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DIFFERENTIATED OLFACTORY RECEPTOR NEURONS FEED BACK TO INHIBIT NEUROGENESIS BY NEURONAL COLONY-FORMING PROGENITORS ISOLATED FROM MOUSE OLFACTORY EPITHELIUM. ((J. Shou, J.S. Mumm, P.C. Rim and A.L. Calof)) Department of Anatomy & Neurobiology and Developmental Biology Center, University of California, Irvine, College of Medicine, Irvine, CA 92717.

Generation of olfactory receptor neurons (ORNs) takes place throughout life in the mammalian olfactory epithelium (OE), suggesting the existence of a neuronal stem cell in this system. To identify neuronal stem cells and define conditions supporting their survival and generation of ORNs, we developed an immunological panning method to purify neuronal progenitor cells from embryonic mouse OE. The majority of purified progenitors behave like cells we previously identified as Immediate Neuronal Precursors of ORNs: in defined, serum-free culture, these cells rapidly give rise to ORNs, which die shortly thereafter. When purified progenitors are co-cultured with stroma cells from olfactory turbinates, however, a small fraction of purified progenitors gives rise to proliferative colonies. One morphologically identifiable subset of these colonies continues to generate both ORNs and undifferentiated progenitors as late as 7 days *in vitro*. The frequency at which such colonies arise suggests they are the clonal progeny of an undifferentiated cell which, when cultured in the presence of stroma cells, exhibits the capacity for sustained neurogenesis; this "neuronal colony-forming cell" may be the neuronal stem cell of the OE. Interestingly, development of neuronal colonies can be specifically inhibited when purified progenitors are cultured in the presence of a large excess of ORNs, suggesting that differentiated ORNs provide a signal that feeds back to inhibit neurogenesis by their own progenitors. Preliminary experiments to characterize the neuronal signal indicate that ORNs subjected to repeated freeze-thaw are still capable of inhibition, but boiled ORNs are not. These results suggest that heat-labile macromolecule(s) produced by ORNs mediate a growth inhibitory signal for neuronal progenitor cells. *Supported by grants to ALC from NIH (DC02180) and the Council for Tobacco Research (3663).*