Chromatin remodelling during nucleotide excision repair

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Abstract/Resumo

Nucleosomes are considered dynamic particles that are involved in practically all chromosomal processes, being subjected to highly ordered changes considered as epigenetic information, which modulates DNA accessibility. Nucleosomes exhibit three dynamic properties: a) covalent histone post-translational modifications, b) change of composition due to removal of histones and c) movement along DNA. The latter two are carried out by ATP-dependent chromatin remodeling complexes. ATP-dependent chromatin remodeling factors use ATP hydrolysis to slide or unwrap DNA. These multi-subunit complexes can also catalyze eviction of histone octamers to promote histone variant replacement. Histone post-translational modifications such as the addition of acetyl, methyl, phosphate, ubiquitin, and sumo groups change the properties of histones, modifying histone-DNA or histone-histone interactions. In response to DNA damage, a signal transduction cascade, known as the checkpoint response, is activated. This phenomenon is also referred to as the DNA damage response. The two main features of the DNA damage response mechanisms are cell-cycle checkpoint activation and DNA repair. For both damage signaling and repair, chromatin remodeling is most likely a prerequisite, specially for the nucleotide excision repair system (NER), which removes a wide range of bulky DNA adducts that distort the double helix of DNA, including those induced by UVC. NER is more efficient in naked DNA than in chromatin since it is inhibited by the presence of nucleosomes and heterochromatin, which limit the access of repair proteins to DNA. Thus, the most challenging step in NER is the recognition of DNA lesions in their chromatin context. Apart from ATP-dependent chromatin remodeling factors and histone modifications, repair factors themselves could cause chromatin rearrangements (i.e. the CSB protein, a SWI/SNF ATP-dependent chromatin remodeling protein; and the TFIIH complex that contains XPD and XPB helicase subunits). A functional connection between chromatin remodeling and the initiation steps of NER will be described.

Keyword/Palavras-chave: Chromatin remodelling; Nucleotide excision; Repair factors

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