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DNA N6-methyladenine modification from unicellular eukaryotes to mammals

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The same genomic sequences of four nuclear DNA bases, A, T, G, and C, code all heritable gene information required for various types of cells in mammalian individuals. Essentially, the methylation of Cytosine at the C-5 position in genome provides a biochemistry-based plasticity required for establishing functionally varying cells in mammals. By this modification, the gene expression can be comprehensively or specifically regulated and chromatin structures be dynamically manipulated. Meanwhile, the methylation of the other nuclear base adenine at the N-6 position (N6-methyladenine, 6mA), which is the dominant DNA modification in genomes of bacteria and shows diverse functions (e.g., regulation of DNA replication initiator factors, control of transposon activity, regulation of DNA gene expression, host-pathogen interactions and guiding DNA repair), is absence in high eukaryotes. Intriguingly, 6mA was also found in unicellular eukaryotes. Until recently we and other groups discovered this 6mA modification predominated in Drosophila melanogaster and Caenorhabditis elegans, respectively. These observations compulsively prove the presence of 6mA in high eukaryotes. Interestingly, in addition to the functions revealed in bacteria, 6mA may mark active transcription start sites and transposon activity and regulates embryonic development. These findings suggest that 6mA is a potential epigenetic mark in eukaryotes. However, it is not clear whether 6mA DNA modification is conservatory and present in mammalian genomes. These recent findings further prompted us to search 6mA modification in mammals again. If so, how 6mA distributes in various tissues and how 6mA distributes in genome. Consistent with previous work, recent work show very low levels of 6mA DNA modification in genomes of frogs, mice, and human cells (approximately 1 6mA for every 1.2 × 106 deoxyadenosine residues. We speculated that 6mA DNA modification can dynamically function in certain cells or stage in a meaningful abundance. Now we showed the prevalence of 6mA in genomes of mice and human cells by developing a unique analytical technology.

Biography

Hailin Wang has his expertise in epigenetics, in particular, DNA methylation and demethylation. He developed ultrasensitive analytical technologies (UHPLC-MS/MS, qPCR, genome-wide sequencing) for characterization and functional study of DNA 5-methylcytosine and its oxidation intermediates. He for the first time showed the enhancement of genome-wide 5-hydroxymethylcytosine by nutrient vitamin C, revealing a role of vitamin C in the regulation of DNA modification, and his study established a direct lin among vitamin C, Tet dioxygenases, and DNA methylation. He further extended these technologies for study of other DNA modifications, and as a world-wide seminal work, he discovered new DNA modification (N6-methyladenine) in high eukaryotes (Cell, 2015). He also has his expertise in ultrasensitive analytical technologies (e.g., capillary electrophoresis-laser induced fluorescence polarization, single molecule fluorescence imaging, and UHPLC-MS/MS) for detection of carcinogenic DNA adducts and for study of DNA-repair proteins interactions. He published 100 peer-reviewed papers on leading journals, including Cell, Cell Stem Cell, Mol Cell, Proc. Natl. Acad. Sci. USA, J. Am. Chem. Soc., Nucleic Acids Research, Analytical Chemistry.

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