ARMI SPECIAL SEMINAR

2024

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The epigenetic enigma of the MLL/SET1 histone 3 lysine methyltransferases

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Abstract

The enigma of the MLL/SET1 histone 3 lysine 4 methyltransferases
H3K4 trimethylation universally characterizes active promoters and the core H3K4 methyltransferase complex is the most highly conserved aspect of epigenetics. However, consequent expectations of central roles in gene expression have not been sustained.

Although each of the six mammalian H3K4 methyltransferases (SETD1A,B, MLL1-4) are required in mouse development, they do so for very different reasons and without the need for their H3K4 methyltransferase activities. MLL1-4 are very large including the two largest known nuclear proteins. None of the four are required in early mouse development or embryonic stem cells (ESCs) until MLL4 (KMT2D) is required for establishment of the embryonic anterior-posterior axis (1). Although MLL2 (KMT2B) is the major H3K4 methyltransferase in oogenesis (2) and for bivalency in ESCs (3), knockout embryos are apparently normal until E6.5 and die around E10 (4). Mll2 conditional knockout ESCs can be differentiated towards neural stem cells until the process stops when Pax6 positive neural rosettes arise after one week. Using Micro-C/Hi-C correlations, we find that loss of MLL2 perturbs 3D chromatin looping and propose that MLL2 is a multivalent chromatin tethering factor that secures long-range regulatory interactions during lineage commitment.

1. Ashokkumar et al (2020) Development 147:dev186999. 2. Denissov et al (2014)Development, 141, 526-37. 3. Andreu-Vieyra et al. (2010) PLoS Biology, 17, 8(8). 4. Glaser etal (2006) Development 133, 1423- 32. 5.

EVENT DETAILS

DATE:
Monday 5th February

TIME:
2:00pm

VENUE:
Room G19
Ground floor
15 Innovation Walk
Monash University
Clayton Campus

HOST:
A.Prof. Edwina McGlinn

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The Australian Regenerative Medicine Institute (ARMI) acknowledges the generous support of Monash University and the Victorian State Government.