

# THE DEVELOPMENT OF A BIOLOGICAL NOVELTY: A DIFFERENT WAY TO MAKE APPENDAGES AS REVEALED IN THE SNOOT OF THE STAR-NOSED MOLE *CONDYLURA CRISTATA*

KENNETH C. CATANIA<sup>1,\*</sup>, R. GLENN NORTHCUTT<sup>2</sup> AND JON H. KAAS<sup>1</sup>

<sup>1</sup>Department of Psychology, Vanderbilt University, 301 Wilson Hall, Nashville, TN 37240, USA and <sup>2</sup>Department of Neurosciences, 0201, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0201, USA

\*e-mail: Catania@ctrvax.vanderbilt.edu

Accepted 8 July; published on WWW 30 September 1999

## Summary

The nose of the star-nosed mole *Condylura cristata* is a complex biological novelty consisting of 22 epidermal appendages. How did this new set of facial appendages arise? Recent studies find remarkable conservation of the genes expressed during appendage formation across phyla, suggesting that the basic mechanisms for appendage development are ancient. In the nose of these moles, however, we find a unique pattern of appendage morphogenesis, showing that evolution is capable of constructing appendages in different ways. During development, the nasal appendages of the mole begin as a series of waves in the epidermis. A second deep layer of epidermis then grows under these superficial epidermal waves to produce 22 separate, elongated epidermal cylinders embedded in the side of the mole's face. The caudal end of each cylinder later erupts from the face and rotates forward to project rostrally, remaining attached

only at the tip of the snout. As a result of this unique 'unfolding' formation, the rostral end of each adult appendage is derived from caudal embryonic facial tissue, while the caudal end of each appendage is derived from rostral facial tissue. This developmental process has essentially no outgrowth phase and results in the reversal of the original embryonic orientation of each appendage. This differs from the development of other known appendages, which originate either as outgrowths of the body wall or from subdivisions of outgrowths (e.g. tetrapod digits). Adults of a different mole species (*Scapanus townsendii*) exhibit a star-like pattern that resembles an embryonic stage of the star-nosed mole, suggesting that the development of the star recapitulates stages of its evolution.

Key words: ontogeny, phylogeny, evolution, recapitulation, homology, star-nosed mole, *Condylura cristata*.

## Introduction

Animal appendages come in a variety of forms, such as the legs, wings and antennae of arthropods, the fins of fish, the limbs and digits of mammals and the defensive spines of sea urchins, to name a few. Despite a wide variety in structure and function, all these appendages originate in the same basic way, as outgrowths of the body wall (for reviews, see Panganiban et al., 1997; Shubin et al., 1997) or as subdivisions of outgrowths in the case of tetrapod digits (Hamburger and Hamilton, 1951; Hinchliffe and Johnson, 1980). Perhaps this is not too surprising, since recent studies reveal a remarkable conservation of the regulatory genes and signaling molecules that underlie early appendage development (Averof and Cohen, 1997; Basler and Struhl, 1994; Ferrari et al., 1995; Panganiban et al., 1994, 1995, 1997; Popadic et al., 1998; Shubin et al., 1997). The conservation of these regulatory elements across metazoan phyla suggests that new appendages may have arisen primarily from the redeployment of ancient developmental mechanisms (Panganiban et al., 1997; Raff, 1996; but see also Gerhart and Kirschner, 1997a; Williams,

1998). This raises basic questions about the process and course of evolution. Does the invention of new methods of appendage morphogenesis represent a major hurdle to the process of evolution? Or has it simply been most efficient to re-use and modify existing developmental pathways?

One way to address these questions is to examine the development of novel and recently evolved animal appendages to see whether they make use of conserved mechanisms of morphogenesis. The star-nosed mole (*Condylura cristata*) possesses just such a set of appendages in a ring around its snout. The star-nosed mole is a eutherian mammal thought to have diverged from other moles in the last 30 million years (Moore, 1986; Skoczen, 1993). Its nose is surrounded by 22 fleshy and mobile appendages that are not homologous to body-wall extensions in other species. They are unique not only in their location and appearance, but also in their function. They form a touch organ of unparalleled complexity and acuity (Catania, 1995a, 1996). The star functions much like a tactile eye, with a small but high-resolution pair of central appendages

and a number of larger, low-resolution peripheral appendages (Catania and Kaas, 1995, 1997).

One might ask whether these nasal structures are comparable as 'appendages' to the body-wall extensions of other metazoans. Though of relatively recent origin, an examination of their anatomy reveals them to be elaborate structures that integrate a number of tissue systems for their sensory functions (Catania, 1995a, 1996). The outer surface of each appendage is an epidermal layer covered with complex tactile sensory organs termed Eimer's organs. Each appendage is densely innervated by a separate branch of the infraorbital nerve, which runs through its center. The appendages are moved by a series of tendons that attach to muscles on the side of the face, and each appendage has its own blood supply (Grand et al., 1998). In addition, the touch centers of the central nervous system of the star-nosed mole are subdivided to represent sensory information from each appendage in a separate module (Catania and Kaas, 1995, 1996). Thus, these appendages are clearly on a par with other animal appendages in complexity, and their evolution has involved the integrated manipulation of multiple tissue systems, including the dermis, epidermis, tendons, muscles and peripheral nervous and circulatory systems.

Were established mechanisms of appendage morphogenesis co-opted to produce this recently evolved set of appendages? We examined the development of the nasal appendages in embryonic and juvenile moles and found that they form in a manner unlike any developmental sequence previously described.

