

NEWS AND COMMENTARY

Evodevo

Darwin's finch beaks, *Bmp4*, and the developmental origins of novelty

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For the past 25 years, a cadre of evodevotees has been struggling to unify the fields of evolution and development. A recent paper published in the journal *Science* by Abzahnov *et al* (2004) reports on the role of the growth factor *Bmp4* during the evolution in the beak morphology of Darwin's finches on the Galápagos Islands. These data show that evolutionary changes to the developmental program of large- versus small-beaked species of Darwin's finch arise from shifts in the heterochronic – timing of ontogenetic events – and heterotopic – spatial expression of ontogenetic events – expression of *Bmp4*.

Stephen J Gould (1977) popularized the term heterochrony, which now serves as a mantra chanted at evodevo journal clubs around the globe. If Gould were alive today, he would undoubtedly be raving about the latest evodevo findings on *Bmp4*.

Heterotopy (Edelman, 1987) and heterochrony (Gould, 1977) capture the five-dimensions of ontogeny and phylogeny: the three spatial dimensions of the developing embryo and the two temporal dimensions of development and evolution. It is no wonder that the synthesis of evolution and development is so difficult to achieve. Einstein only had to worry about the four dimensions involved in the fabric of space and time.

Intriguingly, Abzahnov *et al* (2004) show that heterochronic manipulations of *Bmp4* expression during chick development can reproduce the comparative patterns observed among Darwin's finches. The investigators first attached the chicken *Bmp4* gene to a retroviral vector, RCAS, to allow them to infect a group of cells in a specific layer of developing cells and thus precociously express the *Bmp4* gene. Mesenchymal versus ectodermal cells can be targeted with the retroviral construct because the virus does not cross the basement membrane separating these two cell layers.

Mesenchyme cells of chicken embryos infected with the RCAS:*Bmp4* construct

at stage 23 to 24 precociously express *Bmp4* at stage 26 rather than at stage 29 as is normally the case. Such heterochronic shifts yield a chick embryo that develops into the large-beaked morphology characteristic of the aptly named *Geospiza magnirostris*, which likewise expresses *Bmp4* earlier in mesenchymal cells than any of the other members of the ground finch genus.

What is even more intriguing is the effect of a heterotopic shift in the expression of *Bmp4* in different cell layers. If the same RCAS:*Bmp4* construct is used to infect ectodermal cells of the developing beak, the effect achieved on beak morphology of chick embryos – smaller and narrower beaks – is opposite to that achieved by infection of mesenchymal cell layers. Such heterochronic and heterotopic expression of *Bmp4* provide a parsimonious way to achieve both the svelte-beaked form of the most ancestral of the ground finch (*Geospiza*) group of Darwin's finches, *G. difficilis*, as well as the robust-beaked form of *G. magnirostris*.

Abzahnov *et al* (2004) further confirmed that the changes in beak morphology among Darwin's finches were not associated with two of the regulators of *Bmp4*, *sonic hedgehog* (*Shh*) and *fibroblast growth factor 8* (*Fgf8*). The junction where expression of these two regulatory genes meet on the developing cranium has been shown to drive the out-pocketing of cells that eventually develops into beak and to also induce expression of *Bmp4* (Abzahnov and Tabin, 2004).

Even though *Shh* and *Fgf8* interact to control the proper location of *Bmp4* expression on the cranium and thus beak morphology, variation in *Shh* and *Fgf8* were not correlated with differences between large- and small-beaked species of Darwin's finches. The authors did find that a mesenchymal injection of a viral construct with the gene *Noggin*, which antagonizes *Bmp4* signaling, dramatically reduced the size of the

upper beak of the chick. This result does not rule out potential epistatic interactions of other regulatory genes, but it does narrow the search to those that specifically affect *Bmp4* gene expression.

These findings elucidate the developmental origin of an adaptive radiation that serves as the textbook example of evolution. More importantly, it brings us one step closer to understanding how morphological diversity can be achieved with a minimum amount of informational change. The fact that the same growth factor, when applied to mesenchyme versus ectoderm, can achieve completely opposite morphologies provides us with a partial answer to the paradox of the genome. How can the complex morphology of a human require only the coordinated expression of 30 000 genes? The combination of heterochronic and heterotopic changes in the regulation of single genes provides an infinite set of topological shifts to evolve a limitless set of morphological diversity.

The achievement of an evodevo synthesis in a classic example of evolution like Darwin's finches is dramatic. It quickens the blood and warms the hearts of evodevotees, myself included. The insights on development and evolution associated with *Bmp4* are tantalizingly. They bring us closer to smashing the conceptual iron curtain that has been erected in recent years between the fields of evolution and molecular developmental biology. A trend has been emerging in Universities to split biology departments along these lines. Fortunately collaboration in science does not require close spatial proximity, unlike the close proximity involved in inductive developmental interactions.

Even though natural selection on Darwin's finches is still intense (Grant and Grant, 2002), most of the evolved changes in the regulation of *Bmp4* have occurred in the remote past when each member of the ground finch genus first evolved, and thus are inaccessible to us in the present day. One more step that remains to be demonstrated is the role of natural selection in specifically shaping *Bmp4* or its gene regulators.

Perhaps, the answer to this question lies in the elucidation of *Bmp4* expression in a species that simultaneously exhibits both small-, large-, and mega-beaked forms such as the African seedcracker, *Pyrenestes ostrinus* (Smith, 1993, 1997). In African seedcrackers, the small-, large- and mega-billed forms arise from a simple Mendelian factor

(Smith, 1993), and the implication is that such Mendelian variation should be due to *Bmp4* expression. Whether such within-species polymorphism contributed to the morphological radiation of Darwin's finches in the remote past remains unclear. However, such intraspecies polymorphisms will become very useful in our search for the link between proximate causes of development and ultimate causes of natural selection. Thus, elucidating the heterochrony and heterotopy involved in intraspecies

polymorphisms should be the next step, since the action of natural selection in shaping beak shape and perhaps the modifiers and regulators of *Bmp4* is ongoing (Smith, 1993). The findings on Darwin's finches are likely to be general for vertebrates. Selection on *Bmp4* has been demonstrated in African cichlids (Terai *et al.*, 2002; Albertson *et al.*, 2003), another spectacular adaptive radiation of vertebrates.

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