

Role of XRCC5 repeat polymorphism in the development of acute leukemia

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Acute leukemia is a clonal hemopoietic disorder that is frequently associated with genetic instability characterized by a diversity of chromosomal and molecular changes.

Chromosomal aberrations like single and double-strand DNA breaks (SSB, DSBS). induced by ROS and chemo-or radio therapeutic agents may develop into cancer. There are two DSBS repair pathways in mammalian cells: the homologous recombination (HR) and non-homologous end joining (NHEJ). The latter plays a predominant role in repairing DSBS in mammals. A key component of the NHEJ apparatus is the DNA-dependent Protein Kinase (DNA-PK), which consists of a hetero dimeric DNA targeting subunit (i.e., KU70/KU80, encoded by *XRCC6/ XRCC5* genes)

Variable number of tandem repeats located in the promoter region of *XRCC5* (at 201~-159 nucleotide sites for the initiation of transcription) contains three different alleles, which are two 21 nucleotides repeats (2R), one 21 nucleotides repeat (1R), and zero repeat

unit (0R). This polymorphism could affect *XRCC5* promoter activity and protein expression.

The data comprises of 166 cases (116 AML, 50 ALL) reported at Nizam's Institute of Medical Sciences and MNJ Hyderabad and 237 age and sex matched controls. 5ml Blood samples were collected in EDTA vacutainers from cases and controls. Genomic DNA was isolated from blood samples by non-enzymatic/salting out method. The *XRCC5* repeat polymorphism was analyzed by VNTR method.

The results showed that 0R/1R genotype frequency was highly elevated in cases (9.93%) when compared to the controls (1.39%), indicating it as the risk genotype for the development of acute leukemia. 0R/0R and 2R/2R genotype frequencies were slightly elevated in cases (3.72% and 9.31% respectively) when compared to controls (1.27% and 7.59% respectively). The observations were discussed in terms of drug response and disease progression.