

The ins and outs of the evolutionary origin of teeth

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SUMMARY The role of teeth and jaws, as innovations that underpinned the evolutionary success of living jawed vertebrates, is well understood, but their evolutionary origins are less clear. The origin of teeth, in particular, is mired in controversy with competing hypotheses advocating their origin in external dermal denticles (“outside-in”) versus a *de novo* independent origin (“inside-out”). No evidence has ever been presented demonstrating materially the traditional “outside-in” theory of teeth evolving from dermal denticles, besides circumstantial evidence of a commonality of structure and organogenesis, and phylogenetic evidence that dermal denticles appear earlier in vertebrate phylogeny than do teeth. Meanwhile, evidence has mounted in support of “inside-out” theory, through developmental studies that have indicated that endoderm is required for tooth development, and fossil studies that have shown that tooth-like structures evolved before dermal denticles (conodont dental elements), that tooth replacement evolving before teeth (thelodont pharyngeal denticles), and that teeth evolved many times independently through co-option of such structures. However, the foundations of “inside-out” theory have been undermined fatally by critical reanalysis of the evidence on which it was based. Specifically, it has been shown that teeth develop from dermal, endodermal or mixed epithelia and, therefore, developmental

distinctions between teeth and dermal denticles are diminished. Furthermore the odontode-like structure of conodont elements has been shown to have evolved independently of dermal and internal odontodes. The tooth-like replacement encountered in thelodont pharyngeal odontodes has been shown to have evolved independently of teeth and tooth replacement and teeth have been shown to have evolved late within the gnathostome stem lineage indicating that it is probable, if not definitive, that teeth evolved just once in gnathostome evolution. Thus, the “inside-out” hypothesis must be rejected. The phylogenetic distribution of teeth and dermal denticles shows that these odontodes were expressed first in the dermal skeleton, but their topological distribution extended internally in association with oral, nasal and pharyngeal orifices, in a number of distinct evolutionary lineages. This suggests that teeth and oral and pharyngeal denticles emerged phylogenetically through extension of odontogenic competence from the external dermis to internal epithelia. Ultimately, internal and external odontodes appear to be distinct developmental modules in living jawed vertebrates, however, the evidence suggests that this distinction was not established until the evolution of jawed vertebrates, not merely gnathostomes.

INTRODUCTION

The diversity of jawed vertebrates is predicated on the two formative evolutionary innovations of teeth and jaws, the origins of which appear to be becoming increasingly unclear. It was not always so. Just a couple of decades ago a singular dogma hypothesized teeth to have evolved from the tooth-like dermal denticles that comprise or ornament fish scales, the topological distribution of which extended, through vertebrate phylogeny, from the external dermis to the oral cavity, adapted to a tooth function at the jaw margin. This “outside-in” hypothesis has been challenged by a series of fossil discoveries and evidence of differences in the development of external dermal denticles and internal denticles and teeth. This has led to the formulation of a so-called “inside-out” hypothesis, which posits that teeth and tooth-like structures inside and outside the mouth evolved independently of one another (Smith and Coates 1998, 2000,

2001; Johanson and Smith 2003, 2005; Smith 2003; Fraser et al. 2010; Fraser and Smith 2011; Smith and Johanson 2012). Furthermore, teeth are inferred to have evolved multiple times, once in each of the principal lineages of living and extinct jawed vertebrates, from edentate jawed ancestors (Smith and Johanson 2003; Johanson and Smith 2005). Here we examine the evidential basis of these competing hypotheses and consider their viability in light of new evidence on the development of teeth and scales in living and fossil jawed and jawless vertebrates.

TEETH FROM SCALES?

Similarities between teeth and external dermal denticles have been observed at least since the seminal studies of Agassiz, Owen, Williamson and Hertwig (Agassiz 1833–43; Owen 1843,

