Functions and Consequences of Epigenetic DNA Modifications

Normal function of vertebrate cells relies on the integrity of the DNA sequence and patterns modifications, which are deposited on DNA after replication. Methylation of the 5th position of cytosine pyrimidine ring (5mC) is the most common DNA modification. 5mC in the promoter regions result in suppression of expression, which is important for imprinting, X-chromosome inactivation and silencing of repeat elements. We and others identified that the methyl group can be oxidised resulting in 5-hydroxymethylcytosine (5hmC), 5-formylcytosine (5fC) and 5-carboxylcytosine (5caC). While 5fC and 5caC act as intermediates of demethylation in the genome, the role of 5hmC is less well understood and it is active area of investigation. We have identified that 5hmC reduces mutagenicity of 5mC. As well, transition to 5hmC enables higher transcription by repelling methyl-CpG binding proteins. We propose that 5hmC is beneficial in cells, which are metabolically active and long-lived thus enabling higher transcription but maintaining lower mutability.

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