



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, 4/10/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Molecular Logic of Cerebral Cortex Projection Neuron Development, Diversity, Degeneration, and Regeneration

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Abstract:

Jeffrey D. Macklis' laboratory is focused on the development, diversity, selective degeneration, regeneration, and directed differentiation of projection neuron subtypes in the cerebral cortex. His lab studies neocortical projection neuron differentiation; cortical progenitor biology; induction of neurogenesis within murine neocortex; directed cortical neuron subtype differentiation from neural progenitors and pluripotent cells, functional repair of brain and spinal cord circuitry, and connections between development and degeneration of specific neuron types. Given the heterogeneity of CNS neuronal subtypes (of cerebral cortex / neocortical projection neurons in particular), and the complexity of their connections, detailed understanding of molecular controls over specification, differentiation, connectivity, and survival of specific neuronal subtypes and lineages will contribute not only to 1) understanding the development, organization, function, and evolution of CNS circuitry, but also to 2) identification of developmental and degenerative disease mechanisms and mono/polygenic vulnerability genes, to 3) support or regeneration of vulnerable populations in neurodegenerative (e.g. ALS, HSP/PLS, HD, PD) or acquired disease (e.g. SCI), to 4) enabling cellular models of neuron type-specific disease, and to 5) attempts to functionally repair CNS circuitry. We have identified a set of multi-stage, combinatorially interacting developmental controls – both novel and largely uncharacterized transcriptional regulators and other genes, and cell-extrinsic controls – that are instructive for development of specific neuron subtypes as they develop *in vivo* (in particular, for corticospinal motor neuron, callosal, corticothalamic, and related projection neuron populations). These control key developmental processes from progenitor parcellation and progenitor subtype restriction, to subtype-specific differentiation, to acquisition of precise areal identity, to target-specific axonal outgrowth. This work and much other work in the field reveals a nested (~Boolean) “molecular logic” of progenitor-stage and post-mitotic, areally specific, combinatorial molecular controls over the precise development of key neocortical projection neuron populations. Some of these developmental controls are directly implicated or linked to human disease, and might both elucidate disease mechanisms and (polygenic) vulnerability, and enable directed control of neural progenitors (or ES / iPS cells) toward accurate disease models, neuronal support or regeneration, and functional CNS repair.

Recent relevant publications:

1. Custo Greig LF, Woodworth MB, Galazo MJ, Padmanabhan HK, Macklis JD. Molecular logic of neocortical projection neuron specification, development and diversity. *Nat Rev Neurosci*. 2013 Nov;14(11):755-69.
2. Fame, RM, MacDonald, JL, Macklis, JD. Development, specification, and diversity of callosal projection neurons. *Trends Neurosci*, 2010; 34(1) 41-50.



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