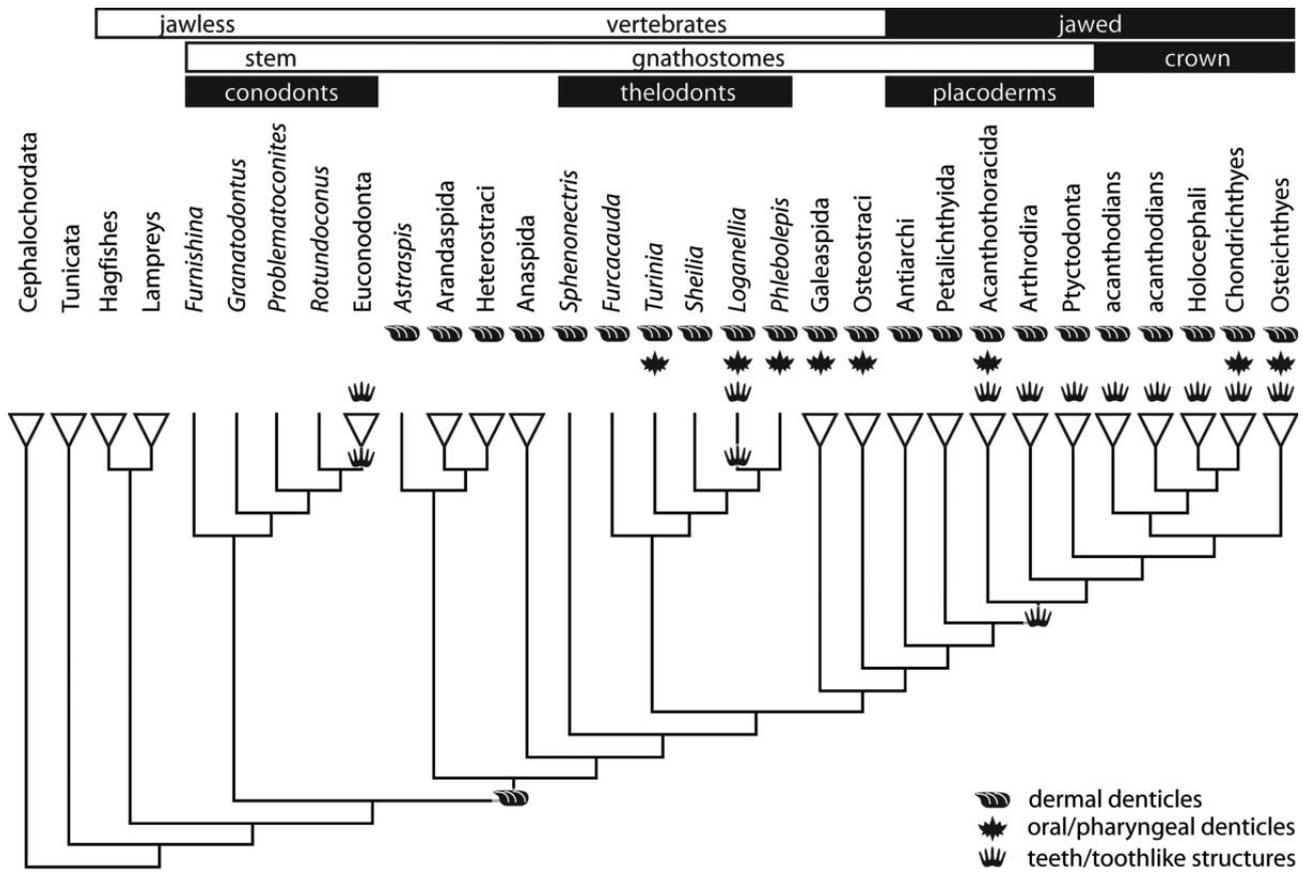


Fig. 1. Distribution of dermal denticles, oral/pharyngeal denticles and teeth/tooth-like structures, plotted on a phylogenetic tree of vertebrates. Phylogeny after Donoghue et al. (2000, 2008), Donoghue and Smith (2001), Brazeau (2009), Davis et al. (2012), Zhu et al. (2013), Murdock et al. (2013), Dupret et al. (2014).

1845; Williamson 1849, 1851; Hertwig 1874a, b, 1876, 1879, 1882). However, in attempting to decipher the evolutionary significance of these observations it is first necessary to establish some phylogenetic context (Fig. 1). Living vertebrates can be divided principally into the jawless and jawed vertebrates. Living jawless vertebrates are limited to the cyclostomes, the hagfishes and lampreys, which have keratinous replacement tooth-like structures (Dawson 1963; Lethbridge and Potter 1981; Krejsa et al. 1990). However, these are not generally considered homologous to the teeth of living jawed-vertebrates, which are comprised of dentine capped with enameloid and bone of attachment. Inferences of dental evolution drawn from living vertebrates are therefore limited to the jawed vertebrates, a grouping comprised of the chondrichthyans (sharks, rays, and chimaeroids) and the osteichthyans (bony fishes including tetrapods).

With an anthropic perspective, it has been something of a tradition to look to chondrichthyans for insights into our ancestry—though they are arguably no less specialized than are osteichthyans. Commonalities of structure and development are most especially obvious in chondrichthyans whose scales are

individual dermal denticles, comprised of a dentine pulp, enameloid cap and bone of attachment, just as are the oral and pharyngeal scales and, indeed, the teeth associated with the jaw. It was not a great inferential leap, therefore, for Hertwig (1874a) to posit that teeth had evolved through the co-option of dermal scales to a jaw location and a tooth function. These similarities were formalized within the lepidomorial (Stensiö 1961) and odontode (Ørving 1977) theories that identified teeth and dermal denticles as derivatives of a homologous developmental unit most popularly recognized as the odontode (Ørving 1977; Reif 1982; Donoghue 2002).

This “outside-in” hypothesis, that teeth evolved from scales, was effectively corroborated by the discovery in fossil jawless vertebrates that external dermal denticles have an evolutionary history that extends into the depths of vertebrate phylogeny (see, e.g., Donoghue and Sansom 2002). This is evidenced by a rich fossil record of jawless vertebrates, often referred to as the “ostracoderms” because they share an extensive dermal armor that, in most groups, includes dermal denticles with a dentine core, an enameloid-cap, and bone of attachment binding them to underlying bony plates. The component “ostracoderm” groups

are related by degree to the living jawed vertebrates and, in phylogenetic branching order, include the jawless heterostracans, anaspids, thelodonts, galeaspids, and osteostracans (Fig. 1). Hence, over a century of unchallenged dogma has made this a textbook view on the evolutionary origin of teeth from scales.

TURNING “OUTSIDE-IN” INSIDE OUT

A singular problem with the “outside-in” hypothesis is that no living or fossil vertebrate evidences tooth-like structures extending undistinguished from the external dermal skeleton to the mouth cavity. Blais et al. (2011) have shown tooth whorl-like scales associated with the outer margins of the mouth in extinct ischnacanthid acanthodians, but these organisms also possess a quite distinct dentition. Indeed, Reif, Smith and colleagues have highlighted that there is never an overlap in the morphology of external scales and internal scales and teeth (Reif 1973, 1978, 1980; Smith and Coates 1998, 2000, 2001). Furthermore, developmental data has been taken to evidence a fundamental distinction between teeth and oral scales, which have been posited to require endoderm for development, and external denticles that develop within the dermis (Smith and Coates 1998, 2000, 2001). A series of three fossil discoveries have been interpreted to challenge the classic “outside-in” hypothesis.

The first of these challenges stems from the reinterpretation of the extinct conodonts as jawless vertebrates. Conodonts are characterized by their mineralized tooth-like “elements” which are comprised of an enamel-like cap and a dentine-like base, which grew together appositionally in a manner analogous or homologous to vertebrate teeth and dermal denticles (Donoghue 1998). Phylogenetic analyses have indicated that conodonts diverged from the lineage leading to jawed vertebrates after it separated from the living jawless vertebrates, the cyclostomes (Donoghue et al. 2000). Conodonts appear tens of millions of years before the first evidence of a dermal skeleton in gnathostomes and, hence, they have been interpreted to indicate that tooth-like structures were present in the vertebrate mouth long before dermal denticles evolved (Smith and Coates 1998, 2000, 2001; Smith 2003; Fraser et al. 2010).

The relevance of conodonts and their tooth-like oral elements to the evolution of a vertebrate dentition was bolstered by the discovery of an oral skeleton in the extinct jawless thelodont *Loganellia* (Van der Bruggen and Janvier 1993). Thelodonts have a shark-like dermal skeleton comprised of individual denticles that are themselves composed of a dentine pulp, an enameloid cap and bone of attachment (Donoghue and Sansom 2002; Žigaitė et al. 2013). The internal scales appear to be identical, with the exception that they aggregated into compound scales through marginal accretionary growth. Those within the pharynx have been described to have grown through polarized growth such that the scales within the aggregates are all

aligned in parallel with their cusps pointing in the same direction (Smith and Coates 2000, 2001). This is reminiscent of the arrangement of teeth within the files of replacement tooth families on the jaws of sharks, and even more so of the fused tooth spirals of extinct acanthodians and Palaeozoic sharks (Van der Bruggen and Janvier 1993). Thus, thelodonts have been interpreted, like conodonts, to evidence the evolution of teeth before jaws, but also for the evolution of tooth-like patterns of replacement that would be later exapted by jawed vertebrates so that replacement teeth could be manufactured ahead of need (Smith and Coates 1998, 2000, 2001; Smith 2003).

