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, 10/16/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Histone H3.3 Nucleosomal Dynamics Regulate Activity-dependent Transcription and Synaptic Development in the Mammalian Nervous System

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Abstract:

Nucleosomal histones have long been considered highly stable proteins in non-dividing cells, with predicted half-lives of months to years. Although this notion has recently been challenged in lower eukaryotes, the existence and functional consequences of such dynamics remain unknown in mammalian cells. Here, we demonstrate that the expression, turnover kinetics and genomic deposition of the replication-independent histone variant H3.3 are tightly regulated by neuronal activity in the developing and adult central nervous systems (CNS). Using a combination of mass spectrometry, genomic and functional analyses, we show that subpopulations of H3.3, but not canonical H3 proteins, turn over rapidly in neuronal chromatin to promote transcriptional events necessary for dendritic and synaptic development and maintenance in the brain in vivo. These findings provide a foundation for understanding the previously underappreciated role of histone dynamics in the regulation of mammalian transcription, neuronal development and adulthood behavioral plasticity.

Recent relevant publications:

1) Maze I, Noh KM, Allis CD. Histone regulation in the CNS: basic principals of epigenetic plasticity. Neuropsychopharmacology. 2013. Jan;38(1): 3-22.

2) Maze I, Noh KM, Soshnev AA, Allis CD. Every amino acid matters: essential contributions of histone variants to mammalian development and disease. 2014 Nature Reviews Genetics. 2014 Apr;15(4): 259-71.

3) Maze I, Wenderski W, Bagot RC, Tzavaras N, Noh KM, Guo Y, Ionete C, Hurd YL, Tamminga CA, Akbarian S, Buchholz BA, Nestler EJ, Blitzer RD, Shen L, Molina H, Allis CD. Histone H3.3 dynamics regulate synaptic development and plasticity in the central nervous system. 2014 Cell In Revision.

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