

Name of the Scholar: Laraib Uroog
Name of the Supervisor: Prof. M. Moshahid Alam Rizvi
Name of the Department: Department of Biosciences

Thesis title: Molecular profiling of FBXW7, EGFR and FOXO3 among Indian Colorectal Cancer patients

Findings

- The two EGFR SNPs rs11543848 and rs2227984 were found to be associated with colorectal cancer. In rs11543848 GA and GA+AA genotypes displayed significant association with all the clinicopathological characteristics but the two haplotype frequencies were not found in strong LD but the genotypes seem to be associated with good prognosis.
- There was a significant difference between CRC cases and controls for FBXW7 SNP rs2255137 in CC genotype and a significant difference in allelic and genotypic frequencies was observed in variant rs6842544 ($p= 0.0295$). The results indicated that FBXW7 rs2255137T>C and rs6842544T>C variant may play a key role as prognostic biomarker for CRC.
- Our study revealed that FOXO3 SNP rs4946936 is strongly associated with colorectal cancer ($p= 0.0393$) where as rs2253310 did not show any statistical significance associated with CRC ($p=0.1213$).
- Somatic EGFR mutations were found in 11(6.35%) of the malignancies. 3 tumors contained E709V mutation in exon 18, 5 samples had E746-A750 deletion mutations in exon 19, 1 sample harbored S768I mutation in exon 20 and 2 A871V mutations were found in exon 21. The results of the western blot and RT-PCR were found to be strongly corroborated for the EGFR protein expression along with IHC with a higher level of EGFR protein in 94 (54.3%) cancer tissues compared to normal tissues
- In total, six mutations were found in the FBXW7 gene in (11%) 173 patients. Out of 19 samples, 7 samples exhibited mutation in exon 15 and 12 samples showed mutation in exon 16. The overall expression of FBXW7 was low (mRNA and protein) in about 56.6% in tumor tissue samples.
- This study has discovered five nonsynonymous mutations in 13 samples in the FOXO3 gene among 173 Indian patients with CRC. None were present in the control population.
- The IHC results revealed FOXO3 protein to be negatively expressed in 63% cases. The FOXO3 protein expression was found to be very highly supported by western blot results. In comparison to normal tissues, cancer tissues have a decreased level of FOXO3 protein. This study demonstrated that expression of FOXO3 mRNA was low in different colorectal cancer in comparison to normal tissues.