DEVELOPMENT OF NOVEL miR-129 MIMIC WITH ENHANCED THERAPEUTIC POTENTIAL TO ELIMINATE RESISTANT COLON CANCER STEM CELLS

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BIOGRAPHY

Jingfang Ju is the Professor in the Department of Pathology at Stony Brook Medicine/Stony Brook University. He received his BS degree from the Northeastern University and PhD in molecular biology and biochemistry at the University of Southern California. He completed his post-doctoral research fellowship at Yale Cancer Center, Yale University. Previously he has served as the Senior Scientist and Team Leader of high throughput genomics at a biopharmaceutical company, CuraGen Corporation in Connecticut.

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Treatment of advanced stage colorectal cancer remains a clinical challenge associated with resistance to fluoropyrimidine based chemotherapy. There is an urgent need to discover and develop new strategies to enhance treatment efficacy in order to improve outcomes for these patients. Non-coding microRNAs (miRNAs) have important functions as oncogenes or tumor suppressor genes in the regulation of cancer development and progression. Recently, miRNAs have emerged as potential therapeutic options. We have identified miR-129 as tumor suppressor miRNA and potential therapeutic candidate in colorectal cancer. The expression of miR-129 expression is progressively lost in colorectal cancer patients and is an important regulator of apoptosis through the targeting of genes such as BCL-2. miR-129 was also found to enhance 5-flurouracil (5-FU) cytotoxicity *in vitro* and *in vivo*. To further developing miR-129 based novel therapeutics in colorectal cancer, we have designed a modified version of miR-129 to enhance stability and efficacy. The miR-129 mimic is significantly more potent in inhibiting proliferation of a panel of colon cancer cell lines than the native miR-129 precursor. The miR-129 mimic induces profound cell cycle arrest at the G1/S checkpoint. We also demonstrated that the miR-129 mimic retains its target specificity to BCL-2, TS and E2F3 as same as the native miR-129 precursor. More importantly, the miR-129 mimic can eliminate resistant colon cancer stem cells. The therapeutic potential of miR-129 was demonstrated *in vivo* mouse colon tumor models as a potent inhibitor of tumor growth and metastasis. As a result, miR-129 mimic has a great potential to be further developed as a novel therapeutic drug for treatment of advanced colorectal cancer.

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