

microRNA93 modulates breast cancer stem cells by regulating their EMT/MET states, proliferation and differentiation

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MicroRNAs (miRNAs) play important roles in normal cellular differentiation and oncogenesis. microRNA93 (mir93), a member of the mir106b-25 cluster, located in intron 13 of the MCM7 gene, although frequently overexpressed in human malignancies may also function as a tumor suppressor gene. Using a series of breast cancer cell lines representing different stages of differentiation and mouse xenograft models, we demonstrate that mir93 modulates the fate of breast cancer stem cells (BCSCs) by regulating the EMT/MET conversion as well as their proliferation and differentiation states. In “claudin^{low}” SUM159 cells, expression of mir93 induces MET associated with downregulation of TGF β signaling and downregulates multiple stem cell regulatory genes including JAK1, STAT3, Akt, SOX4, EZH1 and HMGA2 resulting in cancer stem cell (CSC) depletion. Enforced expression of mir93 completely blocks tumor development in mammary fat pads and development of metastases following intracardiac injection in mouse xenografts. The effects of mir93 on the CSC population is dependent on the cellular differentiation state with mir93 expression increasing the CSC population in MCF7 cells which display a more differentiated “luminal” phenotype. These studies demonstrate that miRNAs can regulate CSC states, the existences of which have important biological and clinical implications.

Biography

Suling Liu, PhD is an Assistant Professor at the University of Michigan. Her research interests have been focusing on Cancer Stem cell Biology. Evidence from this research is of obvious significance for the development of new diagnosis tools and innovative treatments for cancer. After getting PhD from Ohio State University in Dec 2003, her research interest on breast carcinogenesis took her to focus on cancer therapy to find novel treatments to cancer by targeting the cancer stem cells. She has published over 30 peer-reviewed papers together with three manuscripts in preparation and filed four patent applications as a co-inventor; she has been serving as reviewers and in editor board of many journals.