2004 PROGRAM

8:15 a.m. **Registration and Continental Breakfast**
Atrium (Room 1-65), William T. Young Library

9:00 a.m. **Welcome by Dr. Boyd E. Haley, Chairman, Department of Chemistry, University of Kentucky - Auditorium (Room 1-62), William T. Young Library**

9:05 a.m. **Introductory Remarks - Dr. Mark A. Lovell, University of Kentucky**

9:10 a.m. **Dr. Steven A. Goldman, University of Rochester Medical Center**
"Isolation, Induction and Use of Neural Progenitor Cells of the Adult Human Brain"

Recent studies have substantially expanded our conception of the types of progenitor cells that continue to reside in the adult nervous system, and their respective roles in the normal maintenance of the brain and spinal cord. In the adult human, neural stem cells persist within the forebrain ventricular zone, and give rise to a variety of more restricted progenitor phenotypes. The major progenitor pools of the human brain, each of which has now been isolated to purity, include ventricular zone neuronal progenitor cells, hippocampal neuronal progenitors, and parenchymal glial progenitor cells. Each of these phenotypes exists within a local environmental niche, which tightly regulates both the mitotic activity and derivatives of its resident progenitors. Within these niches, both neuronal and glial progenitor cells may reside as transit amplifying pools, by which lineage-biased progenitors expand to replenish discrete mature phenotypes. The largest such pool appears to be that of the parenchymal glial progenitor cell. When isolated and transplanted into neonatal shiverer mice, whose brains lack myelin basic protein and hence otherwise fail to myelinate, these cells can mediate quantitatively substantial and geographically extensive myelination. Remarkably, whereas adult glial progenitor cells only generate oligodendrocytes and astrocytes within their local white matter environment, upon removal from the tissue environment they expand to generate neurons as well as glia. Thus, at least some populations of adult glial progenitors retain both multilineage capacity and mitotic competence, suggesting that the parenchyma, like the ventricular zone, harbors resident neural stem cells.

Besides implanting precursor cells for therapeutic benefit, one may also achieve this end by inducing endogenous stem and progenitor cells. In particular, progenitor cells in the adult ventricular wall may be induced to generate new neurons by over-expressing cognate neuronal differentiation agents, such as BDNF. Moreover, we have noted that the concurrent suppression of astroglial differentiation by resident stem cells, accomplished by over-expressing the soluble bone morphogenetic protein (BMP) inhibitor noggin, can potentiate the BDNF-mediated addition of new neurons to the adult rat neostriatum. The new neurons mature as striatal medium spiny neurons, and successfully project to the globus pallidus, extending processes over several mm of normal adult striatum. The neurogenic effect of BDNF and noggin treatment was also noted in the R62 mouse model of Huntington's Disease, suggesting the potential efficacy of this strategy for replacing medium spiny neurons lost to this disease. Together, these experiments argue that as our understanding of the biology and control of adult neural progenitor cells becomes more extensive, our ability to target, induce and implant these cells for therapeutic purposes will become increasingly manifest.

10:10 a.m. **Dr. Fred Starks**
"Remembrance of Dr. Benton Naff"

10:25 a.m. **Break (Refreshments Available)**

10:45 a.m. **Poster Session, Room 137, Chemistry-Physics Building**

12:00 p.m. **Buffet Lunch, Faculty Club [Please return registration card by March 26, 2004 for reservations]**

2:00 p.m. **Remarks - Dr. Wendy Baldwin, Vice President for Research, University of Kentucky**

2:10 p.m. **Dr. Catherine M. Verfaillie, Stem Cell Institute, University of Minnesota**
"Multipotent Adult Stem Cells"

The quintessential stem cell is the embryonal stem (ES) cell which has unlimited self-renewal and multipotent differentiation potential. Stem cells have also been identified in most tissues. Compared with ES cells, tissue specific stem cells have less self-renewal ability and, although they differentiate into multiple lineages, they are not multipotent. A large number of recent published studies have suggested that tissue specific stem cells may have the ability to generate cells of tissues from unrelated organs. We have identified a population of primitive cells in normal human, rodent, and possibly other mammalian post-natal tissues that have, at the single cell level, multipotent differentiation and extensive proliferation potential, which we named Multipotent Adult Progenitor Cell or MAPC. Single MAPC differentiate *in vitro* into most mesodermal cell types (cells with phenotypic and functional characteristics of osteoblasts, chondroblasts, fibroblasts, adipocytes, skeletal, smooth and cardiac myoblasts, endothelial cells), as well as cells with neuroectodermal and with endodermal features. MAPC undergo 80 to >200 cell doublings without telomere shortening, suggesting that they do not senesce. Mouse MAPC contribute to all tissues of the mouse when injected in a blastocyst, and MAPC engraft *in vivo* in hematopoietic and epithelial tissues in response to local "cues" when injected postnatally. We will discuss studies aimed at determining whether MAPC exist *in vivo* or are a culture phenomenon, to further characterize MAPC using gene expression profiling, and the potential of these cells *in vivo*.

3:10 p.m. **Break (Refreshments Available)**

3:30 p.m. **Dr. Pasko Rakic, Yale University School of Medicine**
"From Stem Cells To Complex Brain Architecture"

The interest in neural stem cells centers mainly on their possible use to replace adult neurons that have been damaged or lost as a result of injury or neurodegenerative disorders. However, inability of the adult human brain to replace its neurons may not be due to the absence of potential progenitors, but to its resistance to accepting newcomers into the existing neural network. In contrast to some non-mammalian vertebrates, such as the salamander, that can replace large portions of their brain and spinal cord, humans have evidently lost this capacity. Thus, overcoming the brain's resistance to the acquisition of functionally competent new neurons will require an understanding of why neurogenesis ceases at the end of specific developmental time windows and why there are regional and species-specific variations in this phenomenon. Our comparative study of developmental cellular events in mouse, monkey and human elucidate both similarities as well as differences in control of cell production that may be relevant for understanding brain evolution as well as for designing strategies for cell replacement therapies.

(http://www.chem.uky.edu/seminars/naff/welcome.html)

UK
Department of Chemistry
University of Kentucky
Lexington, KY 40506-0055

Thirtieth Annual
Naff Symposium on

Chemistry & Molecular Biology

established in the memory of
Anna S. Naff

Adult Stem/Progenitor Cells

SPEAKERS

Steven A. Goldman
Catherine M. Verfaillie
Pasko Rakic

Friday, April 2, 2004

Department of Chemistry
University of Kentucky
Lexington, KY 40506-0055