PROGRESS IN NEUROSCIENCE PINS

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

Thursday, 02/13/14, 3:45 PM
Weill Auditorium

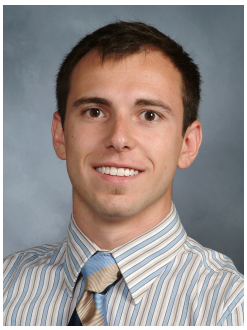
Presentation 1: Unitary production and organization of excitatory neurons in the neocortex

Kate Gao, Neuroscience Graduate Student

Radial glial progenitors (RGPs) are responsible for producing nearly all neocortical neurons, yet a quantitative understanding of RGP division, and neuronal production and organization is lacking. We analyzed excitatory neuron genesis in the mouse neocortex using Mosaic Analysis with Double Markers (MADM), which provides unprecedented single-cell resolution of progenitor division pattern and potential *in vivo*. Remarkably, once they enter the asymmetric neurogenic division phase, individual RGPs across different regions of the developing neocortex produce ~8-9 neurons, suggesting a unitary output in neuronal production. Concordantly, symmetric proliferative divisions of RGPs result in multiplication of the unit. Virtually all RGPs generate both superficial and deep layer neurons organized in vertical clusters with variable topology. Moreover, ~1/6 neurogenic RGPs proceed to produce glia, indicating a coupling between gliogenesis and neurogenesis. These results reveal definitive ontogeny of neocortical excitatory neurons and glia, and suggest a deterministic nature of RGP behaviour in the mammalian neocortex.

Presentation 2: Identity theft: Transformation of cortical pyramidal cells by a transcriptional regulator of inhibitory interneuron fate.

Jeffrey Russ, MD/PhD Student, Neuroscience Program



Adequate inhibitory control of spinal cord circuitry is essential for fine adjustments of information flow between sensory and motor neurons, but goes awry in conditions such as spinal cord injury and cerebral palsy. Understanding the factors that control inhibitory interneuron development and wiring is therefore critical in addressing the symptoms of these debilitating conditions. Ptf1a, an embryonic transcription factor expressed in GABApre interneurons, a population of spinal presynaptic inhibitory interneurons that directly modulates proprioceptive sensory neuron activity, is known to be a crucial regulator of neurotransmitter phenotype in these cells. Ptf1a induces transcriptional cascades that promote an inhibitory, GABAergic fate while suppressing an excitatory, glutamatergic fate (Fujitani, 2006; Glasgow, 2005; Pascual, 2007). However, while it is understood that Ptf1a is necessary for a GABAergic fate in certain interneurons, the ability of Ptf1a to dictate a highly specific neuronal identity, both endogenously and ectopically, remains unclear. Thus, the objective of this project is to study the role of Ptf1a in neuronal identity specification by examining its sufficiency to induce inhibitory interneuronal characteristics when misexpressed in excitatory cortical pyramidal cells.

Presentation 3: The role of $Ca_V1.2$ L-type Ca^{2+} channels in cocaine seeking behavior

Anni Lee, Neuroscience Graduate Student

A hallmark of cocaine addiction is the high rate of relapse despite abstinence from drug or extinction of drug-memory associations. Such persistent cocaine seeking behavior is thought to result from long-lasting maladaptive neuroadaptations. Neuronal Ca^{2+}-activated molecular and epigenetic changes play an important role in cocaine's long-term behavioral effects. Our laboratory has identified a significant role of $Ca_V1.2$ voltage-gated L-type calcium channels in cocaine-induced neuronal plasticity. Utilizing the cocaine conditioned place preference (CPP) behavioral paradigm as an animal model of cocaine seeking behavior, we are exploring the role of $Ca_V1.2$ within the brain's reward circuitry in extinction versus maintenance of long-term cocaine seeking behavior. Using virus-mediated knockout of $Ca_V1.2$, we found that $Ca_V1.2$ in the infralimbic and prelimbic cortices, regions important for extinction learning, do not mediate extinction of cocaine CPP. This is consistent with no change in $Ca_V1.2$ mRNA levels in these regions. In contrast, we find an increase in $Ca_V1.2$ mRNA specifically in the dorsal hippocampus following withdrawal but not following extinction. To further explore $Ca_V1.2$ signaling mechanisms in the dorsal hippocampus during maintenance of cocaine CPP, we examined changes in histone deacetylases (HDACs) which are downstream of Ca^{2+} signaling and shown to mediate cocaine's effects, and found increases in HDAC2 and HDAC5. Further studies to directly link the increase in $Ca_V1.2$, HDAC2 and HDAC5 and their signaling pathways in the maintenance of cocaine CPP following withdrawal are currently ongoing.

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