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Chemo resistance mediated by micro RNAs in cancer

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Abstract

Research involved in the translational regulation of suspected genes in cancer has come to a new frontier in recent years. Mounting evidence showed that post-transcriptional and translational controls mediated by various regulatory molecules, such as RNA binding proteins and non-coding miRNAs, are critically important. Our laboratory was first discovered that a number of miRNAs were regulated by tumor suppressor p53. Such regulatory mechanism was important in regulating cell proliferation and cell cycle control. To investigate the impact of miRNA in chemoresistance to fluoropyrimidines and antifolates, we discovered that miR-215 suppresses the expression of both thymidylate synthase and dihydrofolate reductase. In addition, the expression of miR-215 was directly regulated by p53. The expression of miR-215 was significantly associated with colorectal cancer patient survival. miR-140 modulates chemosensitivity by suppressing HDAC4 expression, and the levels of miR-140 and miR-215 were elevated in colon cancer stem cells. Our recent studies have shown that miR-194 was directly involved in epithelial-to-mesenchymal (EMT) transition, a critical event for tumor progression and metastasis. The expression of BMI-1 protein was suppressed by miR-194 directly at the 3'-UTR region of BMI-1 mRNA. miR-502 regulates autophagy in colon cancer by targeting Rab1B. miRNA based therapeutics, diagnosis and prognosis may emerge in the near future to benefit cancer patients.

Biography

Jingfang Ju, Ph.D. is Co-Director of Translational Research Laboratory at Stony Brook University. He received his Ph.D. in Biochemistry/Molecular biology from University of Southern California and postdoctoral fellow at the Cancer Center of Yale University. His group was the first to discover that non-coding microRNAs are part of the p53 tumor suppressor network. Currently Dr. Ju is focusing on elucidating the molecular mechanism of miRNA mediated cancer stem cell chemoresistance. Dr. Ju's group made the initial systematic discovery that miRNA is stable in archival FFPE specimens (RNA, 2007), this has open the opportunity for miRNA based biomarker discovery.