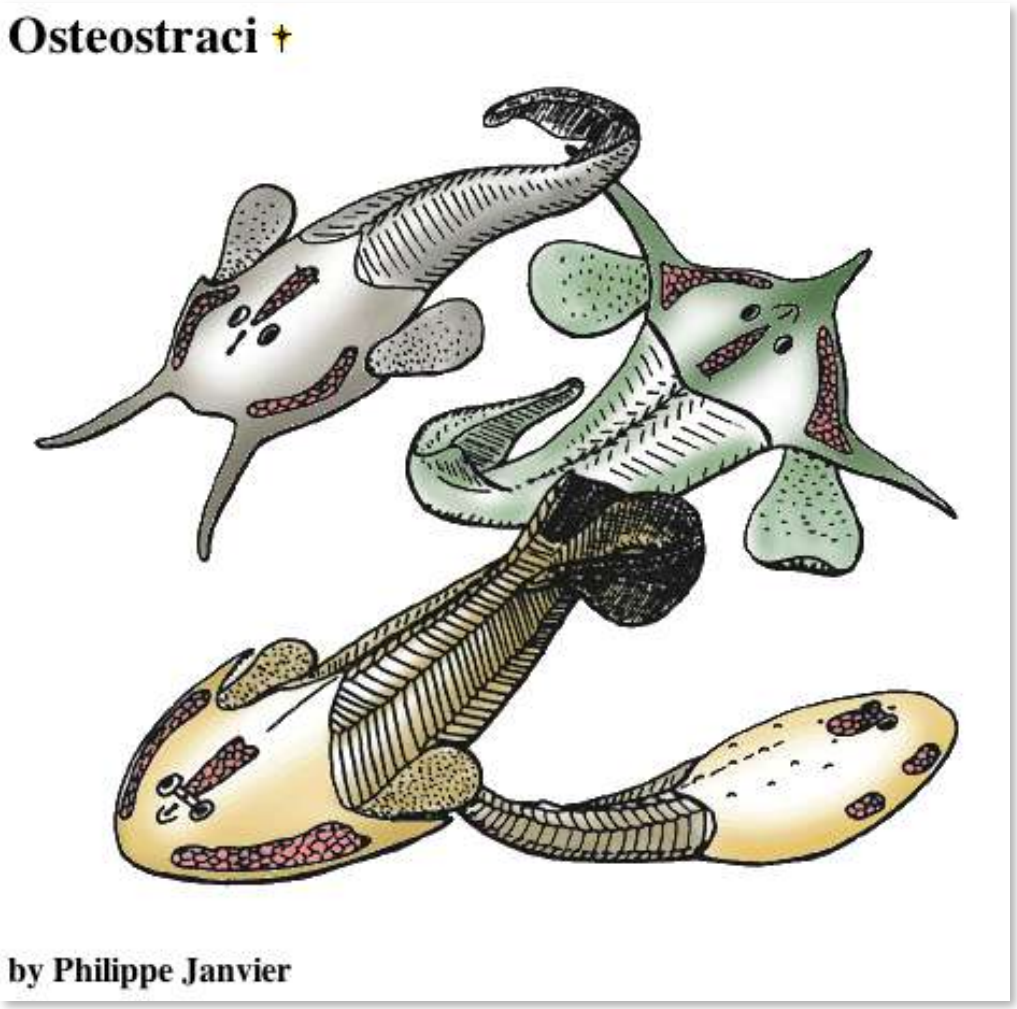
Fig. 5 Schematic chick and mouse skulls showing the contributions of neural crest, paraxial and lateral mesoderms to the cranial skeleton. The avian map is based on transplantation and retroviral lineage tracings in the chick embryo; hyobranchial structures, all of which are derived from neural crest cells, are not shown. The mouse map is based largely on the location of neural crest cells, as identified by expression of *LacZ* driven by a *Wnt1* promoter in *cre-lox* transgenic embryos (Jiang et al. 2002). Origins of mouse laryngeal cartilages are by extrapolation from avian data, with the caveat that birds do not have a thyroid cartilage. Blue dots indicate the locations of crest cells present at sites of calvarial sutures. Abbreviations (Figs 5, 9 and 11): Ang, angular; Art, articular; Bs, basisphenoid; Den, dentary; Eth, ethmoid; Lac, lacrimal; Ls, laterosphenoid*; Mc, mandibular cartilage; Nc, nasal capsule; Os, orbitosphenoid*; Pal, palatine; Pfr, prefrontal; Po, postorbital; Ps, presphenoid; Ptr, pterygoid; Qd, quadrate; Qju, quadratojugal; San, surangular; Sqm, squamosal; *regions of the pleurosphenoid.

Embryonální původ hlavových kostí: kuře vs. myš - deriváty neurální lišty modře

Mesenchym původu neurální lišty

Rozsáhlé zubní a skeletální deriváty,
pancíře, hlavové i trupové desky:
vše deriváty buněk neurální lišty?





Development 140, 2923-2932 (2013) doi:10.1242/dev.093534

An exclusively mesodermal origin of fin mesenchyme demonstrates that zebrafish trunk neural crest does not generate ectomesenchyme

Raymond Teck Ho Lee[1], Ela W. Knapik[2], Jean Paul Thiery[1,3,4] and Thomas J. Carney[1,*]

SUMMARY

The neural crest is a multipotent stem cell population that arises from the dorsal aspect of the neural tube and generates both non-ectomesenchymal (melanocytes, peripheral neurons and glia) and ectomesenchymal (skeletogenic, odontogenic, cartilaginous and connective tissue) derivatives. In amniotes, only cranial neural crest generates both classes, with trunk neural crest restricted to non-ectomesenchyme. By contrast, it has been suggested that anamniotes might generate derivatives of both classes at all axial levels, with trunk neural crest generating fin osteoblasts, scale mineral-forming cells and connective tissue cells; however, this has not been fully tested. The cause and evolutionary significance of this cranial/trunk dichotomy, and its absence in anamniotes, are debated. Recent experiments have disputed the contribution of fish trunk neural crest to fin osteoblasts and scale mineral-forming cells. This prompted us to test the contribution of anamniote trunk neural crest to fin connective tissue cells. Using genetics-based lineage tracing in zebrafish, we find that these fin mesenchyme cells derive entirely from the mesoderm and that neural crest makes no contribution. Furthermore, contrary to previous suggestions, larval fin mesenchyme cells do not generate the skeletogenic cells of the adult fin, but persist to form fibroblasts associated with adult fin rays. Our data demonstrate that zebrafish trunk neural crest does not generate ectomesenchymal derivatives and challenge long-held ideas about trunk neural crest fate. These findings have important implications for the ontogeny and evolution of the neural crest.