### Materials and methods

To examine the development of the nasal appendages that form the star, we collected a developmental series of embryos from wild-caught star-nosed moles (*Condylura cristata* Illiger 1811). For post-natal stages, captured pregnant moles were housed in our laboratory where (for the first time) they gave birth and raised litters of young in captivity. Star-nosed moles are seasonal breeders and give birth to a single litter of young in the spring (Eadie and Hamilton, 1956). We were able to collect pregnant females during March and April using Sherman traps under Pennsylvania scientific collecting permit number COL00087. The day of fertilization is unknown because mating took place in the wild, and all embryos were therefore staged by crown-rump length. Moles were killed with Nembutal (110 mg kg<sup>-1</sup>), and embryos were fixed in a mixture of 1% paraformaldehyde and 2% glutaraldehyde in phosphate buffer (for scanning electron microscopy or serial sections) or in 4% paraformaldehyde in phosphate buffer (for neuronal tract tracing). Postnatal development was examined in newborn moles from females that gave birth and raised young in the laboratory. Pregnant females were kept in moist peat moss, given free access to water and fed night-crawlers (*Lumbricus terrestris*) *ad libitum*. Juvenile moles were killed and fixed as above.

Tissue from each stage was examined under the scanning

electron microscope and serial thin-sectioned for light microscopy. In addition, innervation patterns were determined using the lipophilic neuronal tracer 1,1'-dioctadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate (DiI) (Molecular Probes Inc.) and a scanning confocal microscope. For scanning electron microscopy, specimens were dehydrated through an ethanol series to 100% ethanol, and then transferred into a critical-point dryer where the alcohol was replaced with liquid carbon dioxide. After drying, specimens were sputter-coated with gold and viewed in a Cambridge 360 Stereoscan scanning electron microscope.

To examine the histology of the nose, tissue was post-fixed in 1% osmium tetroxide, dehydrated in a graded ethanol series and transferred into propylene oxide. Tissue was embedded in Embed 812 epoxy resin (EM Sciences). Semi-thin serial sections (1–2 µm) were cut transversely on an LKB ultramicrotome and stained with 1% Toluidine Blue. To determine innervation patterns, the tip of the snout was removed from selected paraformaldehyde-fixed specimens, and DiI crystals were applied to exposed nerve fascicles. After 4 weeks of transport at room temperature, the tissue was examined under the scanning confocal microscope. All procedures were approved by the Vanderbilt University Animal Care and Use Committee and are in compliance with NIH guidelines for the care and use of laboratory animals.

### Results

In this study, the development of the nasal appendages is examined for a series of five prenatal (Figs 1–3) and three postnatal stages (Fig. 4). The star is formed by 11 symmetrical pairs of appendages surrounding the nostrils. The appendages are numbered from 1 to 11 on each side of the face, beginning with the dorsal-most appendage. Figs 2 and 3 show DiI-filled and labeled nerve fibers for selected specimens, illustrating important stages in the development of innervation patterns.

The earliest stage described is the 9 mm crown-rump length embryo (Fig. 1A). At this stage, there is no sign of the nasal appendages that will eventually form the star. The tip of the nose appears smooth and uniform in the scanning electron microscope. Transverse sections through the nasal epidermis (nose sections, Fig. 1A) also reveal a smooth thin epidermis approximately 40 µm in thickness surrounding the underlying dermis and mesenchyme. At this early stage, the epidermis is contacted by many fascicles of nerve fibers that form a dense subcutaneous network (Fig. 2A). At high magnification (not shown), growth cones are visible at the distal ends of the nerve fascicles. But there is no indication, however, from either the epidermal tissue or the innervation patterns of how or where the appendages of the star will later form.

The first signs of the nasal appendages are seen in 11 mm embryos (Fig. 1B). A series of rostro-caudally oriented swellings appears along the side of the face. Each swelling is the precursor to a single nasal appendage, and each consists of simply a 'buckling' or slight wave in the epidermis. The swellings form first along the midline, and later laterally so that