The third challenge to dogma has come from analysis of tooth structure in early fossil jawed vertebrates. The earliest known jawed vertebrates are the extinct “placoderms,” long interpreted as the sister-lineage to the living jawed vertebrates, the chondrichthyans and osteichthyans (Schaeffer 1975, 1981; Janvier 1996). The “placoderms” have generally been considered edentate, having sufficed with bony gnathal elements that developed occlusal fangs and grooves. However, analysis of the most derived “placoderms” has revealed the presence of tooth-like structures composed of dentine and exhibiting of successional replacement (Johanson and Smith 2003, 2005; Smith and Johanson 2003). Similarly, only the most derived of the extinct acanthodians, variably interpreted as stem-gnathostomes, stem-osteichthyans or stem-chondrichthyans, possess teeth (Smith and Johanson 2003). Thus, teeth are interpreted to have evolved independently in “placoderms,” acanthodians, chondrichthyans and osteichthyans, all from edentate forebears, and all exhibiting evidence of successional replacement of the sort that is interpreted to have evolved in the pharyngeal scale complexes of the jawless thelodonts.

Evidently, teeth and oral scales have an evolutionary history that is long and distinct from that of external dermal denticles. They are similar developmental modules, as has been captured by odontode theory (Ørvig 1977; Reif 1982; Donoghue 2002), but the “inside-out” hypothesis views these similarities as having evolved independently. Proponents of this hypothesis argue that internal and external odontodes may share a (somewhat nebulous) “deep homology” (Johanson and Smith 2005). This view has been most clearly articulated by Fraser et al. (2010) who postulate that internal and external odontodes have an ancestry shared in a developmental module that gives rise to an unmineralized structure, such as a taste bud, which share aspects of their gene regulatory network. In this sense, internal and external odontodes can be considered in some manner paralogous.

TESTING THE “INSIDE-OUT” HYPOTHESIS

The evidential basis of the “inside-out” hypothesis has been established to contradict the “outside-in” hypothesis—that teeth, tooth patterning, and oral tooth-like structures, have an

evolutionary history that precedes jaws and, indeed, the dermal skeleton itself. It is based also on evidence of a key developmental distinction that, while external dermal denticles naturally require the dermis for development, endoderm is required for tooth development (Graveson et al. 1997; Imai et al. 1998; Smith and Coates 1998). However, every aspect of the evidence presented in support of the “inside-out” hypothesis has itself been challenged, through analyses of the pattern of development of teeth and tooth-like structures in fossil vertebrates, and of the processes of dental development in living jawed vertebrates.

Development—epithelial plurality

While teeth are generally considered ectodermal organs, developing in association with the epithelium of the oral ectoderm, it is clear that in some jawed vertebrates, teeth also occur in the pharynx in association with pharyngeal endoderm. Distinguishing between these two sources of epithelia is experimentally challenging, but Soukup et al. (2008) have demonstrated unequivocally that endoderm is not an essential aspect of tooth development. Exploiting a germline GFP-positive transgenic axolotl they tracked the germ layer origin of the cells contributing to the enamel-forming epithelia demonstrating that teeth derive not only from ectoderm or endoderm, but also from mixed ecto-endoderm epithelia. In so doing, Soukup et al. also effectively demonstrate the primacy of neural crest cells over epithelia in tooth fate. This evidence is no more compatible with the conventional conception of the “outside-in” hypothesis, than it is the “inside-out” hypothesis. However, it demonstrates, nevertheless, that there is no fundamental germ layer distinction between teeth and oral scales versus dermal denticles, as argued by proponents of the “inside-out” theory.

Additional support for the “inside-out” hypothesis would appear to have emerged with the discovery in zebrafish that dermal scales, unlike teeth (Kague et al. 2012), lack a neural crest contribution (Lee et al. 2013; Mongera and Nüsslein-Volhard 2013). However, zebrafish scales lack the odontode-derivatives that characterize the dermal skeleton of stemgnathostomes (Sire et al. 2009) and, thus, these studies are irrelevant to the question of whether teeth evolved *de novo* or through co-option of dermal denticles (Mongera and Nüsslein-Volhard 2013).

Convergent evolution of conodont and vertebrate mineralized skeletal tissues

Evidence from the fossil record, apparently incompatible with the “outside-in” hypothesis, has also recently been reinterpreted. In particular, this concerns the interpretation of conodonts as the earliest skeletonizing vertebrates and their oral tooth-like elements as evidence of an origin of tooth-homologues long before the appearance of a vertebrate dermal skeleton (Murdock

et al. 2013). This reinterpretation has emerged not from a revision of the phylogenetic position of conodonts, or changed views on the structural, topological and developmental similarities of conodont and vertebrate skeletal tissues (Sansom et al. 1992, 1994; Donoghue 1998; Donoghue and Aldridge 2001), though these are not uncontested (Blieck et al. 2010; Turner et al. 2010). Rather, the proposed homologies of conodont and vertebrate skeletal tissues have been challenged by insights into the evolutionary ancestry of conodonts and the origin of conodont element structure.

If anyone is troubled to think of conodonts they usually contemplate the euconodonts, or “true” conodonts. Euconodont elements have the characteristic tooth-like composition of an enamel-like cap and a dentine-like core, and the earliest euconodont elements are particularly tooth-like in their morphology (Fig. 2E). However, there is a long-standing hypothesis that euconodonts evolved from paraconodonts (Bengtson 1976; Miller 1980; Szaniawski 1987; Szaniawski and Bengtson 1993, 1998; Müller and Hinz-Schallreuter 1998) the elements of which are comprised solely of an equivalent of a euconodont element’s dentine-like base. This hypothesis of ancestry has been contested (Dzik 1976, 1986; Sweet 1988) and morphogenetic models for paraconodonts have been rejected as artifacts of invasive sample preparation (Bengtson 1976; Szaniawski 1987; Szaniawski and Bengtson 1993). Recently, Murdock et al. (2013) employed non-invasive synchrotron tomography to characterize the structure and morphogenesis of paraconodont and early euconodont elements, corroborating the hypothesis that euconodonts evolved from within the paraconodonts. This is evidenced by detailed similarities in the nature, arrangement, and morphogenesis of paraconodont elements and the dentine-like bases of euconodont elements (Fig. 2). The enamel-like crown is an innovation that characterizes and distinguishes euconodonts from their paraconodont relatives.