ARTICLE

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Trunk exoskeleton in teleosts is mesodermal in origin

Atsuko Shimada[1], Toru Kawanishi[1], Takuya Kaneko[1], Hiroki Yoshihara[2], Tohru Yano[2], Keiji Inohaya[3], Masato Kinoshita[4], Yasuhiro Kamei[5], Koji Tamura[2] & Hiroyuki Takeda[1]

The vertebrate mineralized skeleton is known to have first emerged as an exoskeleton that extensively covered the fossil jawless fish. The evolutionary origin of this exoskeleton has long been attributed to the emergence of the neural crest, but experimental evaluation for this is still poor. Here we determine the embryonic origin of scales and fin rays of medaka (teleost trunk exoskeletons) by applying long-term cell labelling methods, and demonstrate that both tissues are mesodermal in origin. Neural crest cells, however, fail to contribute to these tissues. This result suggests that the trunk neural crest has no skeletogenic capability in fish, instead highlighting the dominant role of the mesoderm in the evolution of the trunk skeleton. This further implies that the role of the neural crest in skeletogenesis has been predominant in the cephalic region from the early stage of vertebrate evolution.

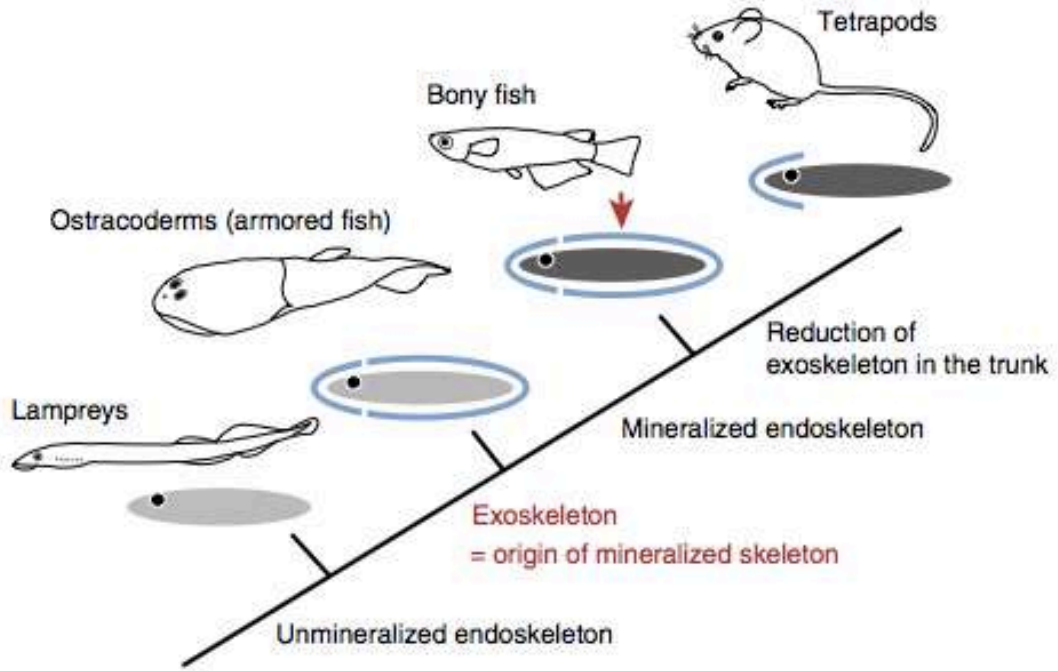

Figure 1 | Origin and evolution of mineralized skeleton in vertebrates. Vertebrates have two distinct sets of skeletons, exoskeleton (dermal skull roofs, teeth, scales, fin rays and so on.) and endoskeleton (neurocranium, vertebra, appendicular skeleton and so on). While the endoskeleton consists of endochondral bones that are preformed by cartilage and later replaced by mineralized bones, the major components of the exoskeleton are the dermal bones that develop in the dermis only by membranous ossification. A mineralized skeleton is thought to have emerged initially as exoskeletonal elements. Bony fish retain the exoskeleton in the form of dermal scales and fin rays. During terrestrial evolution, however, the exoskeleton has been drastically reduced or lost in the trunk region. Outer blue circles show the exoskeleton. Inner solid pale circles show the unmineralized endoskeleton. Inner solid-dark circles show the mineralized endoskeleton. The red arrow indicates the trunk exoskeleton we focused on in the present experiment.

