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Abstract Topic: - Molecular effects of genetic variation

Abstract Title: - p.R72P and PIN3 Ins 16bp polymorphisms of TP53 in Punjabi Population

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Aims: - Somatic mutations in TP53 are found in various cancers mainly in colorectal, head & neck, oesophageal, female genital organs (cervical, ovarian, uterine, vaginal), lung and pancreas. Cellular stresses including DNA damage, hypoxia, and replication/translation stress activate sensor proteins ATM, ATR and p14ARF which phosphorylates p53 leading to its stabilization, oligomerization, and binding to p53RE. TP53 is involved in apoptosis, protection of DNA integrity and maintaining energy homeostasis of cell. TP53 variants impact energy metabolism, influence oxidative phosphorylation and induction of mitochondrial apoptosis. TP53 polymorphism PIN3 regulates gene expression and DNA protein interaction. TP53 p.R72P is non-conservative change located within its proline-rich domain. P72 variant has strong ability to induce apoptosis than R72 variant and contribute to differences in cancer susceptibility. PP genotype is associated with increased cancer risk in Asian, Caucasian and ethnic Kashmiri population. For PIN3 polymorphism, in East Indian, Northern European and South African population, homozygote carriers of A2A2 allele were at increased risk of cancer. Present study aims to investigate PIN3 and pR72P polymorphisms in Punjabi population

Methods: - Genotyping of PIN3 and p.R72P polymorphisms using Direct PCR and PCR-RFLP assay in 86 unrelated healthy individuals. Hardy Weinberg Equilibrium was tested using Chi Square test

Results: - Genotype analysis revealed that of 86 individuals tested for PIN3, 82.56% studied subjects were homozygous for A1A1 genotype, 15.12 % heterozygous for A1A2 genotype and 2.32% homozygous for A2A2 genotype. For p.R72P polymorphism, 20.93% of studied subjects were homozygous for RR genotype, 54.65% heterozygous for RP genotype and 24.42% homozygous for PP genotype. Allele frequencies were; 90.12% (A1) 9.88% (A2) and 48.25% (R) and 51.75% (P) of PIN3 and p.R72P respectively. Results obtained were in accordance with HWE

Conclusions: - Among the studied polymorphisms R72P appears to be associated with potential disease risk as PP genotype and RP genotype were in higher frequency. Case-control approach for screening of studied polymorphisms give insight into etiology and targets for development of therapeutic approaches

Keywords: - Genotype analysis revealed that of 86 individuals tested for PIN3, 82.56% studied subjects were homozygous for A1A1 genotype, 15.12 % heterozygous for A1A2 genotype and 2.32% homozygous for A2A2 genotype. For p.R72P polymorphism, 20.93% of studied subjects were homozygous for RR genotype, 54.65% heterozygous for RP genotype and 24.42% homozygous for PP genotype. Allele frequencies were; 90.12% (A1) 9.88% (A2) and 48.25% (R) and 51.75% (P) of PIN3 and p.R72P respectively. Results obtained were in accordance with HWE