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Identification of biomarkers for precision management of metastatic colorectal cancer

Identification of novel prognostic and predictive biomarkers is purported to improve the classification and management of metastatic colorectal cancer (mCRC) and is the primary thrust of my research.

In this context we have identified a single nucleotide polymorphism (SNP) within DNA-repair enzyme O6-methylguanine DNA methyl-transferase (MGMT) by analyzing 78 mCRC patients. In a univariate analysis, patients with the TT genotype (12% of patients) had a median OS of 61.8 months, while those with homozygous GG or heterozygous GT had a median OS of 29.3 months (P=0.06). Further, in multivariate modeling, patients with the TT genotype had longer survival when compared to those with homozygous GG or heterozygous GT (HR 0.30; 95% CI:0.10-0.89, P= 0.03), after adjusting for known clinical prognostic parameters such as gender, race, age at diagnosis, number of metastatic sites, number of chemotherapy lines received and CEA at diagnosis. The patients with the TT genotype had 70% reduced risk of death. We have also analyzed the expression of DNA excision repair protein ERCC-1 in 56 mCRC patients' pre and post oxaliplatin regimen by immunoblot and real time quantitative PCR. Median PFS was 190 and 237 days in the two groups respectively (log-rank test HR 2.35, CI 1.005-5.479; p=0.0182) Thus, increase in ERCC gene expression post platinum-based chemotherapy is a potential marker of drug resistance. Further in effort to understand the immune responses in mCRC we generated tissue microarray from 137 mCRC patients and performed immune histochemical staining for four different markers of B7 family of immune modulators. The analysis showed that increase expression of B7H3 is a potential biomarker of worse overall survival among patients of different racial origin. Race was designated as non-Hispanic white (NHW, n=25), non-Hispanic black (NHB, n=63), and Hispanic (n=49). Median survival was 747days for NHW and 565days for H patients (p=0.036, HR=1.6, 95% CI=1.03-2.58).

Speaker Biography

Radhashree Maitra is a Senior Scientist at Montefiore medical centre and also an associate professor of biology at Yeshiva University. She completed her bachelor's degree in chemistry (honours) with specialization in Biochemistry. She did her masters in Biochemistry with specialization in molecular Biology and also a Ph.D in Biophysics, molecular biology and genetics from Calcutta University in 1997. She qualified for UGC (University Grants commission, India) National Eligibility Test (NET) award in 1989 and then "Senior Research Fellowship" award from CSIR-INDIA in 1993. She did her first post-doctoral research at Washington University in St. Louis, Missouri and her second postdoctoral research at Albert Einstein College of Medicine of Yeshiva University, Bronx New York. She has around 28 original peers reviewed publications.

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