

LAUSANNE INTEGRATIVE METABOLISM AND NUTRITION ALLIANCE (LIMNA)

Thursday January 8, 2015 10.30am
Conference Room: AI 1153 (*) EPFL – Lausanne

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“A H3K9/H3K27 methylation crosstalk to repress gene expression in embryonic stem cells”

Hosts: Kristina Schoonjans and Johan Auwerx

Abstract

G9a/GLP and Polycomb Repressive Complex 2 (PRC2) are two major epigenetic silencing machineries, which in particular methylate histone H3 on lysines 9 and 27 (H3K9 and H3K27), respectively. Polycomb proteins are essential for maintaining gene repression during development and consequently play pivotal roles in various biological processes, such as cellular pluripotency, differentiation and plasticity. Although evidence of a crosstalk between H3K9 and H3K27 methylations has started to emerge, their actual interplay remained elusive. Here, we show that PRC2 and G9a/GLP interact physically and functionally. Moreover, we show that G9a enzymatic activity modulates PRC2 genomic recruitment to a subset of its target genes. Furthermore, combining different genome-wide approaches, we demonstrate that PRC2 and G9a/GLP share an important number of common genomic targets, encoding developmental and neuronal regulators. Additionally, we found genomic co-localization between G9a, PRC2 and the neuronal regulator REST, and showed that G9a forms a ternary complex with REST and PRC2. We could observe that one-third of G9a target sites co-localize with PRC2 and found G9a/PRC2 co-bound sites to be enriched around promoters and CpG islands as compared to G9a alone. Interestingly, the G9a-binding sites, excluding G9a/PRC2 co-bound sites, are instead enriched in LTRs. Taken together, our findings reveal that the 'crosstalk' between H3K9 and H3K27 methylations is mediated, at least in part, by the G9a-mediated recruitment of PRC2 to a subset of genes. Interestingly, we found that this mechanism is likely to be prevalent in the maintenance of neuronal gene silencing.

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