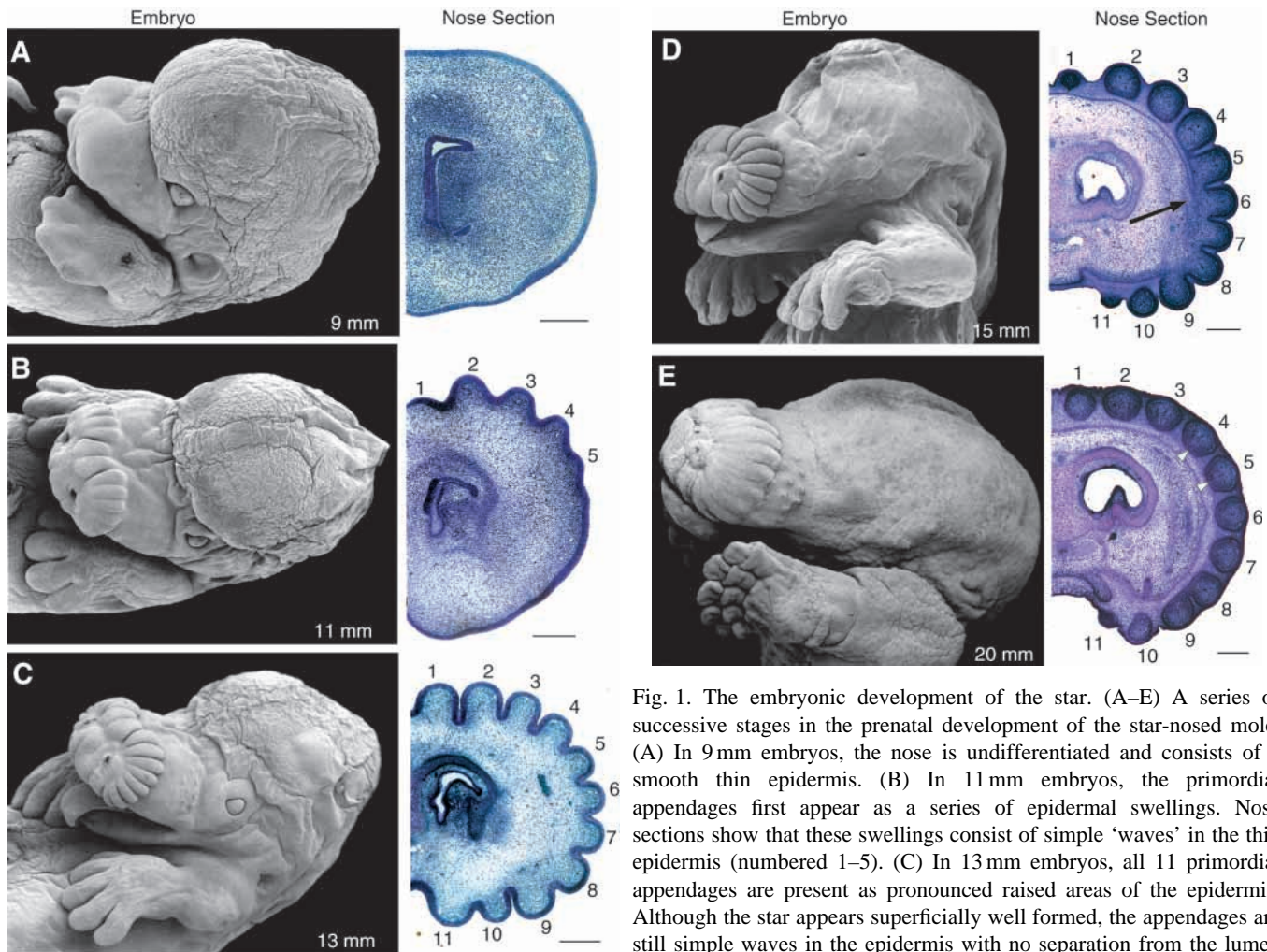


Fig. 1. The embryonic development of the star. (A–E) A series of successive stages in the prenatal development of the star-nosed mole. (A) In 9 mm embryos, the nose is undifferentiated and consists of a smooth thin epidermis. (B) In 11 mm embryos, the primordial appendages first appear as a series of epidermal swellings. Nose sections show that these swellings consist of simple ‘waves’ in the thin epidermis (numbered 1–5). (C) In 13 mm embryos, all 11 primordial appendages are present as pronounced raised areas of the epidermis. Although the star appears superficially well formed, the appendages are still simple waves in the epidermis with no separation from the lumen of the central snout. (D) In 15 mm embryos, the bottom wall of each

appendage forms as a new deep layer of epidermis (arrow) extends to separate each epidermal wave from the dermis and mesenchyme of the snout. (E) Just before birth, in 20 mm embryos, there is a proliferation of cells in the epidermis of the snout, and each separate appendage forms a cylinder embedded in the hypertrophied epidermis (arrowheads). At the same time, the external pattern of appendages on the snout is obscured. Scale bar, 250  $\mu$ m.

the precursors to appendages 1–5 and 10 and 11 appear before the swellings for the lateral appendages. Transverse sections through the snout reveal the epidermal waves that make up the appendages (Fig. 1B). At these early stages, the myelin-poor nerve fascicles are not apparent in light microscopy, but DiI labeling reveals a very dense innervation of the epidermis. The crest of each epidermal wave is contacted by numerous nerve fascicles that project from the center of the snout (Fig. 2B). The simple conformational change of the epidermis into crests and troughs seems to be the first foundation for the selective elimination or preservation of innervating nerve fibers. Where the waves have formed, nerve fibers densely contact the crests of the waves and are sparse in the troughs (Fig. 3A1), but in the lateral areas where the waves have not yet formed, there is a uniform distribution of nerve fibers (Fig. 3A2).

In 13 mm and 15 mm embryos, all 22 appendages of the star are clearly apparent (Fig. 1C,D). Here, the star appears remarkably adult-like, as if the appendages were folded against

the side of the face, but this external appearance is an illusion. In 13 mm embryos, the appendages are still simple waves or swellings of the epidermis (see nose section, Fig. 1C) and are open to the mesenchyme of the central snout. The epidermis of the waves has become more densely innervated from ingrowing fibers, and the nerve fascicles are well segregated to individual crests in the epidermis (Figs 2C, 3B). At high magnification, there is not yet any sign of the orderly arrangements of nerve fibers that characterize the punctate epidermal sensory organs in the adult skin (Catania, 1995a). Instead, the nerve fascicles end in amorphous collections of terminals extending numerous filopodia and often distinct growth cones (arrowhead, Fig. 3B2).

During these stages (13–15 mm crown–rump), a complex sequence of tissue growth and movement takes place, separating each of the epidermal waves into a distinct unit with a lumen and surrounding walls. A new deep layer of epidermis begins to grow beneath the innervated epidermal waves. This



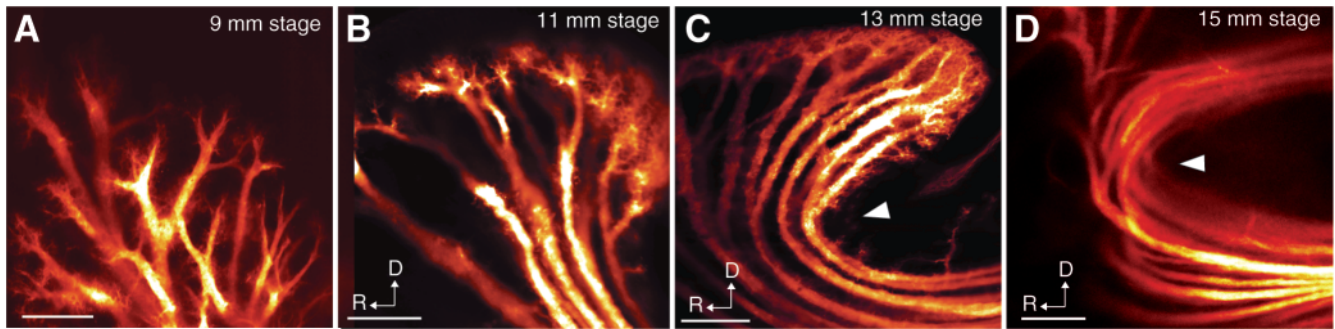


Fig. 2. The innervation of the nose at selected developmental stages, revealed by the lipophilic neuronal tracer DiI. (A) In 9 mm embryos, there is a uniform innervation of the epidermal walls that form the snout, but no pattern that reflects the appendages. (B) In 11 mm embryos, the crests of a series of epidermal waves (see Fig. 1B) are densely innervated from below. The innervation of a single epidermal crest is viewed from the side, showing the many nerve fascicles terminating at the skin surface. (C) The bottom epidermal wall of each appendage forms from caudal to rostral. In 13 mm embryos, just prior to the growth of this lower layer of epidermis (see arrowhead, Fig. 1D), the deep portion of the innervating fascicles begins to move rostrally (arrowhead). (D) In 15 mm and later embryos, the innervating nerve fascicles must make a complete 'U-turn' to go around the deep layer of epidermis and reach their peripheral skin targets (see also Fig. 1E).