In so far as it goes, none of this has any impact on the homology of conodont and vertebrate skeletal tissues. To those already convinced, the structural, topological and developmental similarities of conodont and vertebrate skeletal tissues remain as compelling as ever. These characteristics are necessary to identify homology, but they are not sufficient; to demonstrate homology requires that enamel and dentine were present in the common ancestor of conodonts and other vertebrates. Since we now know that the enamel-like cap of euconodonts is an innovation peculiar to that lineage, we also know that it cannot have been present in the last ancestor that euconodonts and, for that matter, paraconodonts shared with other skeletonizing vertebrates. This leaves open the possibility that through paraconodonts, euconodonts inherited dentine from such an ancestor. However, the interpretation of the presence of dentine in euconodonts has relied heavily on the topological and developmental relationship between the basal tissue and the enamel-like crown (Donoghue 1998; Donoghue and Aldridge 2001; Dong et al. 2005). Odontoblast canaliculi have been

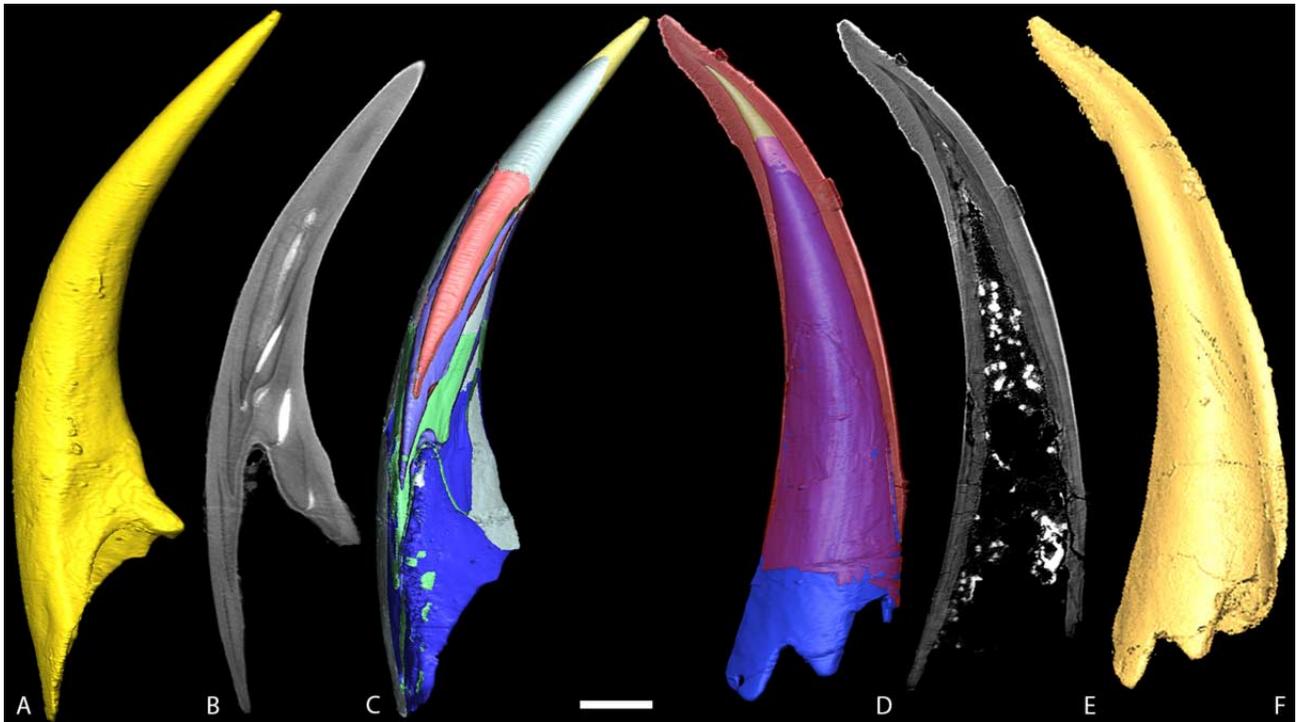


Fig. 2. Growth and microstructure of paraconodont and euconodont elements. (A–C) Paraconodont *Furnishina* sp., Threadgill Creek section, Wilberns Formation, 1,115 feet above base of Cambrian strata, central Texas, USA. (A) Surface model derived from SRXTM data. (B) Tomographic orthoslice of the same specimen showing the growth arrest lines. (C) Segmentation of the component growth stages with the oldest in yellow at the tip and the youngest in gray at the base (D–F) Euconodont *Proconodontus posterocostatus*, Gros Ventre Formation, Late Cambrian, Bighorn Mountains, Wyoming, USA. (D) Segmentation of the component growth stages of the basal body with the oldest in yellow at the tip and the youngest in blue at the base. (E) Tomographic orthoslice of the same specimen showing the growth arrest lines. (F) Surface model derived from SRXTM data. Relative scale bar represents 36 μm (A–C) and 53 μm (D–F).

documented only rarely in euconodont basal tissue (Sansom et al. 1994; Smith et al. 1996; Dong et al. 2005) and never in paraconodonts. Instead these lamellar and spheritic tissues have been interpreted as atubular and spheritic dentines, which they resemble (Smith et al. 1996; Donoghue 1998; Smith and Sansom 2000; Donoghue and Aldridge 2001; Dong et al. 2005). Yet, without evidence of development in association with an enamel homologue, the key plank supporting the interpretation of basal tissue as dentine-like, this conjecture of homology, too, must be rejected. Evidently, conodont elements represent an independent experiment in evolving a vertebrate dentition, and it has no relevance to debate over the origin of gnathostome teeth. Evidence of oral teeth evolving before dermal denticles must be rejected and with it a key piece of founding evidence for the “inside-out” hypothesis (Murdock et al. 2013).

