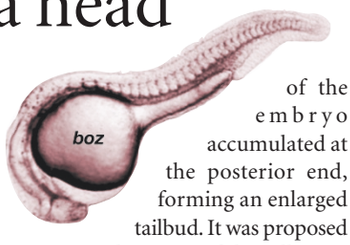
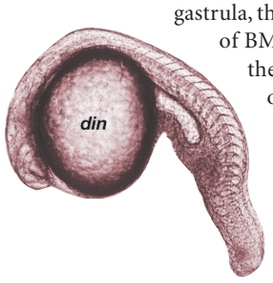
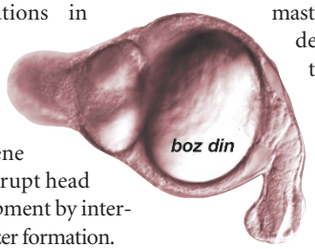
DEVELOPMENT

How to get a head

In recent years, considerable progress has been made in elucidating the genetic pathways underlying head development. The mechanisms are highly conserved through evolution and, as Manzanares *et al.* recently reported in *Nature*, many of the genes that have been elaborated for vertebrate head development also have functional homologues in more primitive organisms that lack head structures, such as *Amphioxus*. An essential requirement for head induction is the correct specification of neural ectoderm in the gastrulating embryo, which in turn relies on suppression of bone morphogenetic protein (BMP) signalling. In the zebrafish gastrula, there is a gradient of BMP activity, with the highest levels observed ventrally. Ectopic dorsal BMP signalling results in ventralization of the embryo and loss of neural tissue and other anterior structures, whereas BMP inhibition causes dorsalization of the embryo with excessive production of neural tissue. BMP antagonists such as Chordin and Noggin are secreted from the dorsal (Spemann's) organizer. Mutations in genes involved in Nodal signalling, including *squint* and *cyclops*, or in the homeobox gene *bozozok* (*boz*), disrupt head and trunk development by interfering with organizer formation.







Although the effects of some of these mutations are quite severe, no single mutation is known to abolish formation of anterior structures completely. However, as Gonzalez *et al.* have recently shown in *Genes and Development*, mutations in just two genes — *boz* and the Chordin gene *chordino* (*din*) — act synergistically to prevent head and trunk formation. In the *boz din* mutant, most of the cells of the embryo accumulated at the posterior end, forming an enlarged tailbud. It was proposed that most of the cells normally destined for the neural lineage had been respecified as nonneural ectoderm. This was confirmed by the dorsal expansion of nonneuronal ectoderm marker *gata3* expression at the expense of the expression domain of the neural marker *HuC*. Although the embryos showed a generalized increase in apoptosis, this could not explain the selective loss of dorsoanterior tissues. Furthermore, to show that excessive BMP signalling was responsible for the loss of anterior structures, the authors introduced the *swirl*^{tc300} (*swr*) mutation, which downregulates BMP signalling, into *boz din* mutants. As predicted, most anterior structures were restored in the *boz din swr* triple mutants.

The authors propose a model in which the interaction of just two genetic pathways, one involving *bozozok* and the other involving Chordin, is both necessary and sufficient to permit development of the head and trunk through inhibition of BMP signalling. Therefore, although no single factor has emerged as a master regulator of anterior development in vertebrates, the genetic mechanisms involved have been shown to be surprisingly simple.

Heather Wood

References and links

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WEB SITE Lilianna Solnica-Krezel's lab
ENCYCLOPEDIA OF LIFE SCIENCES BMP antagonists and neural induction | Vertebrate central nervous system: pattern formation

Images courtesy of Lilianna Solnica-Krezel, Vanderbilt University, Nashville, Tennessee, USA.

COGNITION

Knowing your onions

Categorization is the fundamental ability that underlies the allocation of stimuli into useful classes such as animal, vegetable and mineral. Without this ability, perceptual input would make little sense. Although we are beginning to understand the complex processes leading to perception, we know very little about the neural basis of categorization. Now, writing in *Science*, David Freedman and colleagues describe an experimental protocol that might lead to an improvement in this situation in the coming years.

Freedman and colleagues used a three-dimensional morphing system to generate images that reflected linear combinations of three different species of prototype dogs and three different species of prototype cats. By blending different amounts of dog and cat together, they were able to produce a set of stimuli that continuously varied in shape between prototype dogs and cats. Importantly, the set contained a precisely defined category boundary such that stimuli that were near to, but on opposite sides of, the boundary appeared similar, whereas stimuli that were on the same side of the boundary but were far apart could appear to be dissimilar. This type of sharp boundary is a classic feature of perceptual categorization and allows for the dissociation of physical similarity and category membership. Two monkeys were trained to categorize the stimuli set as either cat or dog. Freedman *et al.* then looked for neurons that reflected the different categories.

A population of neurons in the lateral prefrontal cortex reflected the category of the visual stimuli. A typical neuron was more active in response to one of the categories (for example, dog) and responded similarly to each of the stimuli from that category irrespective of the amount of dog in the stimulus. Further analysis of the response properties revealed that the typical neuron was more sensitive to category than identity. Finally, the monkeys could be trained with stimuli that were assigned to a new category, illustrating the plasticity of this system.

The authors were careful to note that the prefrontal cortex is unlikely to be the only area of the brain involved in perceptual categorization. The development of approaches such as this suggest that it may not be long before we have definitive evidence on this point.

Peter Collins

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WEB SITE Earl Miller's lab