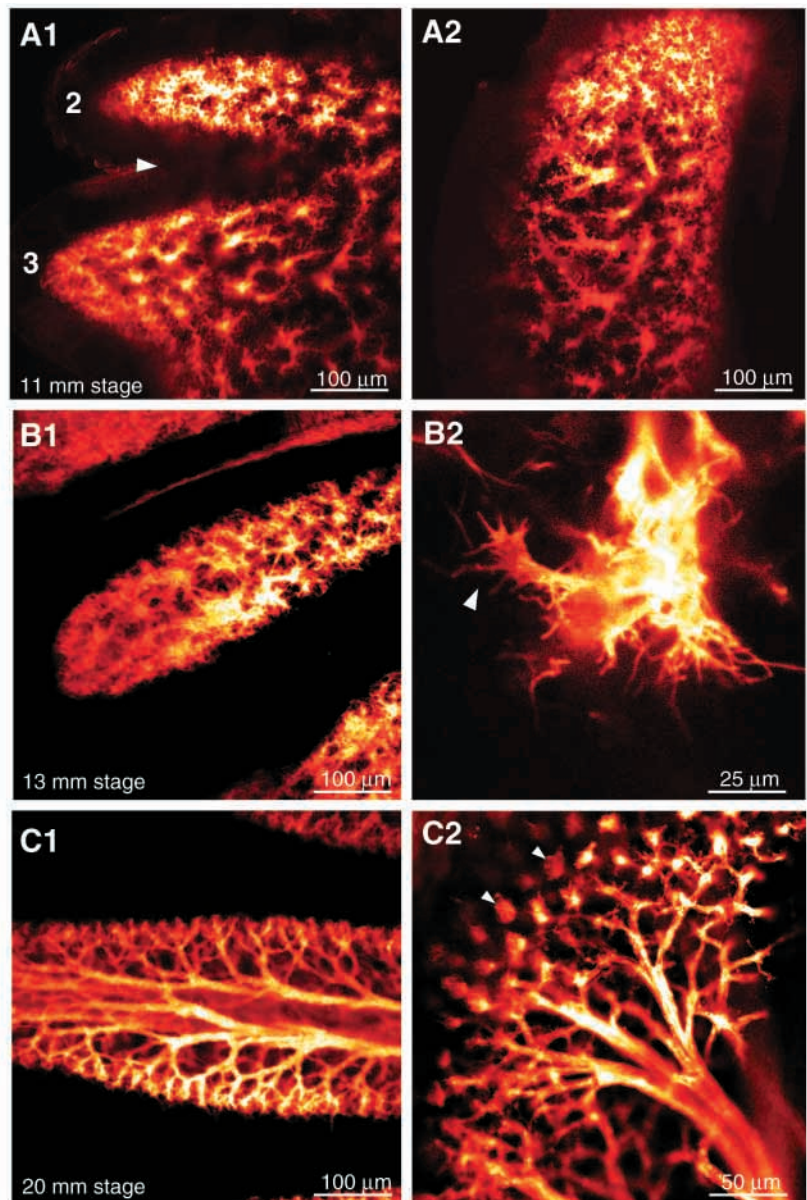


Fig. 3. Refinement of innervation patterns during the course of development. (A1,2) In 11 mm stage embryos, two different areas of the nose reveal the beginnings of appendage-specific innervation patterns. In A1, an area where the epidermal crests and troughs have formed shows dense innervation of the crest and loss of innervation from the trough (arrowhead) between the precursors to appendages 2 and 3. In a more lateral area (A2), where crests and troughs have not yet formed, there is a uniform pattern of innervation. (B1,2) At a later stage, the innervation of the crests is more refined (B1). Higher magnification (B2) reveals the presence of numerous filopodia and growth cones (arrowhead). The adult pattern of punctate neurite distribution has not yet emerged. (C1,2) In 20 mm embryos, the epidermal cylinders of each appendage have formed, and the internal walls are very densely innervated by many nerve fascicles (C1). A punctate distribution of neurites has formed in a pattern similar to the adult distribution (C2). The clusters of nerve terminals reflect the future distribution of epidermal sensory organs in the adult (see Catania, 1995a,b and arrowheads in Fig. 6).

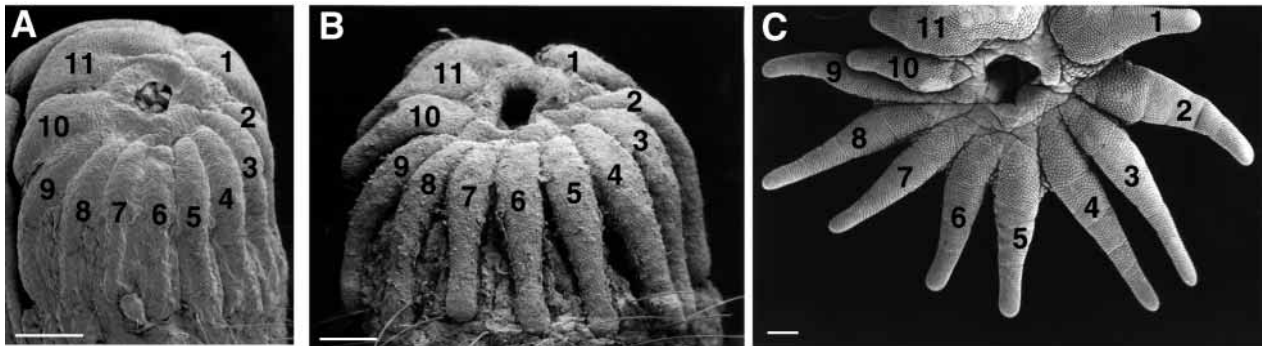


Fig. 4. Postnatal development of the star. (A) In newborn moles, the appendages remain embedded in the epidermis of the face. (B) At approximately 1 week, the appendages emerge from the side of the face as the surrounding epidermis sloughs. (C) Shortly thereafter the appendages detach and bend forward into the adult pattern. As a result of this 'backward' formation, the rostralmost tissue of the adult nose is derived from the caudalmost tissue of the embryonic nose (see Fig. 5C). Scale bars, 500  $\mu$ m.