Thelodonts with teeth—by any other name

The discovery of compound oral and pharyngeal denticles in the thelodont *Loganellia* was a remarkable discovery (Van der Bruggen and Janvier 1993), but direct evidence that these complexes accreted by polarized toothwhorl-like marginal addition has been wanting. Oral and pharyngeal scales have

been discovered subsequently in articulated remains of other species of thelodonts (Wilson and Caldwell 1998; Donoghue and Smith 2001; Märss and Wilson 2008), but they occur in aggregate only in *Loganellia*, *Pezopallichthyes*, and *Phlebolepis*. Rücklin et al. (2011) conducted synchrotron tomographic analyses of these scale aggregates from the mouth and pharynx of *Loganellia scotica* demonstrating that they grew through successive addition of individual denticles that have a histological composition identical to those of the dermal skeleton. Rücklin et al. (2011) showed that oral aggregates show no preferred pattern of addition around pioneer scales, while those of the pharynx show evidence of precisely polarized successive addition of individual denticles along a single vector, united by underlying sheets of acellular bony tissue that maintain the integrity of these compound elements. However, our subsequent analyses of additional material, carefully dissected from articulated remains of another specimen of *L. scotica* (Fig. 3), indicate that the topological distinction between two morphotypes is not as clear as has been suggested previously (Van der Bruggen and Janvier 1993).

Our original study (Rücklin et al. 2011) was based on disarticulated remains that had been acid-extracted from articulated individuals of *L. scotica* as part of the original study

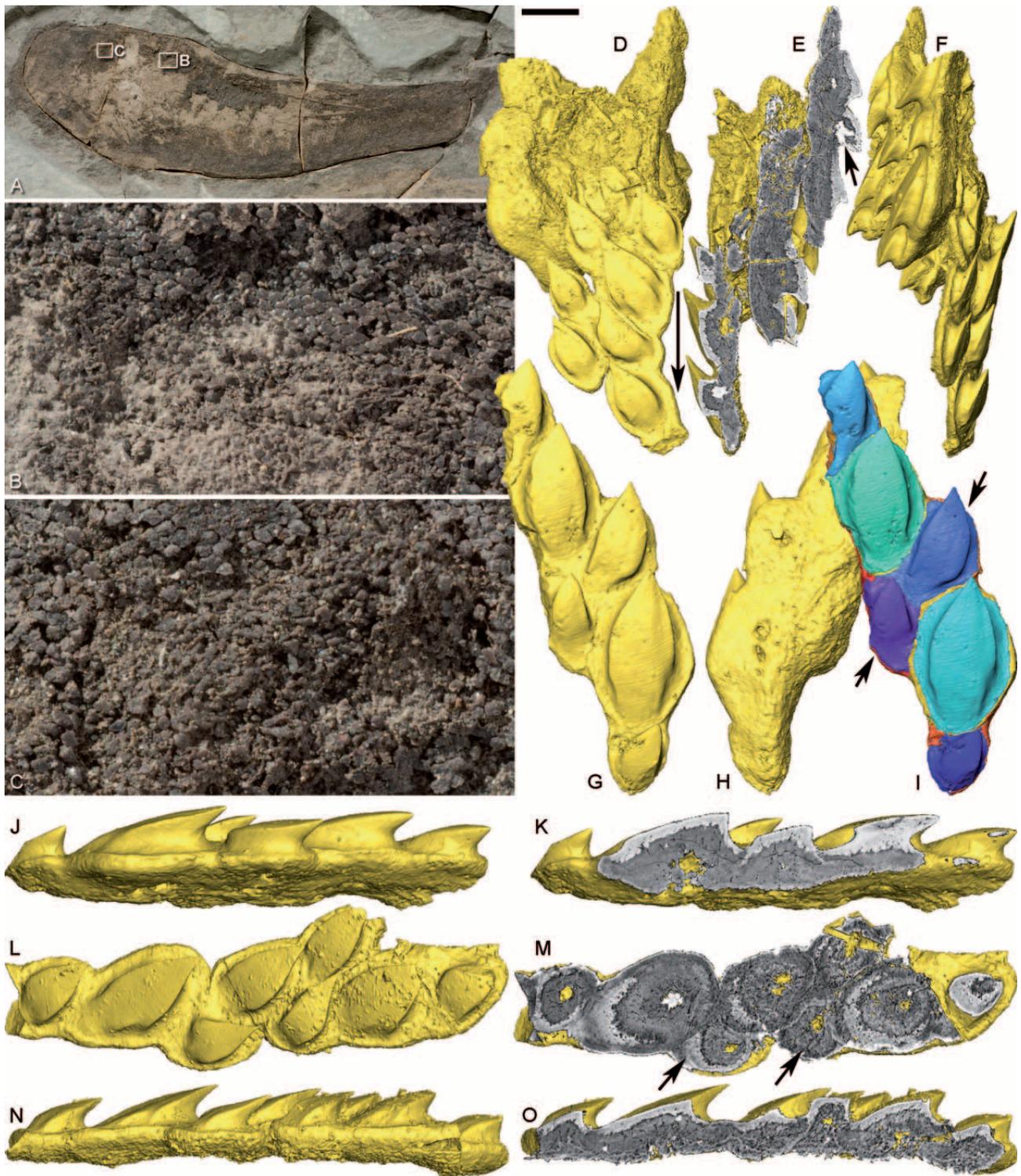


Fig. 3. *Loganellia scotica* from the Silurian of Scotland (MB.f.4013), morphologically complete specimen with internal scales in situ and detailed SRXTM images of internal scales. Overview (A), posterior pharyngeal area (B) and anterior pharyngeal area (C). Pharyngeal scale aggregate of polarized, sequentially added denticles and others with marginally added denticles (D–F). Unpolarized pharyngeal scale aggregate with denticles that differ in size (G–I). Elongated pharyngeal scale aggregate with sequentially added denticles and randomly added denticles (J–O). Long arrow indicates direction of polarized growth (D) and short arrows randomly added denticles (E, I, M). Relative scale bar represents 25 mm (A), 2.5 mm (B), 1.7 mm (C), 81 μm (D–F), 54 μm (G–I), and 57 μm (J–O).

by Van der Bruggen and Janvier (1993). We sampled compound denticle morphotypes assuming their topology as described in this study. However, we have subsequently manually dissected compound denticles directly from the oral and pharyngeal regions of an additional articulated specimen of *L. scotica*. This has shown that though polarized denticle aggregates occur in the pharyngeal region, they occur among a spectrum of otherwise unpolarized denticle aggregates such as that described previously from the oral region. For example, Figure 3, D–F shows an aggregate of scales in which polarized, sequentially added denticles occur in association with others that differ in size, and are added to their margins.

