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## *Abstract*

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**Grant Number:** 1R01NS036176-01  
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**PI Title:** ASSOCIATE PROFESSOR  
**Project Title:** REGULATION OF CORTICAL NEUROGENESIS

**Abstract:** DESCRIPTION: The overall goals of the project are to define the molecular mechanisms that regulate neuronal differentiation in the developing cerebral cortex. To identify and characterize such molecular mechanisms, primary cultures of cortical precursor cells have been developed that allow the process of neuronal differentiation to be studied in vitro. The differentiation of cortical neurons in these cultures can be regulated by at least three signals: bFGF, which acts as a mitogen, NT-3, which acts to promote differentiation, and a membrane-associated signal which cooperates with bFGF to inhibit differentiation. Preliminary studies indicate that this membrane-associated signal is likely to be a ligand for one or more of the mammalian Notch proteins. Experiments using the cortical precursor cultures as well as embryonic slice cultures will be used to determine the mechanisms by which these three signals act to regulate neuronal differentiation. The specific aims of the proposal are; (i) an analysis of the role of bFGF- and NT-3- induced signaling in the regulation of cortical neurogenesis; (ii) a functional analysis of mammalian Notch-mediated interactions in the control of neuronal differentiation. The control of neuronal differentiation is a central problem in nervous system development, and the findings from the proposed experiments should be of much scientific as well as clinical interest. A number of neurological diseases, such as paraventricular and laminar heterotopias, micrencephaly, and lissencephaly are characterized by the failure of proper neuronal differentiation in the cortex. The consequences are severe, and include mental retardation, motor dysfunction, and neonatal death. Cure for these disorders will require the identification of the underlying molecular defects, and the proposed investigations of mechanisms of neuronal differentiation should prove to be useful in devising such strategies.

**Thesaurus Terms:**

cerebral cortex, developmental neurobiology, neurogenesis  
developmental genetics, fibroblast growth factor, gene induction /repression, neurotrophic factor  
laboratory mouse, tissue /cell culture, transgenic animal

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