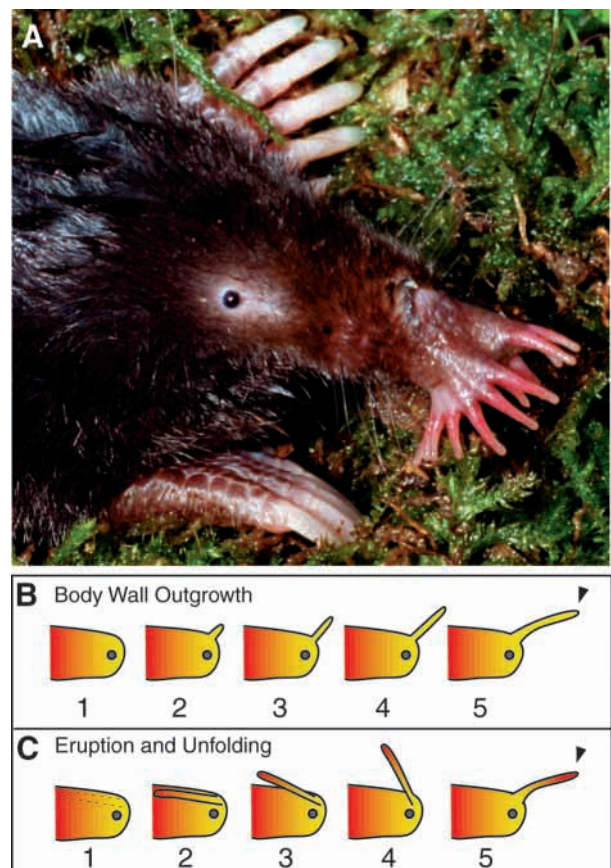
layer forms the bottom wall of each appendage, separating the connective tissue of the dermis within each appendage from the dermis and mesenchyme that form the center of the snout (arrow, Fig. 1D). The deep epidermal layer grows from the posterior snout towards the anterior snout, and the troughs of the waves simultaneously extend slightly downward to meet and fuse with the new layer of epidermis. At the same time, the deep portions of the innervating nerve fibers move ahead of the extending epidermis to maintain contact with their targets (arrowheads, Fig. 2).

Towards the end of this process, in 20 mm embryos (just prior to birth), there is a proliferation of epidermal cells that seems to involve the entire rostral snout. As a result, each primordial appendage forms a separate epidermal cylinder within the hypertrophied epidermis (arrowheads, Fig. 1E) open to the deep connective tissue only at the rostral end, near the nares. The many nerve fascicles innervating an appendage must pass through this small remaining opening, making a 'U-turn' to reach targets within the appendage (arrow, Fig. 2D).

With these processes complete, the basic outline of the appendages is in place. Each now consists of a separate cylindrical unit with a densely innervated epidermal wall (Fig. 3C1). At this stage (20 mm), the nerve terminals that contact the skin surface form a series of clusters in a periodic pattern consistent with the distribution of sensory organs seen later in the adult (arrowheads, Fig. 3C2).

In newborn moles (Fig. 4A), the appendages remain embedded in the facial epidermis, giving an external appearance that is surprisingly less adult-like than previous embryonic stages. But the nasal appendages soon emerge from

Fig. 5. An adult mole and two ways that nasal appendages might develop. (A) A star-nosed mole emerges from its tunnel, showing the unusual star consisting of 22 fleshy appendages. The appendages are densely innervated epidermis, have a rich blood supply and are moved by tendons that connect to facial muscles. (B) A simplified diagram of appendage formation through body-wall outgrowth. Some variation of body-wall outgrowth is a basic stage in the formation of nearly all animal appendages. This mechanism may be conserved from a Precambrian ancestor of modern metazoans (see text). (C) The unique developmental sequence for the nasal appendages of the star. Rather than developing by outgrowth, they begin as longitudinal cylinders embedded in the side of the face. The cylinders of epidermis subsequently emerge and rotate forward, so that the original embryonic orientation of the precursor tissue is reversed. The colors denote the embryonic origins of the tissues that make up the appendages in each of the two processes. During the formation of the nasal appendages, caudal embryonic tissue of the snout (red) detaches and becomes the most rostral tissue on the adult nose. This is contrasted with the result of body wall outgrowth (arrowheads).





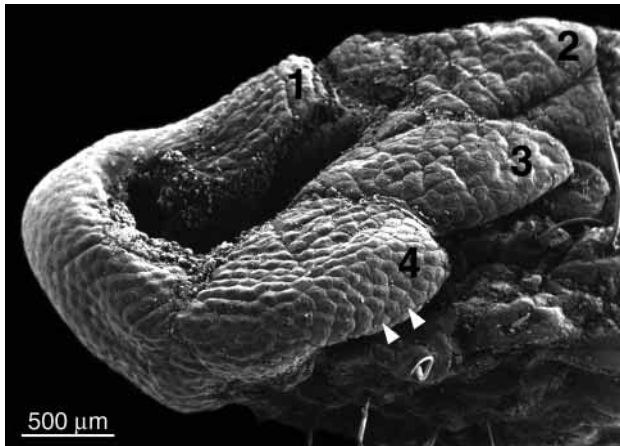


Fig. 6. The adult nose of Townsend's mole (*Scapanus townsendii*) showing separate raised subdivisions of epidermis on the side of the face. The star may have evolved from a similar ancestral condition through progressive elevation of the raised epidermis, which contains numerous sensitive touch organs called Eimer's organs (small raised domes, arrowheads). The same small receptor organs cover the appendages of the star-nosed mole (Catania, 1995a,b). The receptors in *Scapanus townsendii* are elevated relative to the nearby caudal epidermis that does not contain sensory organs, which may allow for increased tactile receptivity for the sensitive touch organs. Compare the appearance of the nose of this adult mole with the early embryonic stage in Fig. 1B.

the side of the face, presumably through programmed cell death, as the once hypertrophied epidermis sloughs from around the appendages (Fig. 4B). Roughly 1 week after birth, the appendages break free from the side of the face and rotate forward to form the adult star (Figs 4C, 5A).

