Pasko Rakic Receives Neuroscience Award

By Qing Wang

"Understanding the brain's function and its disorders can be helped by studying how it [the brain] develops," explains Yale researcher Pasko Rakic, M.D., Ph.D. For the past three decades, Rakic has made numerous pioneering contributions to the field of neuroscience. His revolutionary discovery of the principles and mechanism of how embryonic nerve cells migrate in the central nervous system has firmly established his reputation in the scientific community. On September 18, 2002, Dr. Rakic was honored with the 15th Annual Bristol-Meyers Squibb Award for Distinguished Achievement in Neuroscience Research, a $50,000 award. The fact that nine of the past twenty five previous recipients of this award have subsequently received the Nobel Prize is testament to its prestige.

After obtaining his medical and graduate degrees at the University of Belgrade, Rakic joined the neurosurgery and neuropathology departments at Harvard Medical School. In 1978 he came to Yale and is now the chair and Dorys McConnell Duberg Professor of Neurobiology.

Rakic is known for developing the radial unit hypothesis to describe the specialization of neurons in early development. According to this "brick-by-brick" building model, each proliferative unit at the base of a radiating column generates the neurons in the column, which then migrate to their final destination by passing their predecessors. In a related "protomap" hypothesis, Rakic proposes that external signals determine the function of the neurons as they grow and form complex connections. These two hypotheses have become fundamental elements of neuroscience and have provided insight into the development of the cerebral cortex and the pathogenesis of brain disorders such as autism, schizophrenia, Alzheimer's, mental retardation, and childhood epilepsy.

Currently Rakic and his 14-member research team are working on deleting and manipulating genes that participate in programmed cell death and stem cell differentiation. Their recent findings suggest that these genes also maintain neuronal connectivity in the adult brain and are involved in the initiation of neurodegenerative diseases. Thus, Rakic hopes to further study how the regulation of these genes may help prevent or slow down the progression of such diseases.

Pasko Rakic

"We are now living in an extremely exciting time, since the introduction of new methods in neurobiology allows us to study development of a complex structure such as the cerebral cortex at a level of analysis that was not possible in the past," says Rakic.

News

"Synthetic Gene Delivery Systems"

Tetelman Lecture: Mark Davis' Smart Drugs

By Qing Wang

What are conventional drugs made of? Most are known as small molecule therapeutics derived from natural products such as plants, microbes, and other organisms. These small molecules easily reach the target area of a treatment, but at the same time can cause collateral damage to healthy tissue. A recent biomedical trend is to develop macromolecules such as protein, DNA, and RNA into therapeutic agents. However, therapeutic macromolecules cannot easily penetrate the cells that they are indented to treat. The 2002 Tetelman Fellowship recipient, Mark E. Davis of Caltech, is a leading scientist in the development of a delivery system to actively transport gene therapeutics into cells. On October 15, Davis described his gene therapy research in a lecture sponsored by the Yale Engineering Sesquicentennial and Tetelman Fellowship program. Endowed in 1979 by Damon Wells, the Tetelman fellowship is sponsored by Jonathan Edwards College and honors eminent scientists who have made significant contributions to their fields.

"Think of nucleic acids themselves as a drug," suggested Davis. If a gene mutation prevents an individual from producing a functional protein, scientists can insert the correct gene to produce the needed protein. The challenge lies in creating a non-immunogenic vector to deliver the gene into individual cells. Encapsulating DNA plasmids in the hydrophilic polymer cyclodextrin, Davis and his research group have added radicals to regulate charge expression and to recognize pH changes so that the vector can penetrate the cell membrane and release the DNA once in the cell. Davis has also added targeting mechanisms so that these "smart" polymers enter only certain types of cells. For example, a polymer with surface-attached galactose will target hepatocytes, or liver cells.

Davis hopes that this gene delivery system will eventually enable gene therapy to treat AIDS and cancer, and even promote natural wound healing in the elderly, eliminating the need for sutures.