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275. A Transgenic Approach for Determining the Role of Bone Morphogenetic Proteins in the Development of Olfactory Receptor Neurons. André Wineland,[1] Ira L. Blitz,[2] Richard C. Murray,[1] and Anne L. Calof[2]. [1]Hendrix College, Conway, AR 72032; [2]Univ. of California, Irvine, CA 92697.

Mouse olfactory receptor neurons (ORNs) are generated throughout life from progenitor cells that reside within the olfactory epithelium (OE). Proliferation of progenitors and survival of ORNs are positively and negatively regulated by bone morphogenetic proteins (BMPs) in vitro and several *Bmps* are expressed in and around the OE (Shou et al., 2000, Development 127, 5403) suggesting that BMPs may regulate olfactory neurogenesis in vivo. To test this, we generated transgenic mice that overexpress BMP4 or Noggin in the OE to alter intrinsic BMP signaling. To allow detection of the proteins, *Bmp4* and *noggin* cDNAs were epitope-tagged and demonstrated to be functional and properly secreted. Expression was directed to ORNs using the tissue-specific genomic regulatory elements from the *Omp* gene (Danciger et al., 1989, PNAS 86, 8565). Ten *Omp-Bmp4* and eight *Omp-Noggin* lines were generated and transgene expression was demonstrated using RT-PCR, immunoblotting, or histochemistry. The line with the highest level of expression was chosen for further analysis. Decreased numbers of both proliferating progenitors and apoptotic cells were detected in the OE of both types of transgenics. In addition, the OE of *Omp-Bmp4* transgenics showed decreases in ORN number and OE thickness, and altered expression of GAP43, a phosphoprotein involved in neuron maturation and axon growth. These findings demonstrate that regulation of BMP levels is crucial to the development and maintenance of neuron number in the OE, and suggest that BMPs also regulate the rate of ORN turnover. (Supported by grants to ALC: NIH (DC-03583 and HD-38761) and MOD.)