Mesenchym původu neurální lišty

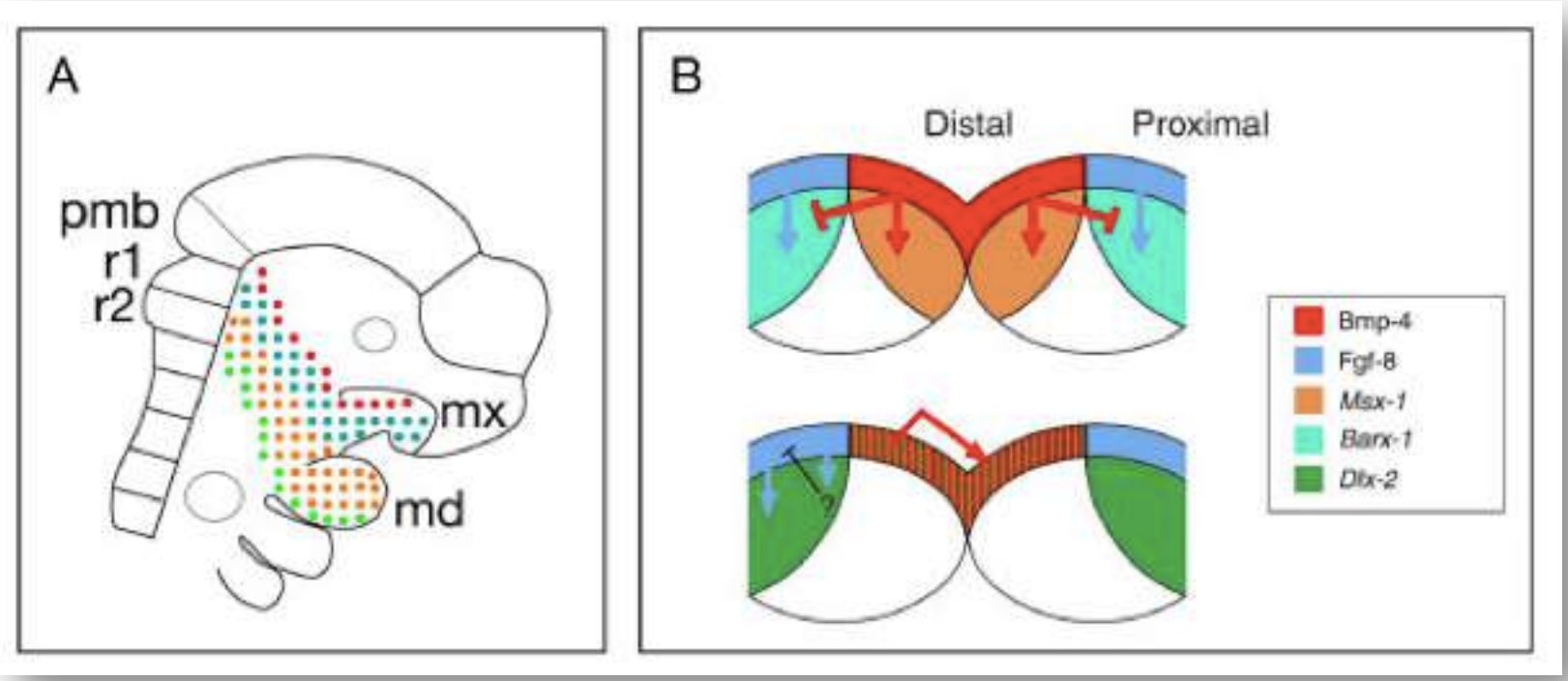

Fig. 3. Patterning the murine dentition. (**A**) Neural crest cells migrate into the maxillary (mx) and mandibular (md) processes of branchial arch 1 in distinct streams originating from the posterior midbrain (pmb) and rhombomeres (r) 1–2. (**B**) Signalling interactions establishing homeobox gene expression in the mandibular arch. The upper panel depicts regulation of *Barx-1* and *Msx*-1 at E10.5. Complementary domains of Fgf-8 (blue) in the proximal and Bmp-4 (red) in the distal regions of the mandible result in reciprocal expression of *Barx-1* (light blue) and *Msx-1* (brown) in the proximal and distal mesenchyme, respectively. The lower panel represents regulation of *Dlx-2* by Fgf-8 and Bmp-4 at E10.5. Bmp-4 (red) induces *Dlx-2* (green) in the distal epithelium via an intra-epithelial signal. Fgf-8 (blue) in the proximal epithelium induces *Dlx-2* in the underlying mesenchyme. In addition, Fgf-8 also inhibits *Dlx-2* in the epithelium of this region by an unknown signal that passes via the mesenchyme. Adapted from Tucker et al. ('98) and Thomas et al. (2000).

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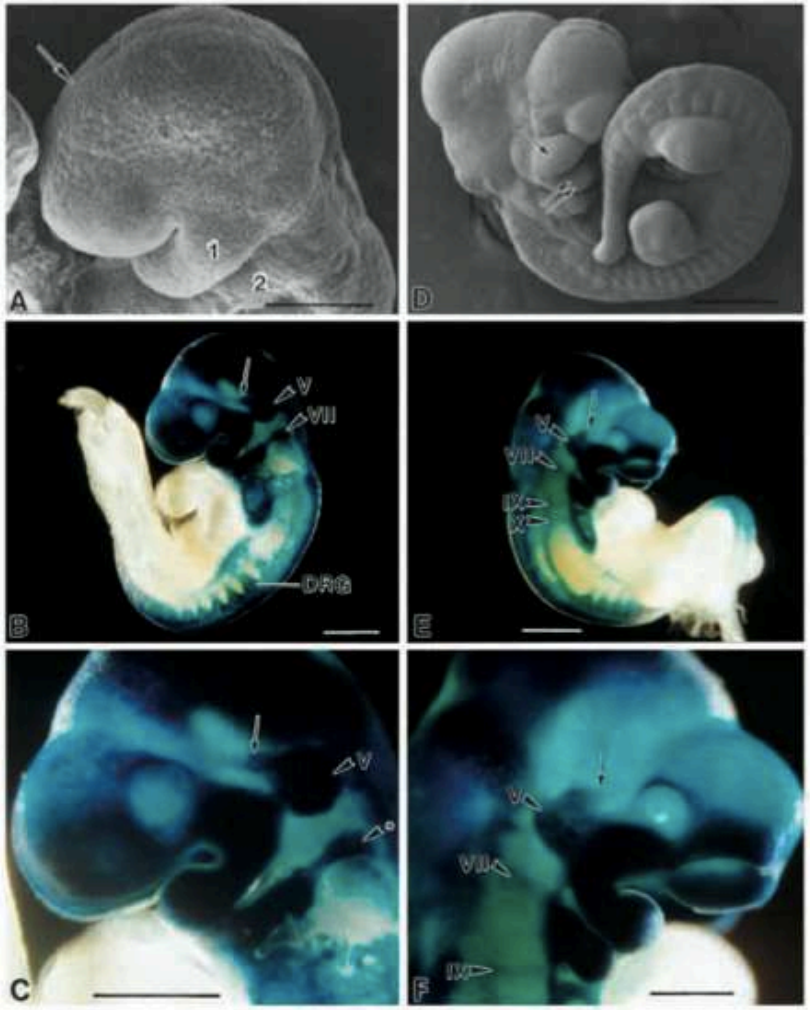
DEV4301

Fate of the mammalian cranial neural crest during tooth and mandibular morphogenesis

Yang Chai[1,*], Xiaobing Jiang[2,5], Yoshihiro Ito[1], Pablo Bringas, Jr[1], Jun Han[1], David H. Rowitch[3], Philippe Soriano[4], Andrew P. McMahon[3] and Henry M. Sucov[5]



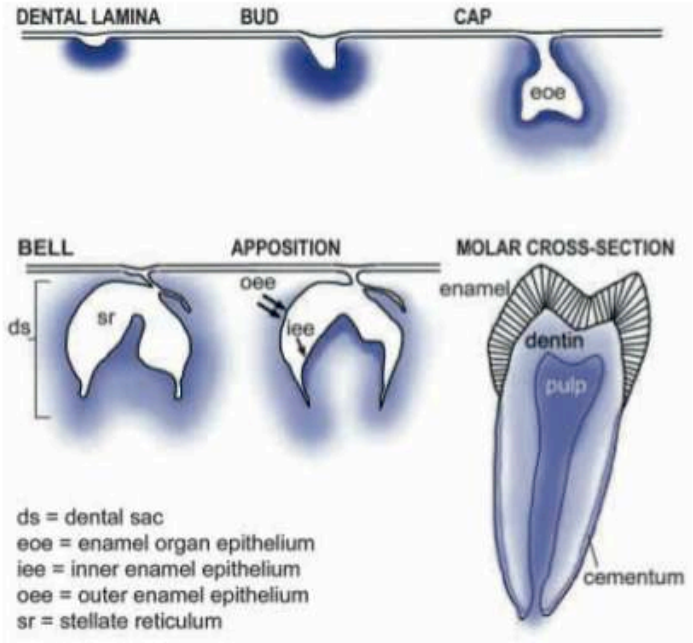


Fig. 5. Schematic drawing of life cycle of tooth with contribution from CNC cells. When tooth development is initiated with the formation of dental lamina, its underlying mesenchyme is almost entirely populated with CNC-derived cells (dark blue). As the tooth develops from bud to cap stage, CNC-derived cells are concentrated (dark blue) at the interface with the epithelium while the peripheral portion of the dental sac is less populated (light blue) with CNC-derived cells. In adulthood, CNC-derived cells contribute to the formation of dentine, pulp and cementum.

