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Novel TP53 three dimensional (3D) hot spot mutations at codon 36, 72 and 240 in oral squamous cell carcinoma: A promising diagnostic tool for future immunotherapies

Abid Azhar¹, Saima Saleem¹, Abdul Hameed², Zubair Abbasi³, Mansoor Ahmed Khan¹ and Navid Rashid Qureshi⁴

¹University of Karachi, Pakistan

²Institute of Biomedical and Genetic Engineering (IB&GE), Pakistan

³Karachi Medical and Dental College (KMDC), Pakistan

⁴Liaquat College of Medicine and Dentistry (LCMD), Pakistan

Oral squamous cell carcinoma (OSCC) is the leading cause of death in the developing countries like Pakistan. This problem aggravates because of the excessive use of available chewing products. In spite of widespread information on their use and purported legislations against their use, the Pakistani markets are classical examples of selling chewable carcinogenic mutagens. Reported studies indicated that these products are rich in reactive oxygen species (ROS) and polyphenols. TP53 gene is involved in the suppression of tumor. It has been reported that somatic mutations caused by TP53 gene are the foundation of the cancer. This study aims to find the loss of TP53 functions due to mutation/polymorphism caused by genomic alteration and interaction with tobacco and its related ingredients. Total 260 tissue and blood specimens were collected from OSCC patients and compared with age and sex matched controls. Mutations in exons 2-11 of TP53 were examined by PCR-SSCP. Samples showing mobility shift were directly sequenced. Two mutations were found in exon 4 at nucleotide position 108 and 215 and one in exon 7 at nucleotide position 719 of the coding sequence in patient's tumor samples. These result in substitution of proline with arginine at codon 72 and serine with threonine at codon 240 of p53 protein. These polymorphic changes, found in tumor samples of OSCC, could be involved in loss of heterozygosity and apoptotic activity in the binding domain of TP53. The model of the mutated TP53 gene elaborated a nonfunctional unfolded p53 protein, suggesting an important role of these mutations in p53 protein inactivation and malfunction. This nonfunctional 3D model also indicates that exogenous tobacco related carcinogens may act as DNA-damaging agents affecting the structure of DNA. The interpretations could be helpful in establishing the pathways responsible for tumor formation in OSCC patients.

abid.azhar@kibge.edu.pk