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Single Nucleotide Polymorphisms in Exon 4 and Exon 11 of PARK2 Gene and their Insilico Rationalization in Colorectal Cancer Patients of North India

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Abstract—*Genetic alterations in PARK2 have been reported frequently across several human cancers as well as in hereditary Parkinson's disease. The study included a total of 650 genetically unrelated subjects of North Indian ethnicity comprising 300 colorectal cancer cases and 350 healthy controls. The study was approved by Institution Ethics Committee of Department of GIT G B Panth Hospital New Delhi and the Institutional Human Ethical Committee of Jamia Millia Islamia, New Delhi as per ICMR guidelines. Participating subjects provided 3–5 ml of venous blood samples used for isolating genomic DNA by standard phenol–chloroform extraction method as established in the lab. SNPs rs1801474, rs 1801334 were analyzed using the Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) assay. Restriction enzymes ALwNI and TaqI were used for rs1801474 and rs 1801334. Structural analysis, such as root mean-square deviation (RMSD), root-mean square fluctuation (RMSF), and radius of gyration, were analysed using RMS, RMSF, and gyrate respectively, with the built-in functions of GROMACS. Chi-square (χ^2) 3x2 test was performed. Hardy-Weinberg equilibrium (HWE) for both the SNPs were evaluated. The variant genotypes rs1801474 G/A, 1801334 G/A were significant and notably associated with colorectal cancer risk ($P<0.05$) and the non synonymous changes in the loop region lead to deviation in structure of both S167N and D394N when compared to wild type. The D394N change specially leads to compactness of PARK-2 protein due to increased hydrogen bonding thereby reducing its dynamicity. In conclusion our study revealed a significant association of PARK2 SNPs in colorectal cancer, as well as their relations with other clinical parameters highlighting their contribution towards colorectal cancer susceptibility in North Indian population.*