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Fate of the mammalian cranial neural crest during tooth and mandibular morphogenesis

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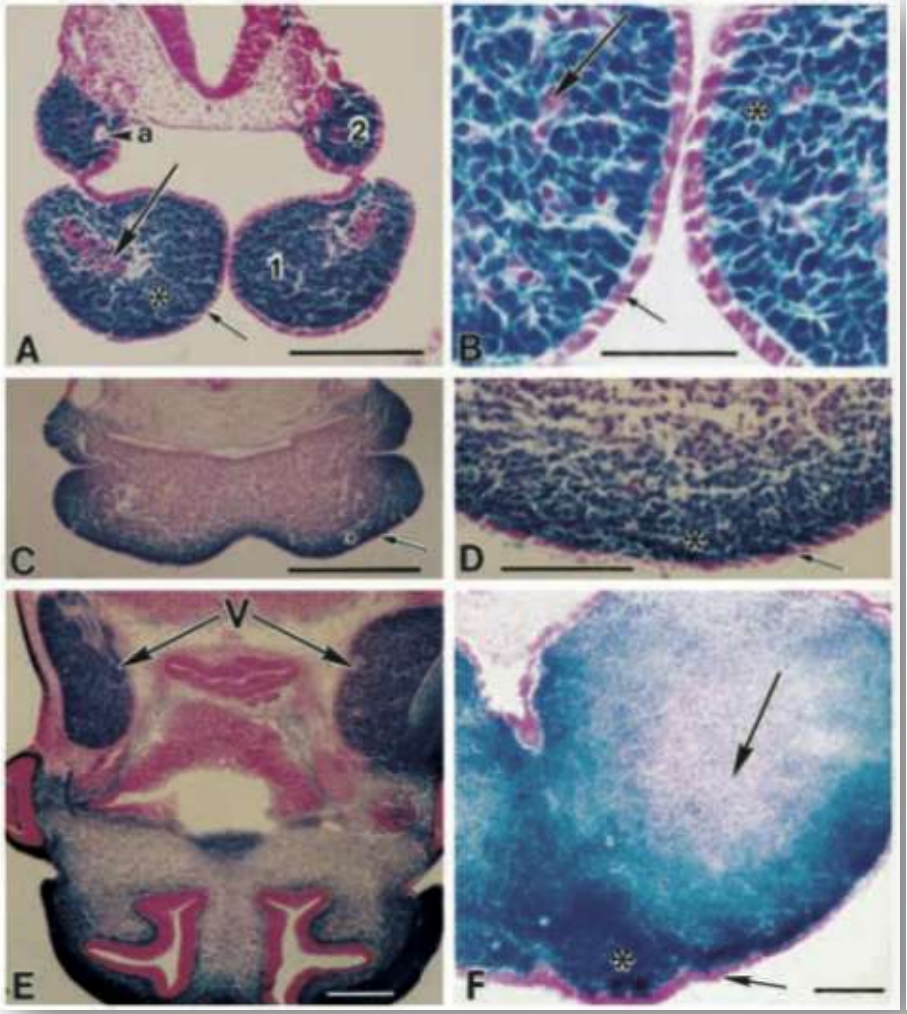
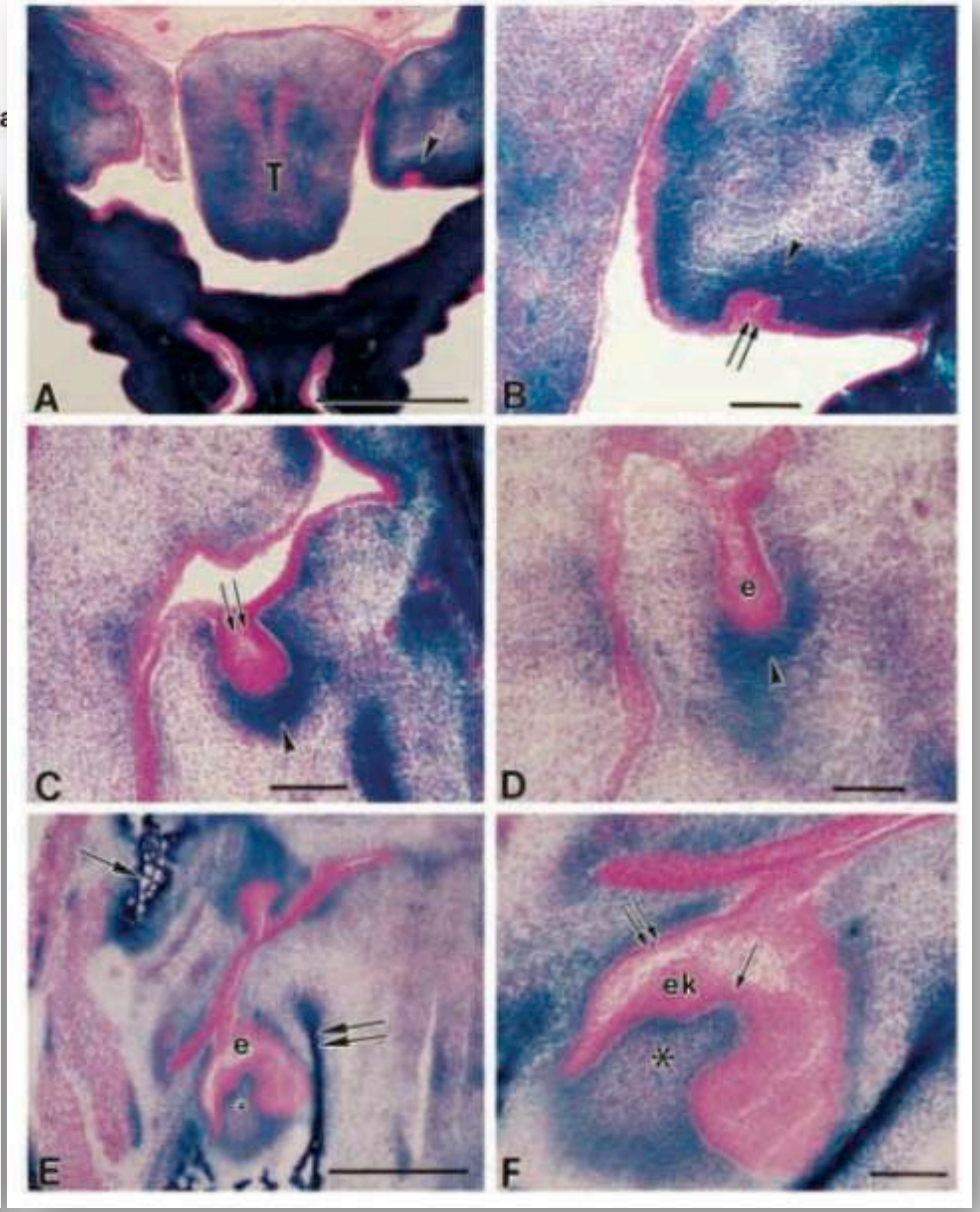
Philippe Soriano[4], Andrew P. McMahon[3] and Henry M. Sucov[5]





