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47. **BMP11—A Candidate Negative Regulator of Olfactory Neurogenesis.** H.-H. Wu,* P. Chern,* J. E. Johnson,† and A. L. Calof.*
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In vivo studies suggest that olfactory epithelium (OE) neurogenesis is regulated by signals produced by olfactory receptor neurons (ORNs), which inhibit proliferation of neuronal progenitors. This hypothesis is supported by experiments showing that OE neuronal progenitors cultured with high numbers of ORNs generate fewer neurons. Some BMPs also act in this way: BMPs 2, 4, and 7 act on neuronal progenitors in the ORN lineage to inhibit neurogenesis. Nevertheless, in the olfactory mucosa, these BMPs are not expressed exclusively in ORNs. Therefore, other negative regulators may be important in OE neurogenesis. One candidate is BMP11. *In situ* hybridization shows that Bmp11 is exclusively expressed in OE, but not in adjacent stroma or respiratory epithelium. BMP11 belongs to a class of BMPs that includes the negative regulator of muscle growth, GDF8. Since GDF8 is 90% identical to BMP11, we tested GDF8 effects on OE neurogenesis. GDF8 strongly inhibits neurogenesis in a dose-dependent manner. Unlike BMPs 2, 4, and 7, however, GDF8 treatment has no effect on MASH1+ progenitors, suggesting that GDF8 acts at a different cell stage or through a different signaling pathway. Experiments with OE cultured from GFP reporter mice suggest that GDF8 inhibits development of Ngn1-expressing immediate neuronal precursors, the progeny of MASH1+ progenitors. Current experiments are directed toward identifying the receptors that mediate this action and determining whether OE responses to other growth factors are affected by GDF8 signaling. (Supported by NIH Grants DC03583 and HD38761 to A.L.C.)