To be sure, the linear aggregates of pharyngeal denticles compare closely in structure and developmental pattern to the statodont toothwhorls seen in some Paleozoic sharks and acanthodians. As such, they merit consideration as rudimentary teeth, or at least evidence for the evolution of tooth-like patterns of successional replacement prior to the origin of jaws and, indeed, without their co-option to a tooth function. However, it has to be considered that this comparison is borne out only through judiciously selecting from among a greater range of more variable and less organized denticle aggregates, only those that are linear and exhibit polarized development.

Whether or not these structures are in any manner homologous to the teeth of living jawed vertebrates depends on whether it can be demonstrated that tooth-like patterning could have been inherited phylogenetically from the last common ancestor that *Loganellia* shared with dentate jawed vertebrates. The toothwhorl-like structures in the pharynx of *Loganellia* fail this test of conjunction since they appear to occur only in *Loganellia* (Fig. 1), and *Loganellia* is derived within the thelodont clade (Donoghue and Smith 2001; Wilson and Märss 2009). Furthermore, thelodonts are remote from clades that otherwise possess teeth or exhibit evidence of successional dental or tooth-like patterning (Donoghue and Smith 2001; Rücklin et al. 2011). Evidently, compound scales were not present in the oro-pharyngeal region of the last ancestor shared by thelodonts and gnathostomes. Thus, any similarity between oropharyngeal denticle development and gnathostome tooth replacement must be a consequence of convergence—not evidence that dental patterning evolved in the pharynx of jawless vertebrates prior to the origin of jaws.

“Placoderm” teeth and the origin of tooth replacement in jawed vertebrates

The view that the teeth of jawed vertebrates evolved convergently through the co-option to a tooth function of oral/pharyngeal denticles, inheriting *Loganellia*-like successional dental patterning, is also beginning to appear increasingly unlikely. This is not because claims of “placoderm” teeth are unfounded. Quite to the contrary, the presence of tooth-like histological structure, development and replacement has been

corroborated by high resolution tomographic analyses of arthropod “placoderms.” Indeed, claims that the tooth-like features associated with the bony jaws of arthropods are entirely superficial and mirror similar structures in the external dermal skeleton (Burrow 2003; Young 2003) have themselves been demonstrated to be false. Rücklin et al. (2012) have shown, for instance, that the tooth-like structures associated with the infamously jaw-like dermal pectoral spines of antiarchs are merely focal developments of compact bone and show no semblance of a tooth-like structure. However, the tooth-like structures associated with the mandibular “infragnathal” of arthropod “placoderms” have a clear dentine structure that developed in association with a looped vasculature and pulp, was bound to the underlying jaw ossification by an extensive bone of attachment, and that these teeth developed successively ahead of function. The supragnathal teeth, which occlude with their infragnathal counterparts, exhibit a common structure and display the same pattern of successional development. However, in both the infragnathals and supragnathals, these teeth lack a capping tissue of enamel or enameloid (Fig. 4, C, D, H, and F). It is not known whether the absence of a hypermineralized capping tissue represents a primitive or a derived condition since this may merely be associated with the parallel loss of dental tissues associated with the dermal skeleton seen in all of the principal lineages of “placoderms” (Giles et al. 2013).

The proposition that “placoderm” teeth are convergent on chondrichthyan and osteichthyan teeth assumed that each had evolved through the co-option of oral/pharyngeal denticle developmental units. Even edentate “placoderms”-like antiarchs show patterns of oral/pharyngeal denticle arrangement strongly reminiscent of tooth-like (especially shark-like) successional replacement (Johanson and Smith 2003, 2005). However, Rücklin et al. (2012) have shown that any semblance of teeth is entirely superficial since these structures show no structural similarity to teeth. Rather than composed of dentine and, perhaps, enameloid, where they have been investigated, they are comprised solely of bone. Thus, they do not even merit the descriptor “denticle” and they certainly cannot be considered manifestations of an odontode-like developmental unit co-opted in some lineages to a tooth function. Therefore these structures cannot be considered as supporting the “inside-out” hypothesis.

With the rejection of this hypothesis, the possibility of demonstrating phylogenetic continuity between the teeth of “placoderms” and crown-gnathostomes might be hopeless except for a recent game-changing revolution in our perception of the evolutionary relationships of early jawed vertebrates. Specifically, the long-standing dogma of “placoderm” monophyly (e.g., Goujet and Young 1995, 2004; Young 2010) has given way to a new phylogenetic milieu in which “placoderms” are perceived as a paraphyletic grade, with component lineages more or less closely related to crown-gnathostomes, reflecting the gradual assembly of gnathostome characters (Brazeau 2009; Davis et al. 2012; Zhu et al. 2013). Within this framework the

