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Effect of genomic instability and mutations on the signaling pathways in colon cancer cells

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Colorectal cancer (CRC) is the third most common cancer diagnosed in the United States and the second leading cause of cancer death. Microsatellite instability (MSI) is present in about 15% of colorectal cancers and plays critical roles in the development and progression of these cancers. Several clinical studies showed that MSI colon cancer has a more favorable prognosis and is less prone to lymph node and distance metastasis. Furthermore, the MSI phenotype may predict the response to treatment with 5-fluorouracil (5-FU) and irinotecan. Recent gene expression studies revealed alteration of the apoptotic and immune response pathways in MSI cells. However, the role of these pathways in the carcinogenesis of CRC and the interaction of these protein biomarkers in MSI CRC cells remain to be determined. The goal of this study is to determine the global effect of microsatellite instability on the signaling pathways and network in colon cancer cells to find out the protein biomarker. We profiled the expression and phosphorylation of 110 proteins in six colon cancer cell lines by using Protein Pathway Array. The pathways and network constituted by these proteins were identified by using Ingenuity Pathway Analysis. Our results showed that 25 proteins and phosphoproteins change more than 1.5-fold between MSI and microsatellite stable (MSS) cells. Sixteen major pathways were affected in MSI cells, including p53 and 14-3-3β pathways, with p53 and HGF being the most important pathways. Finally, although the EGFR/K-RAS/MEK pathway was not affected in MSI cells, collateral pathways such as the p70S6K and p90RSK pathways were activated in MSI cells. Thus, suppression of the p53 pathway and activation of the HGF pathway in MSI cells may be critical in the tumorigenesis of MSI colorectal cancer.

Biography

Miao Cui has completed his MD at the age of 23 years from Nantong Medical College in China. He is working as an associate researcher at Mount Sinai School of Medicine, New York, USA. He has published 1 paper in American Journal of Pathology and Cellular Immunology, respectively, and has 2 paper and 6 book chapters which are under review. He is serving as a reviewer for Journal of Hepatology. He had a poster presentation at 33rd Annual San Antonio Breast Cancer Symposium in San Antonio, Texas and 2010 immunology institute retreat, Mount Sinai School of Medicine, New York.

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