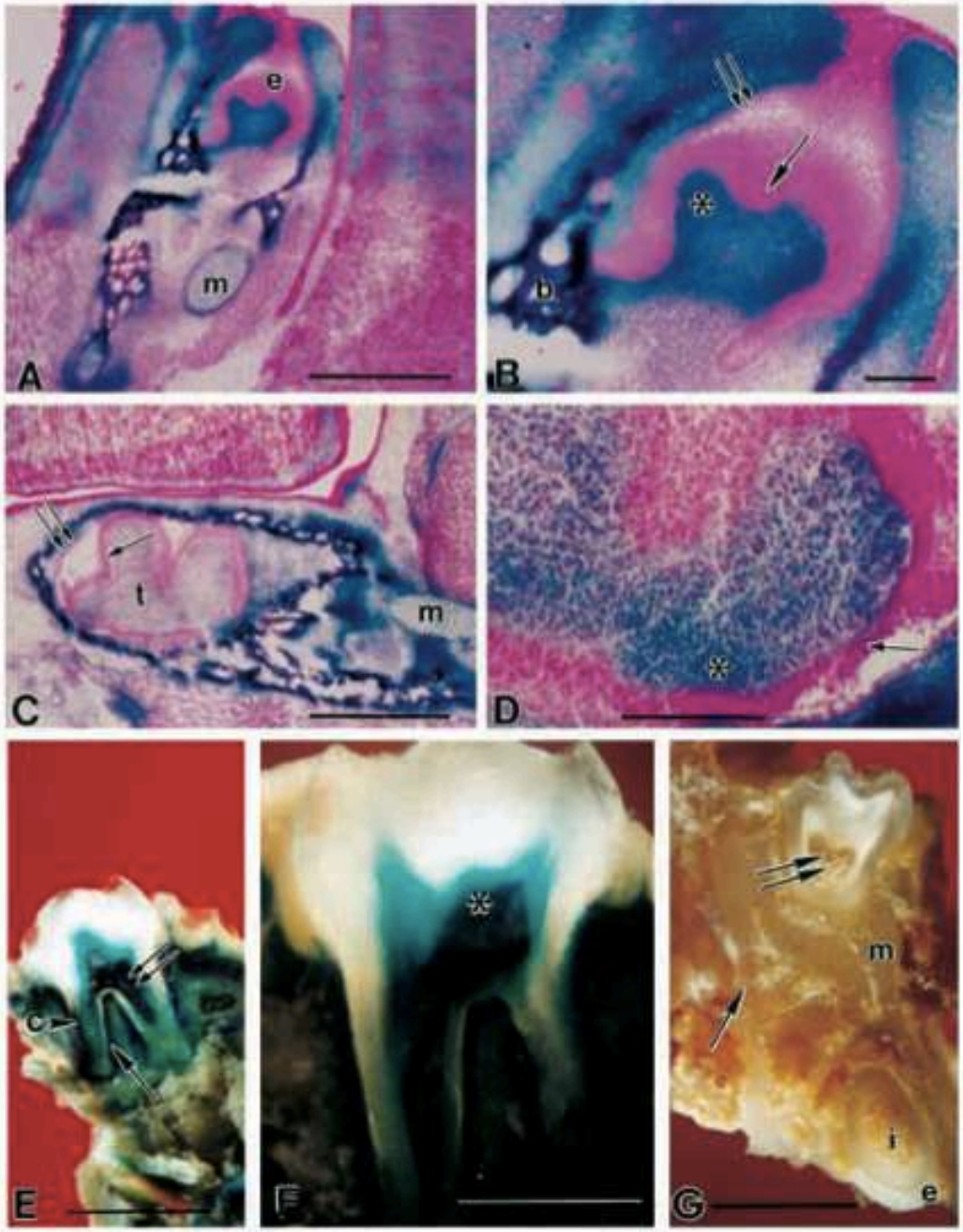


Fig. 4. The contribution of CNC-derived cells during tooth morphogenesis (continued). (A) There is variation in the stage of tooth morphogenesis at a given embryonic time point. Here at E15.5, tooth formation has advanced into bell stage with the folding of the enamel epithelium (e). The dental papilla and Meckel's cartilage (m) show large numbers of CNC-derived cells. (B) Both inner (single arrow) and outer (double arrow) enamel epithelium do not contain β-gal-positive cells. The dental papilla is populated with mainly CNC-derived cells (*), while some β-gal-negative cells are also present. b, mandible. (C) At E17.5, a tooth organ (t) is present within the mandible. Both inner (single arrow) and outer (double arrow) enamel epithelium is free of β-gal-positive cells. (D) The dental papilla is populated with both CNC- (*) and non-CNC-derived cells adjacent to preameloblasts (single arrow). (E) In a cross section of maxilla of a 6-week-old adult transgenic mouse, β-gal-positive cells are present in dentine, pulp (double arrow), cementum (c) and periodontal ligament (single arrow). (F) The adult maxillary molar is shown with β-gal-positive cells in dentine (*), pulp, cementum and periodontal ligament, reflecting their CNC origin. (G) An adult mouse non-transgenic littermate control does not show any labeling in mandible (m), pulp tissue of both incisors (i) and molars. Double arrow, molar pulp; single arrow, mandibular periosteum. Scale bars: A,C,F, 0.5 mm; B,D, 100 μm; E,G, 1 mm.

