PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&
The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 2/27/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

New Insights into Human Cortical Development and Evolution

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Abstract:

Recent insights gained from studies of the developing cerebral cortex are illuminating potential evolutionary steps that contributed to structural and functional features of the human brain. Radial glial cells (RG) undergo self-renewing, asymmetric divisions to generate neuronal precursors that can further proliferate in the subventricular zone (SVZ) to increase neuronal number. Unlike the developing rodent cortex, the developing human cortex contains a massively expanded SVZ (OSVZ) that is thought to account for the bulk of cortical neurogenesis.

We have begun to characterize the types and locations of progenitor cells responsible for human cortical development. We found that large numbers of radial glia-like cells and intermediate progenitor cells populate the human OSVZ. The OSVZ radial glia-like cells, termed oRG cells, have a long basal process but do not have basolateral polarity and lack contact with the ventricular surface. Using real-time imaging and clonal analysis, we demonstrate that the oRG cells undergo self-renewing asymmetric divisions to generate daughter neuronal progenitor cells that can further proliferate. The daughter cells undergo multiple rounds of symmetric division before generating neurons, suggesting that they are a transit amplifying cell population.

oRG cells are probably present in all mammals and are not a specialization of a larger brain with increased cortical area. Instead, an evolutionary increase in the number of oRG cells and their transit amplifying daughter cells likely amplified neuronal production and contributed to increased cortical size and complexity in the human brain.

The diversity of neural stem and progenitor cells observed during human cortical development, consisting of ventricular RG, oRG cells, intermediate progenitors of the inner SVZ, and transit amplifying cells of the OSVZ are not found in the developing mouse brain. These cell types may be important for modeling human neurodevelopmental diseases ranging from cortical malformations to more subtle disorders such as autism and schizophrenia.

Recent relevant publications:

Hansen DV, Lui JH, Parker PR, Kriegstein AR. (2010) Neurogenic radial glia in the outer subventricular zone of human neocortex. Nature Epub ahead of print 2010 Feb 14.

Lui JH, Hansen DV, Kriegstein AR. (2011) Development and evolution of the human neocortex. Cell 146(1): 18-36.

Lamonica BE, Lui JH, Hansen DV, Kriegstein AR. (2013) Mitotic spindle orientation predicts outer radial glial cell generation in human neocortex. Nat Commun. 2013 Apr 9;4:1665.

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