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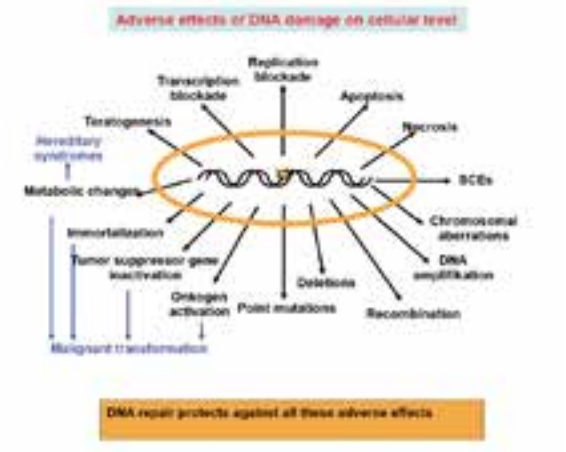
Transcriptional and epigenetic regulation of DNA repair

To maintain genome integrity, DNA is subject to rigorous quality control and repair by proteins that recognize and remove harmful lesions, resulting from endogenous metabolic processes, microbiota activity, food-borne carcinogens and the exposure to external radiation and a plethora of man-made genotoxicants. Most of the DNA repair proteins are constitutively expressed while some others are inducible following genotoxic stress, contributing to adaptation to genotoxic stress. Most DNA repair pathways are complex, involving many enzymes and cofactors, which must be expressed in a balanced way in order to avoid uncoordinated and error-prone repair of DNA lesions. The fine-tuned adaptive regulation of repair genes occurs on the level of transcription by promoter activation mediated by stress-inducible transcription factors. Some DNA repair genes, however, are subject to epigenetic regulation, which occurs notably in cancer cells. The DNA repair gene MGMT is the best-studied example, frequently silenced by promoter hypermethylation in malignant brain tumours, which bears significant therapeutic implications. Moreover, DNA repair processes are involved in regulating gene activity on epigenetic level. The mechanisms of transcriptional and epigenetic regulation of DNA repair genes and biological consequences will be discussed.



Recent Publications

1. Roos W P, A D Thomas and B Kaina (2016) DNA damage and the balance between survival and death in cancer biology. Nature Rev. Cancer 16(1):20-33.
2. Fahrer J and B Kaina (2013) O6-Methylguanine-DNA methyltransferase (MGMT) in the defense against N-nitroso compounds and colorectal cancer, Carcinogenesis, 34(11):2435-2442
3. Christmann M and B Kaina (2013) Transcriptional regulation of human DNA repair genes following genotoxic stress: trigger mechanisms, inducible responses and genotoxic adaptation. Nucl. Acids Res., 41(18):8403-8420
4. Christmann M, B Verbeek, W P Roos and B Kaina (2011) O6-Methylguanine-DNA methyltransferase (MGMT) in normal tissues and tumors: enzyme activity, promoter methylation and immunohistochemistry, Biochimica et

Biophysica Acta, 1816(2):179-190

5. Christmann M, G Nagel, S Horn, U Krahn, D Wiewrodt, C Sommer and B Kaina (2010) MGMT activity, promoter methylation and immunohistochemistry of pre-treatment and recurrent malignant gliomas: a comparative study on astrocytoma and glioblastomas, Int. J. Cancer, 127(9):2106-2118

Biography

Bernd Kaina completed his PhD in Genetics from Universtity of Halle, Germany in 1976. He completed his Postdoctoral training at the Institute of Genetics in Gatersleben and continued his studies on DNA repair in the Department of Molecular Biology in Leiden, Netherlands and at the German Cancer Research Center in Heidelberg and, as a Heisenberg Fellow in the Department of Genetics of the Nuclear Research Center in Karlsruhe, Germany. In 1993, he obtained a full professorship at Institute of Toxicology of the University of Mainz and, since 2003; he acts as a Director of the Institute. His research program focuses on MGMT and the regulation of repair genes, DNA damage signaling, genotoxicity, cancer formation and death of cells exposed to radiation, chemical genotoxins and anticancer drugs. In a translational research program, his group studies the mechanisms of resistance of glioma, melanoma and other cancer cell types to alkylating anticancer drugs.

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