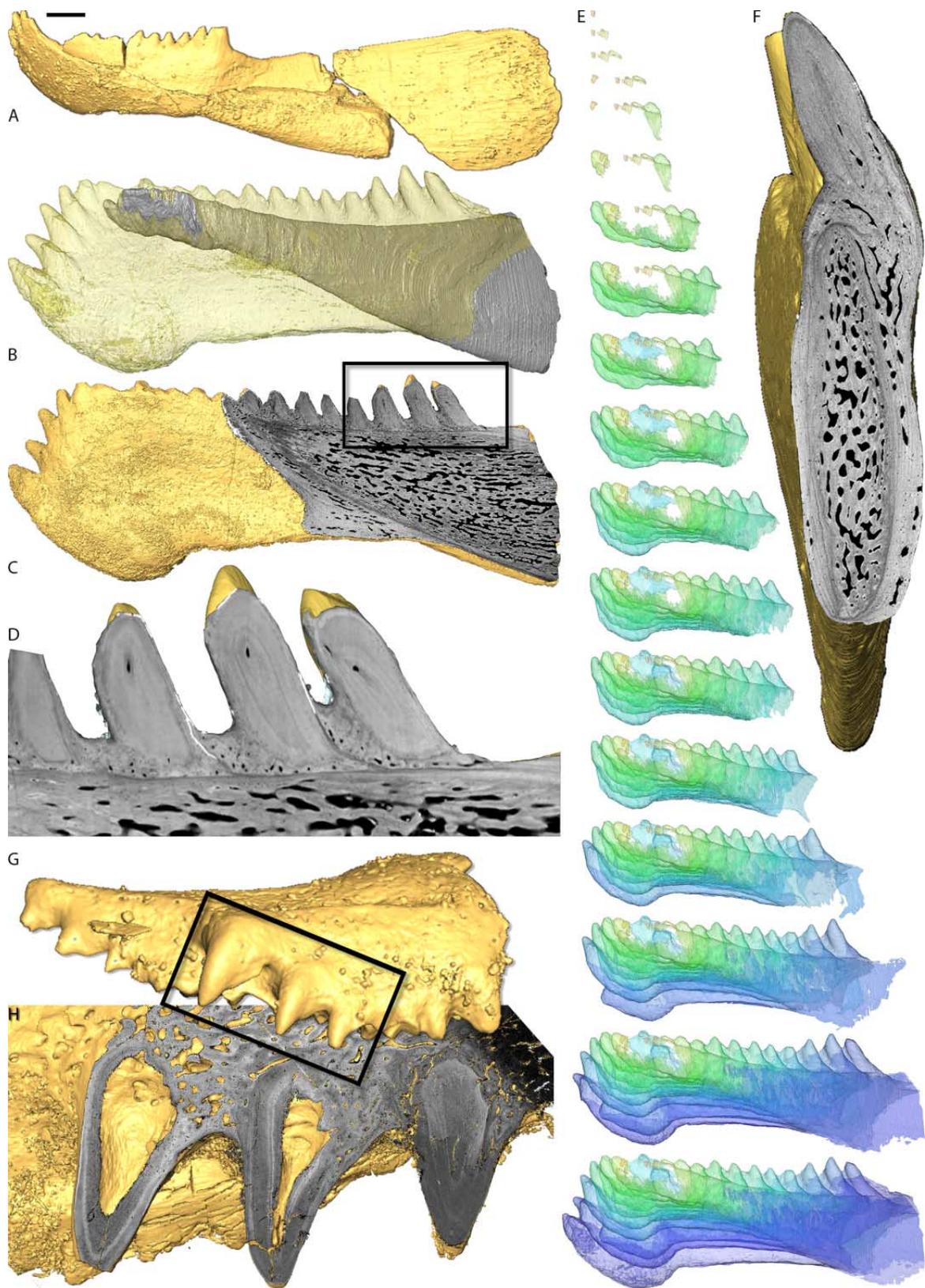


Fig. 4. Jaw elements of *Compagopiscis croucheri*, Late Devonian period, Gogo Formation, Western Australia (WAM 91.4.3). (A) Infragnathal, lateral view of the isosurface based on microCT data, (B) segmentation of the dental (transparent) and elongated jaw elements. Longitudinal section (C) and detailed view of sequential tooth addition (D). Upper jaw element, posterior supragnathal (G) and detailed longitudinal section showing the sequential tooth addition and infill of the pulp cavities with dentine (H). Virtual development reconstructed via sclerochronology in the dental element of the lower jaw (E). Vertical section through the lower jaw elements (F). Relative scale bar represents 1.3 mm (A), 0.9 mm (B, C); 257 μm (D, F), 135 μm (E), 0.75 mm (G), and 225 μm (H).

dentate arthrodirans, long perceived as a remote branch nested deep within a monophyletic grouping of “placoderms,” are now perceived as closely related to the living jawed dentate vertebrates (Zhu et al. 2013). As such, homology of arthrodiran “placoderm” and crown gnathostome teeth appears increasingly likely, if not yet a certainty (Rücklin et al. 2012; Smith and Johanson 2012).

DISCUSSION: IN SEARCH OF THE ONE TRUE TOOTH

Given the contemporary approach of testing homology through molecular signatures and networks of interacting regulatory genes, it seems obvious that, where analyses of fossil fish have failed, we should reach for developmental tests of competing hypotheses on the evolutionary origin of teeth. Unfortunately, testing between the traditional “outside-in” and the “inside-out” hypotheses of dental evolution through comparative development is difficult and maybe impossible since both hypotheses lead to the same predictions about the developmental characteristics of internal and external odontodes. Even the advocates of the “inside-out” hypothesis argue that teeth and dermal denticles are united in a “deep homology” (Johanson and Smith 2005). Thus, the gene regulatory controls on oral and extra-oral odontode development are predicted to share inherited characteristics, no matter how remote the “deep homology” (e.g. if it is rooted in an unmineralized sensory receptor, as Fraser et al. (2010) have argued), but they will also exhibit differences that have accumulated since that time. Though the “outside-in” hypothesis is predicated on a less remote origin of oral from extra-oral odontodes, associated with the origin of jawed vertebrates, it also predicts implicitly that the gene regulatory controls on teeth and dermal scale development will share inherited elements (rooted in dermal odontodes), as well as differences that have accumulated since they, as developmental modules, encountered different selection pressures and contingencies.

In theory, it might be possible to test the “outside-in” hypothesis by comparing the gene regulatory networks underpinning dermal scale development in a jawless vertebrate to those underpinning dermal scale and tooth development in a jawed vertebrate. If teeth evolved from dermal scales we might therefore anticipate that the GRNs of dermal scales and teeth in a jawed vertebrate would be more similar to one another than either are to the GRN underpinning dermal scale development in a skeletonizing jawless vertebrate. This is because the GRNs underpinning tooth and scale development in jawed vertebrates would, following “outside-in” theory, have diverged after the extension of odontogenic competence from the external dermis to the oropharynx, long after the origin of odontogenic competence in the earliest skeletonizing vertebrates. Conversely, following the “inside-out” hypothesis, we should anticipate the

GRNs underpinning dermal scale development in jawless and jawed vertebrates to be more similar to one another than either are to a tooth GRN. This follows, since their GRNs would have diverged, according to inside-out theory, in association with the independent origins of internal and dermal odontodes. In sum, inside-out theory predicts the divergence of internal and external odontode development programs at the base of the gnathostome stem-lineage while outside-in theory predicts divergence late in the gnathostome stem-lineage. Unfortunately, no such test can be realized since there are no living lineages of skeletonizing jawless vertebrates. It is only through comparative analysis of the development external odontodes in such an organism, to the development of internal and external odontodes in crown-gnathostomes, that these two scenarios could be discriminated. Thus, in attempting to decipher the evolutionary history of teeth we have no recourse, but to consider the phylogenetic distribution of oral and extra-oral odontodes in living and fossil vertebrates.

