Arnold Kriegstein, MD, PhD
University of California, San Francisco

Arnold Kriegstein, MD, PhD, is currently a professor of Neurology, the John Bowes Distinguished Professor in Stem Cell and Tissue Biology, and the Director of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at the University of California, San Francisco. Dr. Kriegstein received his MD and PhD degrees from New York University and his undergraduate degree from Yale University. He completed his residence training in neurology at Harvard University and the Brigham and Women's Hospital, the Beth Israel Hospital, and the Boston Children's Hospital, and has held academic appointments at Stanford University, Yale University, and Columbia University.

Dr. Kriegstein has an international reputation for his research in the areas of neocortical development, neural differentiation, and neural stem and progenitor cell biology. He has received several awards including the Stanford University William M. Hume Faculty Scholar, a Javits Award from the NIH, an he was elected to the National Institute of Medicine in 2008.

As Director of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, Dr. Kriegstein oversees one of the largest and most comprehensive stem cell programs in the United States, which encompasses over 120 laboratories carrying out studies aimed at gaining fundamental information about human development, with an eye toward illuminating and treating a broad range of diseases and disorders, from heart disease and diabetes to cancer, and neurological disorders including epilepsy, Parkinson's disease, and brain injury. Dr. Kriegstein's own research focuses on the way in which neural stem and progenitor cells in the embryonic brain produce neurons, and ways in which this information can be used for cell based therapies to treat diseases of the nervous system.

Neural stem and progenitor cells in rodent and human cortical development

Recent work has identified the neural stem cells in the embryonic and adult brain and is unraveling the mechanisms by which new neurons are created and delivered to their correct locations. In addition, insights gained from studies of the developing brain are helping to guide efforts to create unlimited numbers of replacement neurons from stem cell lines. Radial glial cells (RG), long thought to simply guide embryonic nerve cells during migration, have now been identified as neuronal stem cells in the developing brain. In the rodent, RG cells lining the ventricle undergo self-renewing, asymmetric divisions to generate intermediate precursors (IPCs) that can further proliferate in the subventricular zone (SVZ) to increase neuronal number. Unlike the developing rodent cortex, the developing human cortex contains an additional proliferative zone, a massively expanded outer SVZ (OSVZ) that is thought to account for the bulk of cortical neurogenesis. However, the progenitor cell types that populate the human OSVZ have not been defined. Using post-mortem fetal tissue, molecular markers, and slice-culture, we have begun to characterize the types and locations of progenitor cells responsible for human cortical development. We find that the human outer SVZ is populated with both radial glia-like cells (oRGs) and IPCs. The oRG cells lack apical processes and do not contact the ventricle. Our data suggests that they undergo asymmetric self-renewing division to generate IPCs. The IPCs, in turn, undergo symmetric divisions to produce neurons that presumably occupy the same cortical layer. These observations suggest multiple proliferative zones for the generation of cell diversity and cell number in the developing human cortex and help explain the enormous evolutionary increase in cortical size. The presence of multiple neuronal progenitor types needs to be considered when planning stem cell strategies to produce specific cortical neurons.

What is the central hypothesis of my presentation?
Most neural stem cell strategies are based on mouse models of brain development. Human development is likely to be significantly different in important ways.

What is the most important observation I will discus?
We have described a human neuronal progenitor cell type not observed in the developing rodent brain.

What is the translational significance?
Human cortical neurogenesis is complex and not predicted by rodent studies. New stem cell strategies based on human progenitor cell types may need to be developed to reproduce the diversity of human neural cells.