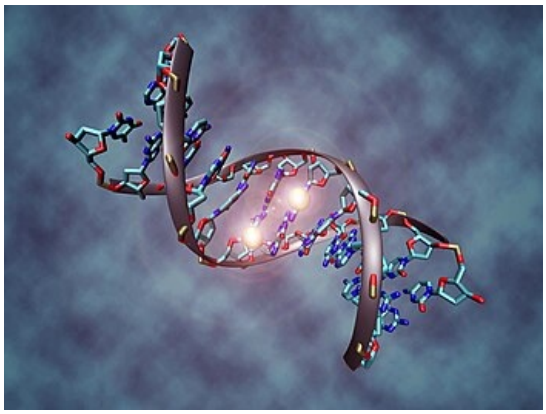
DNA Methylation

'DNA methylation' plays a role in differentiation, X inactivation, imprinting, is involved in the maintenance of chromatin structure and serves to suppress parasitic DNA.

Occurrence and function of methylation



DNA fragment methylation (on two cytosines in the middle of the molecule)

Methylation affects almost exclusively the "cytosine" (position C5) in the "CpG dinucleotide" (CpG = Cytosine Phosphate-Guanine). These dinucleotides in the coding portions of genome u are suppressed, probably disappearing in evolution due to the high mutability of methylated cytosine u. They occur abundantly in repetitive sequences, and so-called CpG islands are accumulated CpG dinucleotides that often occur in the promoter region. About 60% of genes have promoters associated with these CpG islands. These are unmethylated in active genes, where transcription factors bind. Methylation of this region is associated with "gene inactivation", either methylation prevents binding transcription factors, or allows binding of inhibitory complexes containing histone deacetylases and other factors that lead to chromatin rearrangement into an inactive form. . Binding of methylated DNA and an inhibitory complex (containing histone deacetylase) is mediated by "binding proteins" such as MeCP2. The gene encoding this MeCP2 protein is mutated in progressive neurological impairment - Rett syndrome. Methylation is provided enzyme atically by methyltransferases, of which Dnmt1 is the so-called maintenance methyltransferase, which methylates the newly formed DNA strand when replicated according to the methylation pattern of the old strand, Dnm3a, b are "de novo" methyltransferases.

Methylation is a *'reversible process* ', with' *methylation changes during methylation. At the very beginning of embryonic development, at the time of the first divisions of the zygote, global "genome demethylation" occurs. This demethylation is an active enzymatic process (demethylase) in the male genome (sperm DNA is more methylated than egg DNA), the female genome is demethylated gradually during the first divisions of the zygote in the absence of maintenance methylation.* 'Demethylation' *probably leads to* 'gene activation for early embryonic development' *. New methylation begins before implantation, after implantation is completed.*

Methylation changes are also associated with the "malignant" process, in which global genome hypomethylation, especially of repetitive sequences, occurs and specific hypermethylation of some genes. Hypomethylation leads to genomic instability and other genetic changes, mutations, chromosomal aberrations. Hypomethylation also leads to the activation of imprinted protooncogenes. Hypermethylation of CpG promoters tumor suppressor genes (e.g. Rb1, BRCA1), repair genes (e.g. hMLH1), angiogenesis inhibitors (e.g. THBS1) leads to their inactivation. The same changes in genome methylation - *'global hypomethylation'* and *gene-specific hypermethylation* 'are' 'an aging phenomenon' ', which is one of the causes of older age-related tumors.

Related Articles

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Source

- *Text translated with the consent of RNDr. Zdeny Polívkové - 3rd Faculty of Medicine, Charles University*