D-MEM PhD-UNIMI | Doctorate program Milan EXPERIMENTAL MEDICINE

BIOMETRA

UNIVERSITÀ DEGLI STUDI DI MILANO

International PhD Program in Experimental Medicine

D-MEM SEMINAR

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Aula G13 (Via Golgi n°19)

HISTONE VARIANTS H2A.Z AND ITS CHAPERONES: A NOVEL EPIGENETIC MECHANISM IN NEURODEVELOPMENT

Neurogenesis and neurodevelopment are complex processes that heavily rely on dynamic epigenetic mechanisms and their ability to regulate gene expression. In the past decade, a novel epigenetic mechanism involving histone variants and their chaperones has been found to be fundamental to regulate gene expression in post-mitotic cells like neurons. Histone variants' dynamics have been implicated in the regulation of higher brain functions like learning and memory and are involved in numerous neurological disorders. However, little is known about histone variants' dynamics and their role in neurogenesis and neurodevelopment. In our lab, we focus on histone variant H2A.Z and its specific chaperones Anp32e, which removes the variant from chromatin, and Srcap, with the opposite function. We show that H2A.Z is relocated at different genes during neuronal development, with genes losing the variant over time and others gaining it. H2A.Z changes precede gene expression changes, suggesting that H2A.Z's relocation in the genome is fundamental to regulate gene expression. Consistently with this hypothesis, viral-mediated knock-down of Anp32e at early stages of in vitro neuronal development impairs the natural loss of Anp32e from candidate genes and alters their expression. Notably, bulk RNA-seq showed that knock-down of Anp32e causes specific downregulation of genes. involved in neurogenesis and neurodevelopment and significantly impacts dendritic arborization. Overall, these data suggest that H2A.Z's dynamics, orchestrated by its chaperones, during development play a fundamental role in the regulation of neurodevelopment, opening the road for the study of histone variants' genomic relocation as a novel epigenetic mechanism implicated in nervous system development