Gene Section

Mini Review

XRCC3 (X-ray repair complementing defective repair in Chinese hamster cells 3)
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Published in Atlas Database: November 2005

Online updated version: http://AtlasGeneticsOncology.org/Genes/XRCC3ID335ch14q32.html
DOI: 10.4267/2042/38297

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Identity
Hugo: XRCC3
Location: 14q32.3

DNA/RNA

Description
17 800 bp, 9 exons.

Transcription
2,504 bp.

Protein

Description
346 amino acids.

Function
XRCC3 is required for efficient repair of double strand breaks via homologous recombinational repair (link), for correct chromosomal segregation and for repair of DNA cross links. Inactivation of XRCC3 in CHO cells results in increased radiation and cisplatin sensitivity. In human cells, XRCC3 forms a complex with Rad51C which is recruited early to DNA damage. Inactivation of XRCC3 in human cells leads to a two-fold sensitivity to DNA cross-linking agents, impaired Rad51 focus formation, elevated chromosome aberrations and five to seven-fold increased endoreduplication.

Homology
XRCC3 is a paralog to rad51.

Implicated in

No human disease has been linked to inactivation of XRCC3. However, polymorphisms in XRCC3 may be associated with increased cancer risk (see below).

Note: Genetic Epidemiology:
The most frequent polymorphism in XRCC3 is XRCC3 C18067T which results in a Thr to Met amino acid substitution at codon 241. Carriers of the variant T-allele of XRCC3 T241M have higher DNA adduct levels in lymphocyte DNA compared to homozygous C-allele carriers, indicating that the polymorphism is associated with lowered DNA repair capacity. The variant allele of XRCC3 T241M polymorphism has been associated with increased risk of squamous cell carcinoma of the head and neck in one study while another study found no association. No association has previously been found with colon cancer, non-melanoma skin cancer, prostate cancer, gastric cancer, ovarian cancer. Conflicting results have been published on the association with breast cancer, bladder cancer, malignant melanoma and lung cancer. Two frequent SNP are upstream of XRCC3 T241M have also been studied, namely XRCC3 A4541G and XRCC3 A17897G. Neither polymorphism gives rise to amino acid changes. The variant allele of A17897G has been associated with decreased risk of breast cancer and ovarian cancer. The same tendency, but no significant associations was found for lung cancer. XRCC3 A4541G was not associated to risk of breast cancer or lung cancer. However, homozygote carriers of the variant allele had lower risk of serous epithelial ovarian cancer.
References


of the DNA repair genes XRCC1, XRCC3, XPD, interaction with environmental exposures, and bladder cancer risk in a case-control study in northern Italy. Cancer Epidemiol Biomarkers Prev 2003;12(11 Pt 1):1234-1240.


This article should be referenced as such: Vogel U. XRC33 (X-ray repair complementing defective repair in Chinese hamster cells 3). Atlas Genet Cytogenet Oncol Haematol.2006;10(2):105-106.