To summarize this complex developmental sequence (Fig. 5C), the nasal appendages form and emerge from the side of the face and then rotate forward to form the adult pattern. As a result of this 'backwards' formation, the rostral tissue of the appendages is derived from caudal embryonic tissue of the snout while the caudal tissue of the appendages is derived from the rostral embryonic tissue of the snout. There is essentially no outgrowth phase in this developmental sequence, and it results in a reversal of the original embryonic orientation of the tissue that forms the appendages. This developmental sequence is manifestly different from the formation of other animal appendages (Fig. 5B).

### Discussion

The development and evolution of animal appendages have been extensively studied in a number of species. In each case, animal appendages originate as outgrowths of the body wall. Well-known examples include the embryonic formation of arthropod appendages and the tetrapod limb (for an account of postnatal horn and antler development, see Goss, 1983). The legs, antennae, mouthparts and wings of insects form from imaginal disks that telescope outwards to produce each respective structure (Gerhart and Kirschner, 1997b). In

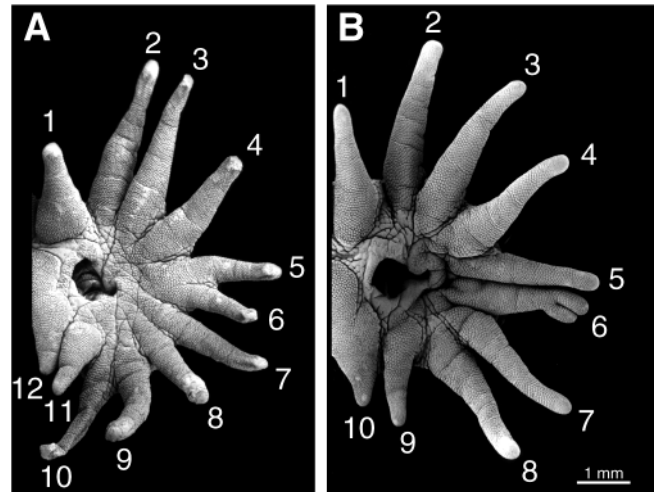


Fig. 7. Two examples of common abnormalities of the star. (A) A nose with an extra nasal appendage on the animal's left side. Sudden duplications such as this could provide the basis for progressive elaboration from an ancestor with fewer appendages (see Fig. 6). (B) A nose missing a nasal ray (although there is a partial duplication of the tip of ray 6). We estimate that approximately 5–6% of the population has an abnormal nose. Clearly, there is relatively widespread variation of the nasal anatomy upon which selection might act, although we have not explored the genetic basis of these variations.

tetrapods, a limb bud extends from the body wall to successively produce differentiated cells in a proximal-to-distal sequence of limb elements (Hinchliffe and Johnson, 1980). Later, the individual digits are initially sculpted by the selective death (Hamburger and Hamilton, 1951) of intervening cells in the handplate, and this is followed by growth (Martin, 1990). Several stages of tetrapod digit formation are shown alongside the nose formation in the mole embryos (Fig. 1A–C) and their development can be contrasted with nasal appendage development.

Tetrapod digits form by separation from a flattened outgrowth or handplate and retain their original embryonic orientation. In contrast, the nasal appendages of the star-nosed mole unfold from the side of the face. This process requires the growth of a new deep layer of epidermis to form both the bottom wall of the appendages and the remaining side of the face from which the appendages later emerge. It also requires the rearrangement of innervating fibers (Fig. 2) and the rich blood supply to the appendages (not shown), and results in the previously described reversal of the orientation of precursor tissues (Fig. 5C). What might account for such an unusual, and seemingly inefficient, way of constructing the nasal appendages?

A remarkable feature of appendage development is the conservation of gene expression during morphogenesis in different phyla. Homologous genes provide anterior–posterior (*hedgehog/Sonic hedgehog*) and proximal–distal (*fringe/Radical fringe*) patterning information in both insects and tetrapods (Shubin et al., 1997). The *Distal-less* homeotic gene

or its homologue are expressed during appendage formation in diverse animal phyla, e.g. during the formation of echinoderm tube feet, onychophoran lobopodia, tetrapod limbs, insect appendages and sea urchin spines (Panganiban et al., 1997). These studies (Panganiban et al., 1997; Raff, 1996; Shubin et al., 1997) suggest that the genetic machinery for appendage formation is phylogenetically ancient and may have helped signal and regulate the formation of body-wall outgrowths in a Precambrian ancestor.