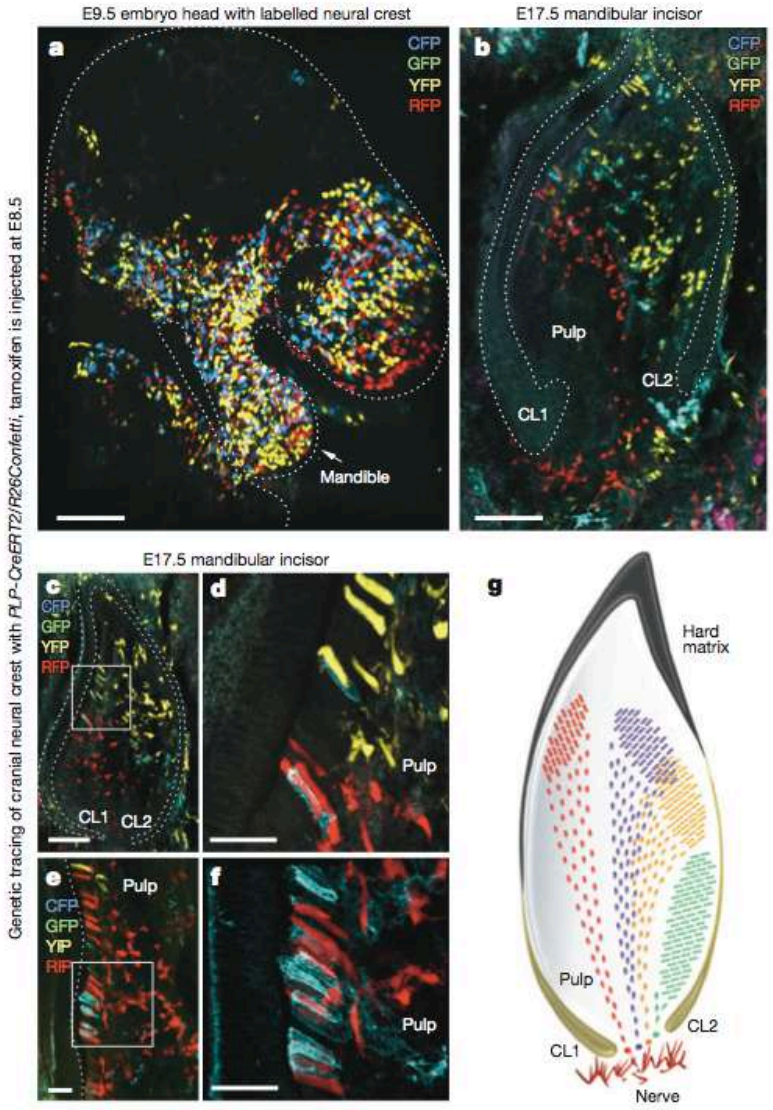
LETTER

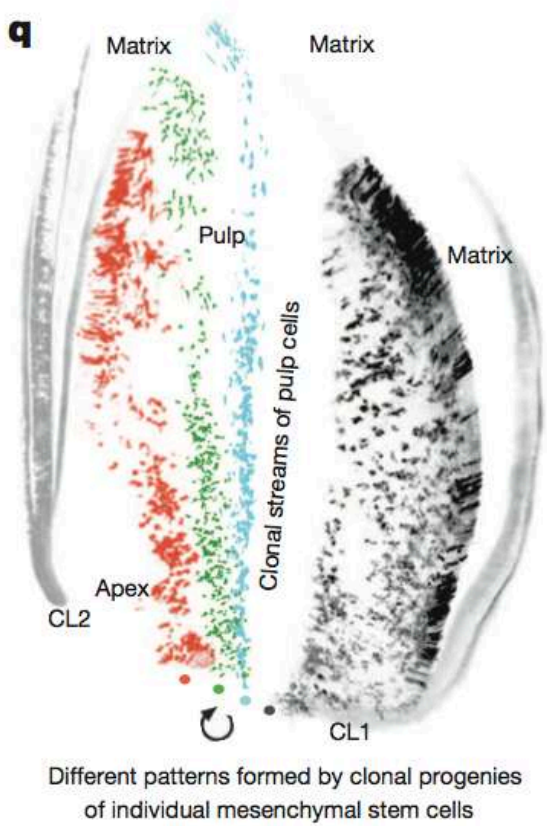
doi:10.1038/nature13536

Glial origin of mesenchymal stem cells in a tooth model system

Nina Kaukua[1]*, Maryam Khatibi Shahidi[2]*, Chrysoula Konstantinidou[3], Vyacheslav Dyachuk[4,5], Marketa Kaucka[4], Alessandro Furlan[6], Zhengwen An[7], Longlong Wang[7], Isabell Hultman[8], Lars Ährlund-Richter[8], Hans Blom[9], Hjalmar Brismar[9], Natalia Assaife Lopes[6], Vassilis Pachnis[3], Ueli Suter[10], Hans Clevers[11,12], Irma Thesleff[13], Paul Sharpe[7], Patrik Ernfors[6], Kaj Fried[1] & Igor Adameyko[4]

Mesenchymal stem cells occupy niches in stromal tissues where they provide sources of cells for specialized mesenchymal derivatives during growth and repair[1]. The origins of mesenchymal stem cells have been the subject of considerable discussion, and current consensus holds that perivascular cells form mesenchymal stem cells in most tissues. The continuously growing mouse incisor tooth offers an excellent model to address the origin of mesenchymal stem cells. These stem cells dwell in a niche at the tooth apex where they produce a variety of differentiated derivatives. Cells constituting the tooth are mostly derived from two embryonic sources: neural crest ectomesenchyme and ectodermal epithelium[2]. It has been thought for decades that the dental mesenchymal stem cells[3] giving rise to pulp cells and odontoblasts derive from neural crest cells after their migration in the early head and formation of ectomesenchymal tissue[4,5]. Here we show that a significant population of mesenchymal stem cells during development, self-renewal and repair of a tooth are derived from peripheral nerve-associated glia. Glial cells generate multipotent mesenchymal stem cells that produce pulp cells and odontoblasts. By combining a clonal colour-coding technique[6] with tracing of peripheral glia, we provide new insights into the dynamics of tooth organogenesis and growth.





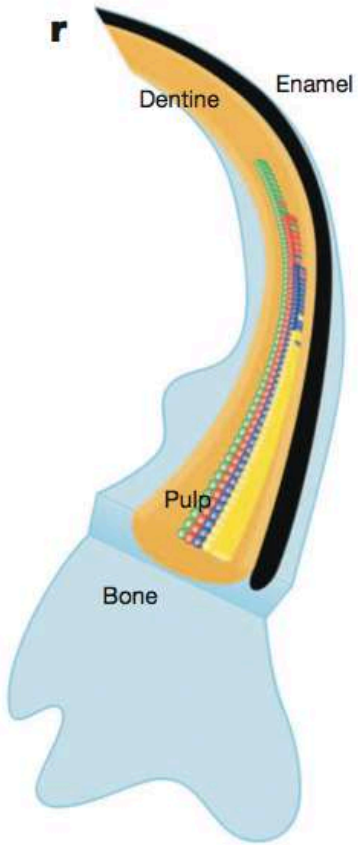


Figure 2 | Clonal contribution of neural crest to tooth development. **a**–**f**, Tracing of neural-crest-derived cells in *PLP-CreERT2/R26Confetti* embryos. **a**, Embryo traced from E8.5 to E9.5, projection of confocal stack. Dotted line demarcates developing head. Arrow: mandible. **b**–**f**, Sections of incisor traced from E8.5 to E17.5. **d**, **f**, Projections of stacks corresponding to areas outlined in **c** and **e**. Note correlation between colours of odontoblasts and adjacent pulp cells. **g**, Illustration of clonally organized pulp and odontoblasts. **b**, **c**, **e**, Dotted line: enamel organ. Scale bars, 100 μm (**a**–**c**); 25 μm (**d**–**f**). CL1 and CL2 indicate labial and lingual aspects of cervical loop.

