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, 02/11/16, 3:45 PM
A-950

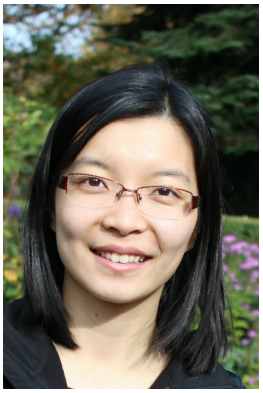
Presentation 1: mRNA methylation as a regulator of neuronal translational homeostasis

Anya Grozhik, Ph.D. Candidate, Neuroscience

Translational homeostasis in neurons is required for long-term synaptic plasticity and memory acquisition and maintenance. Defects in neuronal translation have been associated with diverse conditions such as autism, Fragile X syndrome, and poor memory consolidation. Understanding how translation is regulated in neurons is therefore critical to understanding the etiology of diverse neural conditions. *N*6-methyladenosine (m6A) is an internal, dynamic, and reversible mRNA modification that is found in most cellular mRNAs, and is highly prevalent in neural tissue. Recently, we have shown that m6A is a key regulator of translation in cells. Moreover, we have shown that deletion of the m6A demethylase FTO leads to dysfunction of dopaminergic circuitry, suggesting that m6A-mediated translational regulation may be critical for proper neuronal development. However, the m6A landscape and its function in neurons have not been characterized.To identify m6A residues that may regulate translation in neurons, we wanted to be able to visualize m6A residues at base resolution in cells. However, there are no chemical methods to distinguish between m6A and unmodified adenosine. Here, I show that anti-m6A antibodies induce specific mutational signatures at m6A residues after ultraviolet light-induced antibody-RNA crosslinking and reverse transcription. Using these unique mutational signatures, we map m6A at single-nucleotide resolution in human and mouse mRNA for the first time.

Presentation 2: Ontogenetic origin and organization of thalamic structure and function

Wei Shi, Ph.D. Candidate, Neuroscience



The thalamus, with its intricate cortical, subcortical, and cerebellar connections, is a pivotal node in relaying sensory and motor signals to the cortex as well as supporting higher order cognitive functions. It is composed of ~40 cytoarchitectonically and functionally distinct nuclei, each of which has a different pattern of anatomical connectivity. It is well established that the thalamus emerges from the embryonic diencephalon; however, very little is known about the cellular and developmental principles underlying its complex nuclear formation and functional organization. Here we performed a systematic clonal analysis of mouse thalamus assembly using mosaic analysis with double markers (MADM) and, for the first time, established an ontogenetic map of the mammalian thalamic structure and function both globally and locally at a resolution beyond the conventional single nucleus level. We found that individual radial glial progenitors in the developing thalamus actively divide and give rise to a cohort of neuronal progeny that exhibit striking spatial configuration and functionality. While the anterior clonal cluster displays substantial tangential dispersion and contributes predominantly to non-sensory/motor-related higher order functions, the medial ventral posterior clonal cluster forms prominent radial arrays and contributes mostly to sensory/motor-related activities. Moreover, clones occupying the first-order and high-order sensory/motor nuclei are largely segregated, suggesting a progenitor origin of a cross-modal hierarchical development of sensory/motor pathways. Our study reveals lineage relationship to be a critical regulator of the generally non-laminated thalamus development and function.

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