FULL SPEAKER BIOGRAPHY and ABSTRACT

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Dr. Pasko Rakic received his MD and PhD from Belgrade University where he was Assistant Professor before moving to Harvard Medical School, where he was on the faculty for 8 years before taking the endowed McConnel Duberg professorship at Yale University. He presently is Chairman of the Department of Neurobiology and Director of the Kavli Institute for Neuroscience.

Dr. Rakic's research interests are in developmental neurobiology, particularly cellular and molecular mechanisms of neuronal proliferation, migration and synaptogenesis during development and evolution of the cerebral and cerebellar cortex. He is a member of the National Academy of Sciences (USA); American Academy of Arts and Sciences, Institute of Medicine, and was President of the SFN in 1996. His many honors include Lashley Award, American Philosophical Society, Francois I Medal, College de France, Brystol Myer-Squibb, Pasarow, Henry Gray, Gerard (SFN) and Fyssen International Science Prize, and most recently Kavli Neuroscience Prize for his discoveries of how the neurons in the embryonic brain arrange themselves during development into the complex, densely interconnected circuitry of the adult cerebral cortex.

Neural Stem cell contribution to formation of functional cortical columns

The cerebral cortex is a laminated structure composed of arrays of intersecting radial columns consisting of species-specific combination projection and local circuitry neurons. The origin of the complex species-specific cellular organization of the functional columns begins to already emerge at the time of final divisions of the neural stem cells. During cortical development, excitatory projection neurons originating from the neural stem cells and progenitors within the mosaic of proliferative units of the embryonic ventricular surface migrate along elongated radial glial fibers to form a cellular infrastructure of radial (vertical) ontogenetic columns in the overlaying cortical plate (CP). The clonally related neurons also undergo a lateral shift and transfer from their parental to the neighbouring radial glial fibers intermixing with neurons originating from adjacent proliferative units. We recently discovered that EphA/ephrin-A signalling regulates the shift in allocation of clonally related neurons that is essential for the proper assembly of cortical columns (Torii et al. Nature, in press). In contrast to the relatively uniform distribution of various molecular markers and retrograde tracers in the CP of wild-type mice, we found dramatic alternating labelling of columnar compartments in ephrin-A knockout mice. These distinct columnar patterns appeared to be caused by impaired lateral dispersion of migrating neurons that depends on EphAs-ephrin-As interaction. Thus, in utero electroporation that lateral dispersion, allocation, binding and proper intermix of neuronal classes depends critically on the expression levels of EphAs and ephrin-As during neuronal passage through the subventricular and deep intermediate zone. These findings indicate that an attempt for replacement therapy must include not only induction and/or transplantation of the specific neuronal clones but also activation of a cascade of molecules involved in their proper positioning that affects specific connectivity.
Supported by grants from NIH, NARSAD and Kavli Institute for Neuroscience at Yale.

What is the central hypothesis of my presentation?
The position of neurons within the cortical columns, and indirectly their basic connectivity, is initiated in the proliferative zones at the time of the final cell division of the specified progenitor clones.

What is the most important observation I will discus?
The discovery of one of the probably multiple interacting ligand-receptor molecules involved in allocation and radial migration of cortical neurons.

What is the translational significance?
Replacement therapy in a complex structure such as the cerebral cortex to be successful would require understanding the complex cellular events and molecular interactions that were at play when it was put together in the first place.