JOURNAL OF EXPERIMENTAL ZOOLOGY (MOL DEV EVOL) 312B:416–424 (2009)

Odontoblast: A Mechano-Sensory Cell

HENRY MAGLOIRE[1–3]*, MARIE-LISE COUBLE[1–3], BEATRICE THIVICHON-PRINCE[1–3], JEAN-CHRISTOPHE MAURIN[1–3], AND FRANCOISE BLEICHER[1–3]
[1]*Laboratoire Odontoblast et régénération dentinaire, Université de Lyon, Villeurbanne Cedex, France*
[2]*Faculté d'Odontologie, Université Lyon 1, Lyon Cedex, France*
[3]*CNRS, UMR 5242, IGFL, Lyon Cedex, France*

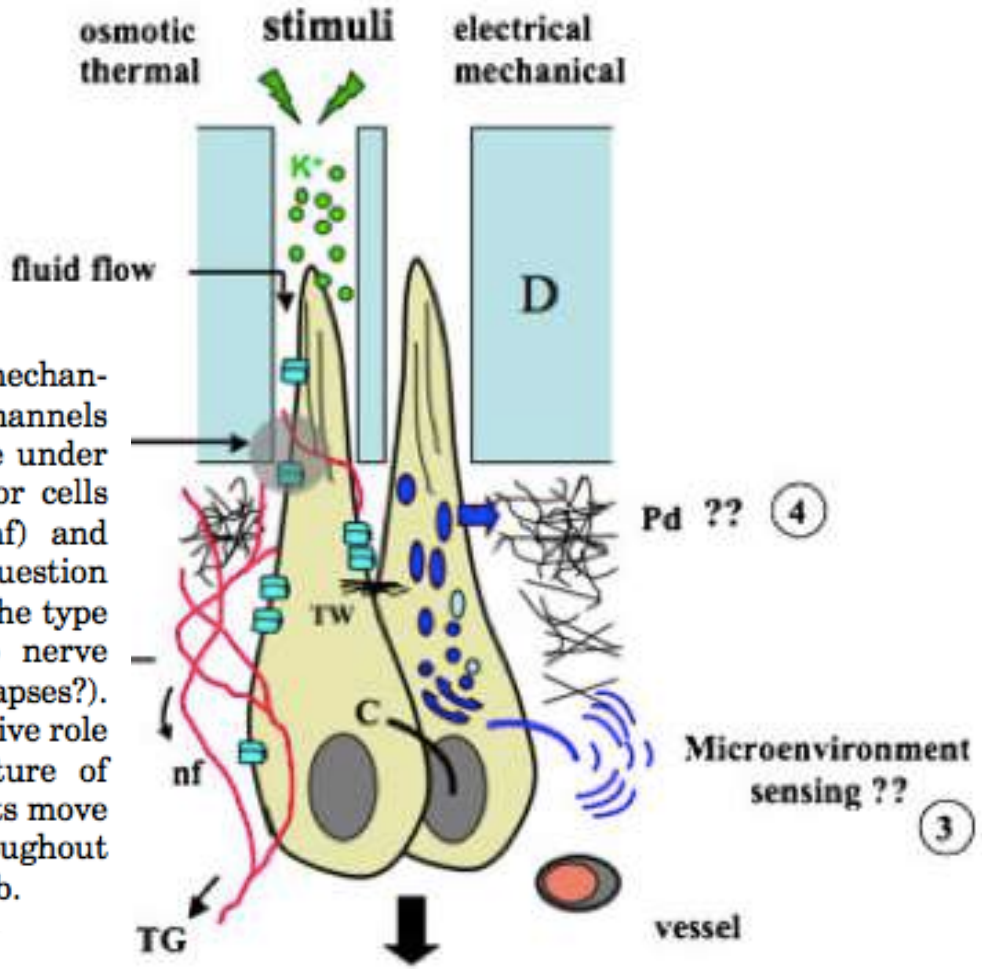


Fig. 7. Schematic representation of hypothetical mechanisms underlining the role of mechano-sensitive ion channels (▭) and cilium structure (C) to odontoblast response under stimuli. Odontoblasts may operate as excitable sensor cells whose excitation is transmitted to nerve fibers (nf) and conducted to the trigeminal ganglion (TG). The question marks (1, 2) refer to the remaining open question of the type of transmission of excitation from odontoblasts to nerve endings (intercellular communication? chemical synapses?). Identically, the question marks (3, 4) concern the putative role of primary cilia in the regulation of the architecture of primary or secondary dentine formation as odontoblasts move centripetally toward the pulp core (black arrow) throughout the life of the tooth. Pd, predentine; TW, terminal web.

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[1]*Laboratoire Odontoblast et régénération dentinaire, Université de Lyon, Villeurbanne Cedex, France*
[2]*Faculté d'Odontologie, Université Lyon 1, Lyon Cedex, France*
[3]*CNRS, UMR 5242, IGFL, Lyon Cedex, France*

srv. zub (odontoda) jako *smyslová papila*; zvápenatění a skeletální fce až sekundární či zároveň?