In the star-nosed mole, however, the development of the recently evolved nasal appendages suggests precursors of a different form, such as sheets of sensory receptors or 'proto-appendages' on the side of an ancestor's snout, which became progressively elevated over successive generations. Such a recapitulatory argument (Dawkins, 1987; Gould, 1977; Northcutt, 1990) is appealing, but would be more compelling with fossil evidence or supporting comparative data. Although no fossilized mole noses have been found, nearly all other extant moles have sheets of the same complex sensory receptors (Eimer's organs) making up the epidermis of their snout in a small, uniform epithelium around the unspecialized nares (Catania, 1995b; Quilliam, 1966; Shibanai, 1988). But in one North American species (Townsend's mole *Scapanus townsendi*), however, we discovered a set of 'proto-appendages' extending caudally on the snout (Fig. 6). The resemblance of the adult nose of this mole to the early embryonic stages of the star-nosed mole (Fig. 1B) is striking. This species might be called the *Archaeopteryx* of moles, representing fairly well what would be expected of an intermediate form between the least specialized moles and the enigmatic star-nosed mole. Of course, this extant species is not an ancestor of the star-nosed mole and, in fact, studies of mole phylogeny suggest that its nose subdivisions evolved independently of the appendages of the star-nosed mole (Whidden, 1995; Yates and Moore, 1990). But *Scapanus townsendii* does illustrate the tenability of such a hypothetical ancestral species. Taken together with the developmental data, it seems reasonable to propose that the star evolved through the progressive elevation of strips of sensory receptors on the side of the face, and that the stages of these ancestral ontogenies have been conserved and built upon to produce the star. The result is a novel developmental sequence that seems to recapitulate many stages of ancestral anatomy (Gould, 1977).

*Scapanus townsendi* has only eight subdivisions on its face, fewer than the 22 modules (11 per side) found on the star-nosed mole. Once the basic developmental mechanism for appendage production was in place, however, they might simply be duplicated to produce the 22 appendages of the star. Such meristic changes are a common occurrence in evolution (Raff, 1996) since duplication of somatic modules provides an efficient means of adding to the body plan without the need to reinvent the regulatory elements that produce each module. In fact, duplications of nasal appendages are common in wild populations of star-nosed moles (Fig. 7). We estimate that over 5% of the population has an abnormal nose, consisting of either extra or fewer nasal appendages (K. C. Catania,

unpublished data). This demonstrates that sufficient variability exists upon which selection might act to increase (or decrease) the number of nasal appendages. It also shows that there seems to be a surprisingly high degree of variation in this presumably critical structure, which contrasts with a much lower rate of mutation in the tetrapod limb (Castilla et al., 1996; Zguricus et al., 1998). Darwin (1859) made special note of such examples in support of the Origin of Species, stating "in those cases in which the modification has been comparatively recent and extraordinarily great... we ought to find the generative variability, as it might be called, still present in a high degree". The argument was that selection has had less time to 'fix' the characteristics of recently evolved complex structures, which are the recent product of selection for variations.

#### *Flexibility or historical constraint?*

At one level, these results demonstrate the flexibility of evolutionary processes. While there seems to be a remarkable conservancy in the basic mechanisms of appendage development across metazoan phyla, there is also clearly the potential for new developmental solutions to this ancient morphogenetic problem. It has been stated that it is difficult to think up anything very different from some actual product of evolution (Maynard Smith, 1990). Here, we find a product of evolution (the developmental sequence of the star) that we might find hard even to imagine prior to this investigation. This is perhaps because the developmental sequence of the nasal appendages is not only unusual, but might also be considered inefficient. To use an old example, it is difficult to envisage an engineer proposing such a literally 'backwards' manner for development of the nasal appendages.

Thus, at a different level of analysis, the development of the nose seems to reflect the constraints imposed by biological history (Gould, 1977, 1979, 1980). Perhaps there are more efficient ways to produce the nasal appendages, such as the outgrowth of the body wall seen for other metazoan appendages, but evolution cannot plan ahead, it can only 'tinker' with the materials at hand (Jacob, 1977). The ontogeny of the star provides a classic example of the outcome of such tinkering. While different developmental stages may be altered during the course of evolution (for a review, see Gould, 1977), several early stages of the development of the nose of the mole may be recalcitrant to change. For example, the crests of the epidermal waves may produce the neurotrophic factors that attract extending neurites to their appropriate appendage-specific targets. This possibility seems to be strengthened by the presence of growth cones extending numerous filopodia beneath the crests, up to at least 13mm stage embryos (Fig. B2). This 'crest-and-trough' stage may have existed in the ancestor, which presumably had a snout similar to *Scapanus townsendi* (Fig. 6). If this and other stages of the development were critical during ancestral ontogenies, as seems likely, then alteration of the nose may have occurred primarily through modifications at the terminal end of ancestral ontogenies, resulting in the apparent recapitulation of nasal appendage evolution during development.

This work was supported by NIH grants MH58909 to K.C.C. and NS 16446 to J.H.K.

