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DNA Modification in embryonic stem cells and cancer

Sriharsa Pradhan
New England Biolabs, UK

Epigenetic gene regulation is modulated by post replicative DNA modification, namely methylation and hydroxymethylation of cytosine residues. However, oxidation of DNA has traditionally been considered a DNA damage event, which is readily removed by DNA repair pathways. Indeed, 5-methylcytosine (5mC) undergoes enzymatic oxidation to 5-hydroxymethylcytosine (5hmC) by the ten eleven translocation (TET) family of enzymes. Although 5hmC was discovered several decades ago, it was only after its recent rediscovery in murine brain and stem cell DNA that it has become a major focus of epigenomic research. Part of the reason for this delay is due to the difficulty in detecting both global and locus-specific 5hmC levels. Several studies have addressed this issue with the development of novel techniques to measure 5hmC, which led to multiple reports detailing 5hmC patterns in stem cells and global 5hmC levels. Based on these studies of 5hmC levels and reports of tissue-specific TET expression, these enzymes are thought to play a role in mammalian development and differentiation. In addition, the TET enzymes are mutated in several types of cancer, affecting their activity and likely altering genomic 5hmC and 5mC patterns. Furthermore, oxidation of 5mC appears to be a step in several active DNA demethylation pathways, which may be important for normal processes, as well as global hypomethylation during cancer development and progression. In this seminar, the author will review the 5-mC/hmC mapping technologies and their distribution in ES and cancer cells. The attendees will get detailed understanding of the technologies currently being used or in development for epigenome analysis.

pradhan@neb.com