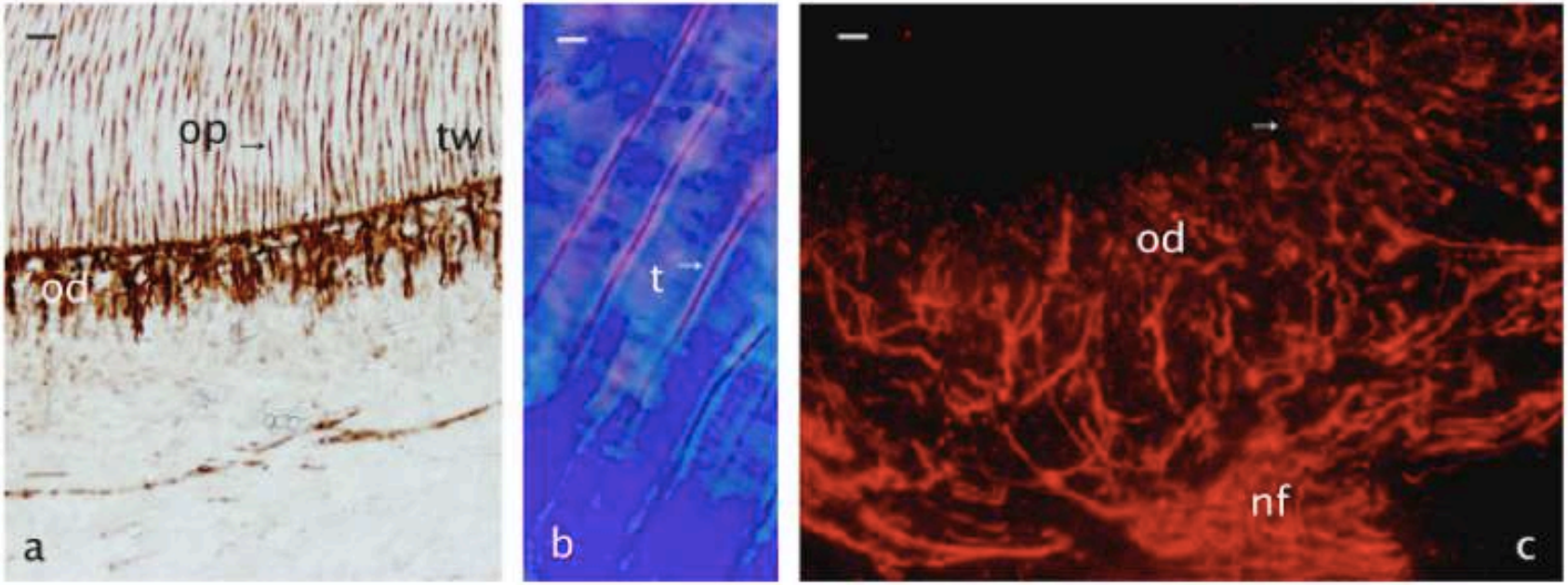

Fig. 1. Pulpal dentinal border of a human tooth. Odontoblasts (od) organized as a single layer with cell processes (op) extending in the dentinal tubules (t). (**a**) Immunoperoxidase detection of β tubulin in decalcified tooth (fixation in 4% paraformaldehyde; demineralization in 10% acetic acid) showing a strong expression in odontoblast cell bodies (od) and processes (op). tw, terminal web. (**b**) Decalcified section of dentine (Bouin's fixation) showing dentinal tubules (t) from the inner third of crown dentine (Masson's trichrome staining). Content of the tubules corresponds to odontoblast cell extensions. The space between processes and tubule walls (arrow) corresponds to the removal of peritubular dentine resulting from the demineralization procedure. (**c**) Frozen section of a carefully isolated pulp showing a dense distribution of nerve fibers (nf) in the odontoblast layer of the crown. The nerve endings and varicosities (arrow) run into the layer (immunodetection of peripherin, marker of intermediate filaments of trigeminal axons). Bar: (a) 20 μm; (b) 10 μm; (c) 10 μm.

THE ANATOMICAL RECORD 297:599–617 (2014)

Sensory Ability in the Narwhal Tooth Organ System

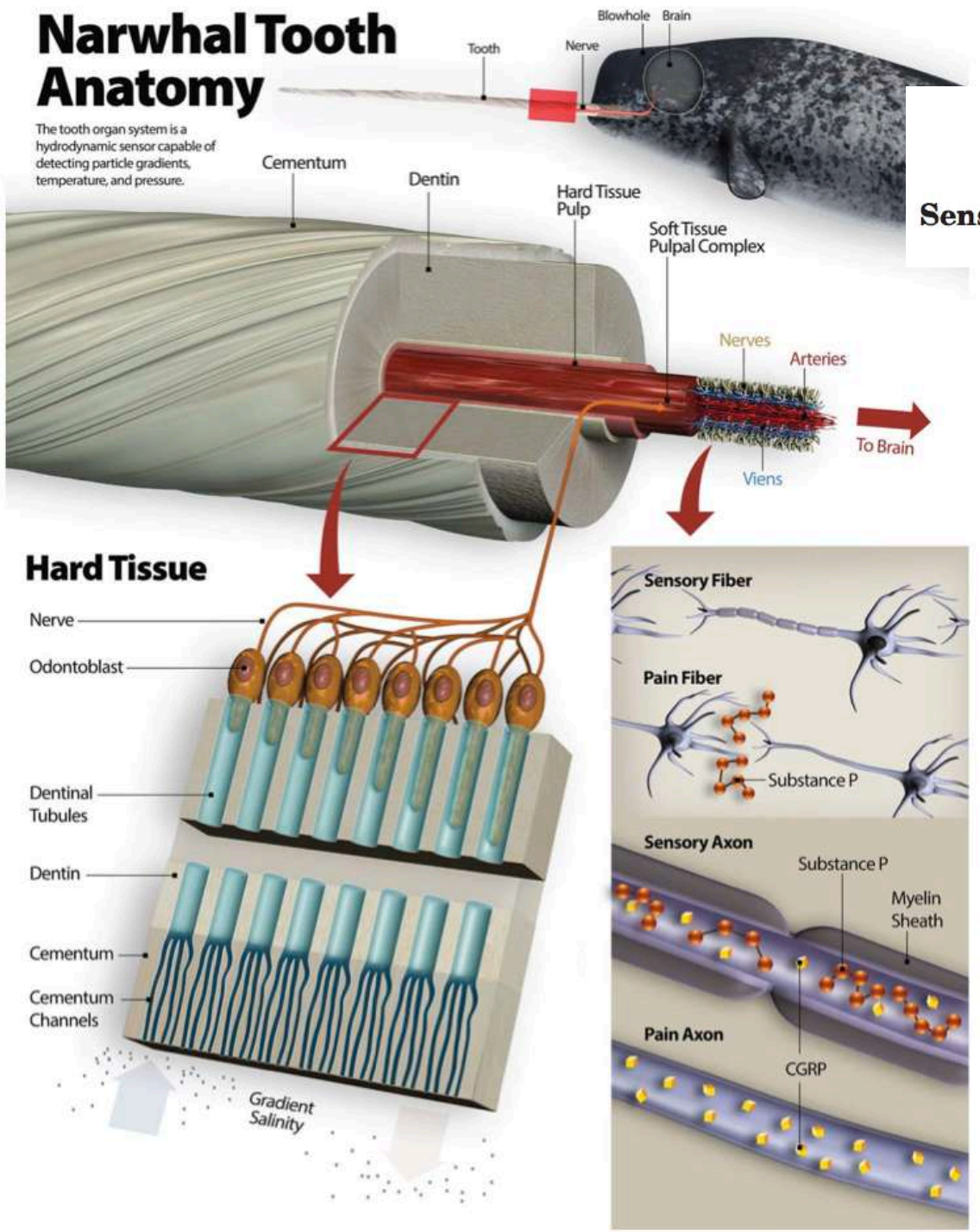

Fig. 9. Sensory model of the erupted male narwhal tusk showing, from bottom left, the introduction of water gradients penetrating cementum channels connected to patent dentinal tubules through the full thickness of the dentinal layer, connecting to odontoblastic processes and cells at the base of the tubules and at the periphery of the pulp, which stimulate nerve tissue connecting the base of tusk tissue to the maxillary branch of the fifth cranial nerve to the brain. Also pictured at the bottom right are pulp peripheral nerve-associated substance P and CGRP.