### References

- Averof, M and Cohen, S. M.** (1997). Evolutionary origin of insect wings from ancestral gills. *Nature* **385**, 627–630.
- Basler, D. and Struhl, G.** (1994). Compartment boundaries and the control of drosophila limb pattern by hedgehog protein. *Nature* **368**, 208–214.
- Castilla, E. E., Lugarinho da Fonseca, R., Dutra, M., Bermejo, E., Cuevas, L. and Martínez-Frías, M.** (1996). Epidemiological analysis of rare polydactylies. *Am. J. Med. Genet.* **65**, 295–303.
- Catania, K. C.** (1995a). The structure and innervation of the sensory organs on the snout of the star-nosed mole. *J. Comp. Neurol.* **351**, 536–548.
- Catania, K. C.** (1995b). A comparison of the Eimer's organs of three North American moles: the star-nosed mole (*Condylura cristata*) the hairy-tailed mole (*Parascalops breweri*) and the eastern mole (*Scalopus aquaticus*). *J. Comp. Neurol.* **354**, 150–160.
- Catania, K. C.** (1996). Ultrastructure of the Eimer's organ of the star-nosed mole. *J. Comp. Neurol.* **36**, 343–354.
- Catania, K. C. and Kaas, J. H.** (1995). The organization of the somatosensory cortex of the star-nosed mole. *J. Comp. Neurol.* **351**, 549–567.
- Catania, K. C. and Kaas, J. H.** (1996). The unusual nose and brain of the star-nosed mole. *BioSci.* **46**, 578–586.
- Catania, K. C. and Kaas, J. H.** (1997). Somatosensory fovea in the star-nosed mole: behavioral use of the star in relation to innervation patterns and cortical representation. *J. Comp. Neurol.* **387**, 215–233.
- Darwin, C.** (1859). *On the Origin of Species by Natural Selection, or the Preservation of Favored Races in the Struggle for Life*. London: John Murray. 191pp.
- Dawkins, R.** (1987). *The Blind Watchmaker*. New York: W. W. Norton & Co. Inc. pp. 91–92.
- Eadie, W. R. and Hamilton, W. J.** (1956). Notes on reproduction in the star-nosed mole *J. Mammal.* **37**, 223–231.
- Ferrari, D., Sumoy, L., Gannon, J., Sun, H., Brown, A. M., Upholt, W. B. and Kosher, R. A.** (1995). The expression pattern of the Distal-less homeobox-containing gene *Dlx-5* in the developing chick limb bud suggests its involvement in apical ectodermal ridge activity, pattern formation, and cartilage differentiation. *Mech. Dev.* **52**, 257–264.
- Garstang, W.** (1922). The theory or recapitulation: a critical restatement of the biogenic law. *Zool. J. Linn. Soc. Lond.* **35**, 81–101.
- Gerhart, J. and Kirschner, M.** (1997a). *Cells, Embryos and Evolution*. Malden, MA: Blackwell Science Inc. pp. 574–575.
- Gerhart, J. and Kirschner, M.** (1997b). *Cells, Embryos and Evolution*. Malden, MA: Blackwell Science Inc. pp. 555–567.
- Goss, R. J.** (1983). *Deer Antlers: Regeneration, Function and Evolution*. New York: Academic Press.
- Gould, S. J.** (1977). *Ontogeny and Phylogeny*. Cambridge, MA: Harvard University Press.
- Gould, S. J.** (1979). The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. *Proc. R. Soc. Lond. B* **205**, 581–598.
- Gould, S. J.** (1980). *The Panda's Thumb*. New York: W. W. Norton & Company.
- Grand, T., Gould, E. and Montali, R.** (1998). Structure of the proboscis and rays of the star-nosed mole, *Condylura cristata*. *J. Mammal.* **79**, 492–501.
- Hamburger, V. and Hamilton, H. L.** (1951). A series of normal stages in the development of the chick embryo. *J. Morph.* **88**, 49–92.
- Hinchliffe, J. R. and Johnson, D. R.** (1980). *The Development of the Vertebrate Limb. An Approach through Experiment, Genetics and Evolution*. Oxford: Oxford University Press.
- Jacob, F.** (1977). Evolution and tinkering. *Science* **196**, 1161–1166.
- Martin, P.** (1990). Tissue patterning in the developing mouse limb. *Int. J. Dev. Biol.* **34**, 323–326.
- Maynard Smith, J.** (1990). Concluding remarks. In *Organizational Constraints on the Dynamics of Evolution* (ed. J. Maynard Smith and G. Vida), pp. 433–437. Manchester: Manchester University Press.
- Moore, D. W.** (1986). Systematic and biogeographic relationships among the Talpinae (Insectivore: Talpidae). PhD dissertation, Albuquerque, University of New Mexico, USA.
- Northcutt, R. G.** (1990). Ontogeny and phylogeny: A re-evaluation of conceptual relationships and some applications. *Brain Behav. Evol.* **36**, 116–140.
- Panganiban, G., Irvine, S. M., Lowe, C., Roehl, H., Corley, L. S., Sherbon, B., Grenier, J. K., Fallon, J. F., Kimble, J., Walker, M., Wray, G. A., Swalla, B. J., Martindale, M. Q. and Carroll, S. B.** (1997). The origin and evolution of animal appendages. *Proc. Natl. Acad. Sci. USA* **94**, 5162–5166.
- Panganiban, G., Sebring, A., Nagy, L. and Carroll, S.** (1995). The development of crustacean limbs and the evolution of arthropods. *Science* **270**, 1363–1366.
- Panganiban, G., Nagy, L. and Carroll, S. B.** (1994). The role of the *Distal-less* gene in the development and evolution of insect limbs. *Curr. Biol.* **4**, 671–675.
- Popadic, A., Panganiban, G., Rusch, D., Shear, W. A. and Kaufman, T. C.** (1998). Molecular evidence for the gnathobasic derivation of arthropod mandibles and for the appendicular origin of the labrum and other structures. *Dev. Genes Evol.* **208**, 142–150.
- Quilliam, T. A.** (1966). The mole's sensory apparatus. *J. Zool., Lond.* **149**, 76–88.
- Raff, R. A.** (1996). *The Shape of Life*. Chicago: University Chicago Press.
- Shibanai, S.** (1988). Ultrastructure of the Eimer's organs of the Japanese shrew mole *Urotrichus talpoides* (Insectivora, Mammalia) and their changes following infraorbital axotomy. *Anat. Anz. Jena* **165**, 105–129.
- Shubin, N., Cliff, T. and Carroll, S.** (1997). Fossils, genes, and the evolution of animal limbs. *Nature* **388**, 639–648.
- Skoczen, S.** (1993). New records of *Parascalops*, *Neurotrichus* and *Condylura* (Talpinae, Insectivora) from the Pliocene of Poland. *Acta Ther.* **38**, 125–137.
- Whidden, H. P.** (1995). The comparative myology of North American moles with comments on the phylogeny of the Talpidae. PhD dissertation, University of Massachusetts, Amherst, USA.
- Williams, T. A.** (1998). *Distalless* expression in crustaceans and the patterning of branched limbs. *Dev. Genes Evol.* **207**, 427–434.
- Yates, T. L. and Moore, D. W.** (1990). Speciation and evolution in the family Talpidae (Mammalia: Insectivora). In *Evolution of Subterranean Mammals at the Organismal and Molecular Levels*. New York: Wiley-Liss. pp. 1–22.
- Zguricus, J., Bakker, W. F., Heus, H., Lindhout, D., Heutink, P. and Hovious, S. E.** (1998). Genetics of limb development and congenital hand malformations. *Plast. Reconstr. Surg.* **101**, 1126–1135.