

MicroRNAs as novel therapeutic adjuvants to treat drug resistant breast cancers

Manjeet K Rao

University of Texas Health Science Center, USA

Resistance to chemotherapy drugs results in poor response rates and treatment failure in more than 90% of patients with metastatic breast cancers. Understanding the mechanisms underlying such resistance is therefore crucial for the development of new, efficacious cancer drugs. Unfortunately, in spite of extensive inquiry in this field, little is known about the key molecules/signaling pathways that regulate this phenomenon. We have discovered that microRNAs (miRNAs) may play critical roles in mediating drug sensitivity/resistance in breast cancers. We have identified miRNAs that are differentially expressed between chemo-resistant and sensitive HER2⁺ breast cancer cells. Specifically, through high-throughput miRNA inhibitor library screens, we have identified miRNAs that sensitize drug-resistant breast cancer cells to paclitaxel and trastuzumab (herceptin), a drug combination commonly used for the treatment of HER2⁺ metastatic breast cancers. Our studies reveal that cognate miRNA/s, which sensitize/de-sensitize resistant tumor cells to drug-induced cell death are differentially expressed in the Her2⁺ metastatic breast cancer patients compared to normal matched controls. Importantly, using liposome-based or biocompatible nanoparticles-based approaches, we have demonstrated that candidate miRNAs can be systemically delivered to sensitize and therefore, eliminate chemoresistant metastatic breast cancers in tumor bearing mice. These findings suggest that certain miRNAs are selectively cytotoxic in a drug-specific manner and these miRNAs may serve as novel biomarkers and provide potent adjuvant therapeutic tools for the treatment of drug-resistant metastatic breast cancers.

Biography

Manjeet Rao completed his Ph.D at the age of 28 years from University of Delhi, India and postdoctoral studies from M. D. Anderson Cancer Center, Houston, Texas, USA. Currently, He is an Assistant Professor at the Greehey Children's Cancer Research Institute, University of Texas Health Science Center, San Antonio, Texas. Rao has published more than 25 papers in reputed journals including Cell, Genes & Development and PNAS and has been serving as an editorial board member of Journal of Cancer Science and Therapy, and reviewer of several journals of repute including PLoS Genetics and Oncogene.

raom@uthscsa.edu