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Epigenetic Mechanisms in the Differentiation of Neural Stem Cells

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Editorial

Epigenetics are heritable modifications on the genome that cannot be explained by changes in DNA sequence [1]. Epigenetic mechanisms for modifications include DNA methylation, histone acetylation, and non-coding RNAs expression [2]. Theses mechanisms play important roles in the differentiation of neural stem cells in the developing brain. The process of brain development encompasses different stages of neurogenesis, migration, differentiation, apoptosis, arborization, synaptogenesis, synaptic sculpting and myelination. Neural stem cells (NSCs) that transform from neuroepithelial cells have a multipotential ability to give rise to neurons and glial cells, that is, astrocytes and oligodendrocytes. Differentiation of NSCs that line the neural tube is tightly regulated spatiotemporally by many genetic factors and epigenetic modifications, which can interact with transcription factors and environmental factors. Epigenetics modifications influence genes activation and silencing at different steps of NSCs differentiation through DNA methylation, histone modification, and non-coding RNAs expression without changes in the DNA sequence [3-5].

Neuronal differentiation in mid-gestation, which precedes glial differentiation, is induced by epigenetic mechanisms through regulation of neurogenic basic helix-loop-helix (bHLH) transcription factors such as Ngn1, Ngn2, and Mash1 [6, 7]. Thereafter, at late gestation, DNA methylation in astrocyte-specific promoter results to glial cells differentiation. So, DNA methylation is one of essential epigenetic factors in differentiation of NSCs during development. DNA methylation is carried out through cytosine methylation of genomic DNA at CpG dinucleotides, which directly interferes with the binding of transcription factors to the target sequences by a family of DNA methyltransferases (DNMTs). The DNMTs family is essential for embryogenesis as their functions are necessary for maintenance of methylation patterns during DNA replication (DNMT1), and for de novo methylation (DNMT3a and DNMT3b) [8, 9].

Histone modification is very complex epigenetic mechanism compared with DNA methylation. H3 and H4 core histones are modified by methylation, acetylation of lysine residue, phosphorylation, ubiquitylation, glycosylation, biotinylation, carbonylation and ADP-ribosylation [10] .Non-coding RNAs such as microRNAs and long non-coding RNA also play roles in gene expression by transcriptional and post-transcriptional regulation, so affect the sequential differentiation of NSCs during brain development.

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