

PRIMARY RESEARCH

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Oxidative stress-induced chromosome breaks within the *ABL* gene: a model for chromosome rearrangement in nasopharyngeal carcinoma

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Abstract

Background: The mechanism underlying chromosome rearrangement in nasopharyngeal carcinoma (NPC) remains elusive. It is known that most of the aetiological factors of NPC trigger oxidative stress. Oxidative stress is a potent apoptotic inducer. During apoptosis, chromatin cleavage and DNA fragmentation occur. However, cells may undergo DNA repair and survive apoptosis. Non-homologous end joining (NHEJ) pathway has been known as the primary DNA repair system in human cells. The NHEJ process may repair DNA ends without any homology, although region of microhomology (a few nucleotides) is usually utilised by this DNA repair system. Cells that evade apoptosis via erroneous DNA repair may carry chromosomal aberration. Apoptotic nuclease was found to be associated with nuclear matrix during apoptosis. Matrix association region/scaffold attachment region (MAR/SAR) is the binding site of the chromosomal DNA loop structure to the nuclear matrix. When apoptotic nuclease is associated with nuclear matrix during apoptosis, it potentially cleaves at MAR/SAR. Cells that survive apoptosis via compromised DNA repair may carry chromosome rearrangement contributing to NPC tumourigenesis. The Abelson murine leukaemia (*ABL*) gene at 9q34 was targeted in this study as 9q34 is a common region of loss in NPC. This study aimed to identify the chromosome breakages and/or rearrangements in the *ABL* gene in cells undergoing oxidative stress-induced apoptosis.

Results: In the present study, in silico prediction of MAR/SAR was performed in the *ABL* gene. More than 80% of the predicted MAR/SAR sites are closely associated with previously reported patient breakpoint cluster regions (BCR). By using inverse polymerase chain reaction (IPCR), we demonstrated that hydrogen peroxide (H₂O₂)-induced apoptosis in normal nasopharyngeal epithelial and NPC cells led to chromosomal breakages within the *ABL* BCR that contains a MAR/SAR. Intriguingly, we detected two translocations in H₂O₂-treated cells. Region of microhomology was found at the translocation junctions. This observation is consistent with the operation of microhomology-mediated NHEJ.

Conclusions: Our findings suggested that oxidative stress-induced apoptosis may participate in chromosome rearrangements of NPC. A revised model for oxidative stress-induced apoptosis mediating chromosome rearrangement in NPC is proposed.

Keywords: NPC, Oxidative stress, H₂O₂, Apoptosis, *ABL*, MAR/SAR

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