OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference on
Biomarkers & Clinical Research

July 2-4, 2012 Embassy Suites Las Vegas, USA

Regulation of breast cancer stem cells by microRNA93 (mir93)

Kevin J. Zhang
University of Michigan Cancer Center, USA

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 has 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

Kevin J. Zhang is a second year student at the University of Michigan and has been conducting research in the Wicha Lab at Michigan's Comprehensive Cancer Center on projects involving stem cells, microRNA, and Aldefluor staining. He attended the National Conference of Undergraduate Research in Ithaca last year. He intends to graduate with an honors thesis in Cellular and Molecular Biology in 2014.

kjzhang@umich.edu