While it may not be possible to employ additional developmental tests to discriminate among the “outside-in” and “inside-out” hypotheses that seek to explain the evolutionary origin of teeth, we have shown that the evidential basis of the “inside-out” hypothesis has not withstood scrutiny. With the rejection of homology of conodont dental elements with oral denticles or with the teeth of jawed vertebrates, there is no longer any evidence that teeth have an evolutionary history that predates dermal denticles. Similarly, the idea that the oral/pharyngeal denticle aggregates of thelodonts reflect an origin of dental replacement patterning prior to the origin of teeth, and exapted to tooth function at the origin of jawed vertebrates, can also be rejected. Rather, the available evidence from the comparative odontology of living and fossil vertebrates, constrained by phylogeny, indicates unequivocally that odontodes are manifest first in vertebrate phylogeny in the external dermal skeleton of jawless vertebrates. There is evidence that odontodes occupied oral locations in at least some heterostracans, where they occur associated with oral plates, but here they appear entirely continuous in their distribution with the denticles of the external dermal skeleton (Purnell 2002). Similarly, as we have discussed, oral and pharyngeal denticles occur in a number of thelodonts (Fig. 1) but, again, they appear continuous in their distribution with the denticles in the external dermal skeleton; in most instances they are also unpolarized. There are denticles associated with the dorsal nasal opening of at least some galeaspid (Thanh et al. 1995). However, it is only in the osteostracans, those jawless vertebrates apparently most closely related to the jawed vertebrates, that oral odontodes occur associated with the median dorsal field of some derived taxa that do not appear to intergrade with the external dermal skeleton (e.g., Janvier 1985). It is unclear whether this is an autapomorphic peculiarity of these derived osteostracans, or foreshadows the modularization of oral versus extra-oral odontodes. However, the evidence in its totality indicates that

extra-oral odontodes are primitive and that odontogenic competence has extended from external to internal oral and pharyngeal epithelia during the assembly of the gnathostome bodyplan (Huysseune et al. 2009, 2010; Rücklin et al. 2011).

It remains unclear, however, whether our search for the evolutionary origin of teeth is a search for the evolutionary appearance of the one true tooth, or whether teeth evolved independently in a number of distinct lineages of jawed stem- and crown-gnathostomes through the cooption of oral/pharyngeal denticles to a tooth function (Johanson and Smith 2003, 2005; Smith and Johanson 2003). The case for a common origin of teeth early in the evolution of jawed vertebrates has been strengthened by the demonstration of successional dental development in arthropods “placoderms” and the revision of phylogenetic hypotheses which resolve arthropods as close relatives of crown-gnathostomes (Brazeau 2009; Davis et al. 2012; Zhu et al. 2013; Dupret et al. 2014). However, there remains uncertainty as to whether the ancestral crown-gnathostome had a dentition.

In particular, the nature of the dentition in acanthodians, which are now interpreted as stem-chondrichthyans (Zhu et al. 2013; Dupret et al. 2014), requires resolution. Blais et al. (2011) have argued for evidence of teeth evolving from scales based on the presence of tooth-like dermal scales associated with the oral margin in acanthodians, though these taxa clearly already possess a dentition distinct from these dermal scales. The only detailed study of acanthodian dental development infers a very peculiar model in which the teeth are focal developments of the dermal bone associated with the jaw (Ørvig 1973). It is very difficult to rationalize this model with the dentitions of osteichthyans and crown-chondrichthyans. Indeed, many lineages of the paraphyletic acanthodians are edentate (Denison 1979), raising the possibility that dentitions have evolved more than once within the chondrichthyans. However, this has to be considered within the context of phylogenetic hypotheses that are in a state of flux, not least since the knowledge of the anatomy of most acanthodians does not extend much beyond scale-studded silhouettes.

The nature, indeed the presence, of a dentition in the earliest osteichthyans is equally unclear, in part because of uncertainty surrounding the phylogenetic position of key taxa, and a paucity of knowledge of their anatomy – for many taxa this is limited to the morphology of individual scales (Friedman and Brazeau 2010). However, it depends also on the correct discrimination of jaw elements for analysis (Botella et al. 2007; Cunningham et al. 2012) and the will to recover data on the structure and development of tooth-like elements from fossils where such data are already known to be present.

Ultimately, however, the search for the evolutionary origin(s) of teeth will depend not merely on the presence and absence of tooth-like structures among the clades of jawed stem- and crown-gnathostomes, but also on tests of their homology. This requires more than similarity in structure, development and location, but

demonstration that the distribution of such structures is congruent with the evolutionary relationships of the groups in which they are encountered. As such, the origin of teeth will depend critically not just on insights from the comparative odontology of living and fossil vertebrates, but also on resolution of uncertainty concerning the phylogenetic relationships among these organisms.

CONCLUSIONS

The evolutionary origin of teeth has been the subject of controversy concerning whether teeth evolved in some manner from the external dermal denticles (the traditional “outside-in” hypothesis), or whether teeth evolved entirely independently (the “inside-out” hypothesis). The foundations of the inside-out hypothesis have been undermined by the reinterpretation of the key pieces of evidence on which it was originally based. Teeth do not require endoderm for development; they can develop from endodermal, dermal and mixed epithelia. Evidence that oral/pharyngeal odontodes emerged before dermal odontodes has been rejected with the reinterpretation of conodont elements as a wholly independent experiment in evolving a vertebrate dentition. Likewise, the tooth-like pharyngeal odontode replacement encountered in a jawless thelodont appears to have evolved independently in this lineage, and does not evidence the origin of tooth replacement mechanisms before teeth. Finally, the hypothesis that teeth evolved independently in disparate lineages of jawed vertebrates through parallel cooption of oral/pharyngeal denticles to a tooth function, has been dealt a fatal blow by the discovery that denticle-like structures in placoderms are not odontode derivatives, and changed phylogenies which suggest that the dentate placoderms are close relatives of living jawed and dentate gnathostomes. Rather, it appears that internal odontodes emerged repeatedly in oral, pharyngeal and nasal regions of extinct jawless stem-gnathostomes, continuous with the dermal scale cover in most instances. This suggests that the traditional “outside-in” hypothesis is the best explanation for the evolutionary origin of teeth through expansion of odontogenic competence from the external dermis to internal epithelia. This is likely a consequence of the primacy of neural crest-derived ectomesenchyme, rather than the origin of the epithelia, in odontode induction.

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