DNA modification in Mammalian Brain

Introduction:

DNA methylation is one of the most important and essential molecule in the epigenetic mark in the mammalian development, genomic imprinting, X-inactivation, chromosomal stability and suppressing parasitic DNA element. DNA methylation in neurons has also been recommended to play an important role for mammalian neuronal functions, and learning and memory.

Epigenetics is a quickly evolving branch of biology that studies how temporal and spatial cellular diversity is achieved from invariable genomic sequences. It tells how a single genome with a defined number of genes can have radically diverse gene expression patterns and allows building a whole organism with different cell types. That every cellular lineage has a different genomic distribution of epigenetic features, such as histone variants, histone modifications and DNA modifications, which engenders distinct gene expression profiles. There are certain examples of DNA, researchers have been successful in describing (i) the epigenetic landscape of embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs), as opposed to somatic cells, (ii) stages of epigenetic alterations during differentiation processes from ESCs or iPSCs to various cellular lineages, and (iii) the epigenetic landscape of cancer cells.

In fact, there are many different and various evidences supporting the importance of epigenetic regulation in neurons, there is more or less information for the neuronal epigenome than for other well-studied cell types, such as ESCs or cancel cells.

It is acknowledged and found that human brain consists of billions of neurons forming a complex network with precise spatio-temporal functions. Each neuron in the human brain works as functional unit which receives, integrates and transmits information. Neurons can very possibly alter their electrophysiological properties and responsiveness towards particular stimuli. Such neuronal plasticity requires sustained alteration of the local synaptic strength as well as sustained alteration of global gene expression in the nuclei, for timescales of hours, days or even years after the initial stimulus was present.

If you have ever tried recalling past events, you have had found it in your memory. Human memory often lasts for many decades, whereas most mRNAs have half lives of minutes to hours and most proteins, including synaptic structural proteins, have half-lives of less than a few days. DNA methylation is a serious candidate for mediating long-term plasticity and memory. DNA methylation is chemically stable with a half-life of over a thousand years. Mammalian DNA methyltransferase (Dnmt) 1 is active on hemimethylated cytosine–guanine dinucleotide (CpG) in double-strand DNA. This allows for the self-perpetuating nature of DNA methylation. The possibility of DNA modification being a key mechanism for neuronal plasticity has been considered since the late 1960s and the disruption of contextual fear conditioning following injection of a methylation inhibitorwas shown in the 1970s. There are many more important discoveries in mammalian brains have been made; First, oxidation products of 5-methylcytosine (5-mC), such as 5-hydroxymethylcytosine (5-hmC), 5-formylcytosine (5-fC) and 5-carboxylcytosine (5-caC).

DNA modifications in the mammalian genome

The mammalian genome 5-methylcytosine (5-mC) one of the earliest discovered. 5-mC mostly appears in the CpG, context in the mammalian genome. When 5-mC is deaminated, 5-mC becomes thymine, which is one of the four bases of DNA.

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