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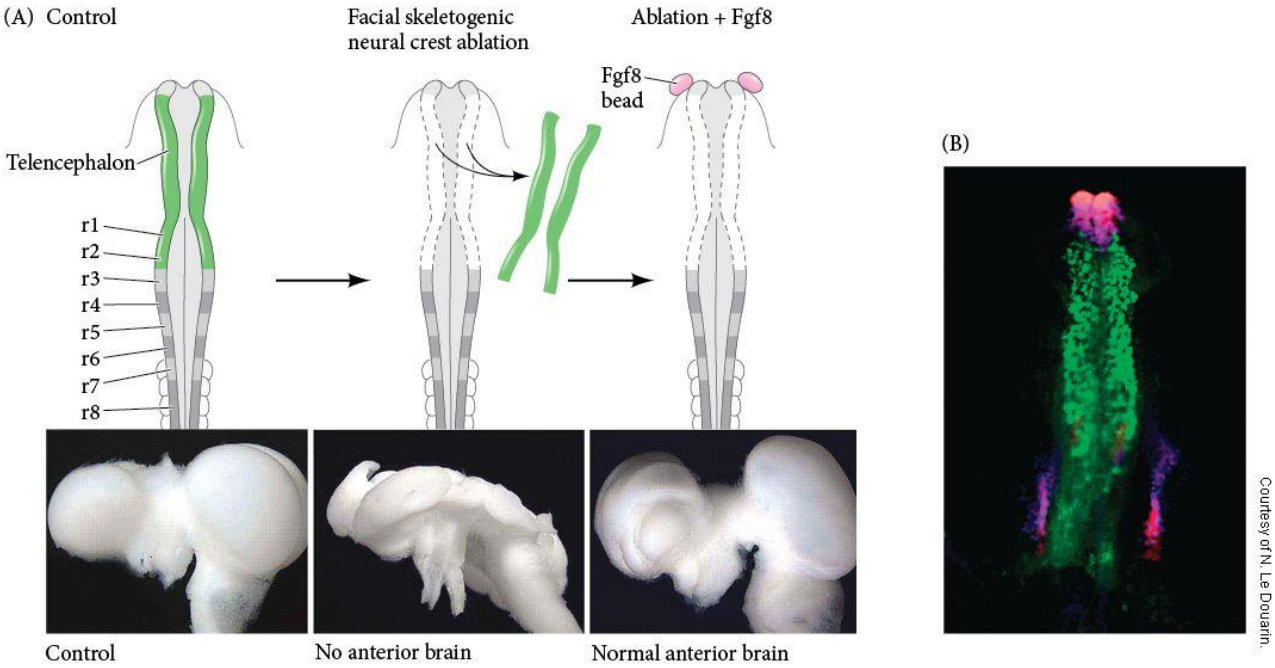
Coordination of Face and Brain Growth

It is a generalization in clinical genetics that “the face reflects the brain.” Although this is not always the case, physicians are aware that children with facial anomalies may have brain malformations as well. The coordination between facial form and brain growth was highlighted in studies by Le Douarin and colleagues (2007). First they found that the region of cranial neural crest that forms the facial skeleton is also critical for the growth of the anterior brain (Figure 1). When that region of chick neural crest was removed, not only did the bird’s face fail to form, but there were major defects in the brain anterior to the otic region and the telencephalon failed to grow. Next they found that forebrain development could be rescued by adding Fgf8-containing beads to the anterior neural ridge (the neural folds of the anterior neuropore). This finding was strange, however, because cranial neural crest cells do not make or secrete Fgf8; the anterior neural ridge usually does. It seemed that removing the cranial neural crest cells prevented the anterior neural ridge from making the Fgf8 necessary for forebrain proliferation.



A after S. E. Creuzet et al. 2006. *Proc Natl Acad Sci USA* 103: 14033-14038, copyright (2006) National Academy of Sciences; S. E. Creuzet. 2009. *Proc Natl Acad Sci USA* 106:15774-15779. Photos from S. E. Creuzet et al. 2006. *Proc Natl Acad Sci USA* 103: 14033-14038, copyright (2006) National Academy of Sciences. Courtesy of N. Le Douarin.

Figure 1 The cranial neural crest that forms the facial skeleton is also critical for the growth of the anterior region of the brain. (A) Removing the facial skeleton-forming neural crest cells from a 6-somite-stage chick embryo stops the telencephalon from forming, as well as inhibiting formation of the facial skeleton. Telencephalon development can be rescued by adding Fgf8-containing beads to the anterior neural ridge. (B) Embryo stained with HNK-1 (which labels neural crest cells green). Fgf8 appears pink in this micrograph.

Looking at the effects of activated genes added to the anterior neural ridge region, Le Douarin and

colleagues hypothesized that the BMP4 from the surface ectoderm was capable of blocking Fgf8. The cranial neural crest cells secreted Noggin and Gremlin, two extracellular proteins that bind to and inactivate BMP4, allowing for the synthesis of Fgf8 in the anterior neural ridge and the development of the forebrain structures. Thus, not only do the cranial neural crest cells provide the cells that build the facial skeleton and connective tissues, they also regulate the production of Fgf8 in the anterior neural ridge, thereby allowing development of the forebrain and midbrain.

Literature Cited

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