Suling Liu, J Cell Sci Ther 2011, 2:4
doi: http://dx.doi.org/10.4172/2157-7013.S1.16

OMICS Group Conferences
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International Conference & Exhibition on
Cell Science & Stem Cell Research

29 Nov - 1 Dec 2011 Philadelphia Airport Marriott, USA

Micro RNA93 regulates breast cancer stem cells

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There is increasing evidence that the growth and metastasis of many tumors, including breast cancer, are driven by a cellular population displaying stem cell properties. Like their normal counterparts, these breast cancer stem cells may be regulated by MicroRNAs (miRNAs). We have previously demonstrated that breast cancer cell lines contain subpopulations with stem cell properties that can be isolated by virtue of their expression of Aldehyde dehydrogenase (ALDH) as assessed by the Aldefluor assay. We compared miRNA expression in Aldefluor-positive and Aldefluor-negative populations in a series of five breast cancer cell lines. We identified specific miRNA expression profiles for each population. Among the differentially expressed miRNAs was miR-93 whose expression was significantly increased in Aldefluor-negative compared to Aldefluor-positive populations. To confirm the regulation of miR-93 during cell differentiation we constructed a miR-93 sensor tagged with GFP and demonstrated that sensor-positive (miR-93-negative) cells had significantly increased tumor initiating capacity in NOD/SCID mouse xenografts compared to sensor-negative (miR-93-positive cells). Furthermore, miR-93-negative cells gave rise to tumors containing both miR-93-negative and miR-93-positive cell populations. Utilizing a tetracycline inducible lentivirus driving miR-93 expression, we found that induction of miR-93 expression decreased the ALDH-positive population *in vitro* as well as in mouse xenografts where this reduction was associated with decreased tumor growth. Furthermore, induction of miR-93 expression immediately upon orthotopic implantation or intracardiac injection completely blocked subsequent tumor growth and metastasis formation. These studies demonstrate that miR-93 plays a functional role in the self-renewal and differentiation of breast cancer stem cells. Furthermore, the TET-inducible miR-93 system allows for the controlled regulation of cancer stem cell function providing a valuable model to simulate the effects of CSC-directed therapies on breast cancer growth and metastasis.

Biography

Suling Liu, PhD is an Assistant Professor at the University of Michigan Comprehensive Cancer Center. Her research interests have been focusing on Cancer biology and 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. This interest brought her to Dr. Max S Wicha's laboratory at the University of Michigan. She has been working on identifying/isolating both normal and cancerous human breast Stem cells and studying the role of Hedgehog pathway, Notch pathway, Bmi-1, BRCA1, tumor microenvironment and microRNAs in the regulation of human mammary stem cell self-renewal and differentiation with most of the molecular and cellular techniques both in vitro and in vivo. She has published over 30 peer-reviewed papers together with three manuscripts in revision and filed four patent applications as a co-inventor; her research has made significant contributions towards out goal of developing more effective therapies for breast cancer.