Cell Therapy-2013

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference and Exhibition on
Cell & Gene Therapy

October 23-25, 2013 Holiday Inn Orlando International Airport, USA

Sex and microRNA in cancer stem/progenitor cells

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Abstract

Malignant immature ovarian teratomas (IOT) most occur in women of reproductive age. However, what roles estrogenic signaling plays in IOT is unknown. Cancer stem/progenitor cells (CSPCs) is known to be regulated by small non-coding RNA, miR21, which linked to ovarian malignancies. In this study, we examined estrogen receptors (ERα and β) roles IOT, and it's relation to miR-21. Estrodiol (E2), PPT and DPN (ERα- and β-specific agonists), as well as ERα- or ERβ-specific shRNAs were applied to PA-1 IOT cells. We found E2/ERα signals promote cell migration and invasion through non-classical transactivation function. The data showed non-genomic E2/ERα activations of focal adhesion kinase-Ras homolog gene family member A (FAK-RhoA) and ERK governed cell mobility. The E2/ERα signaling induces epithelial-mesenchymal transition (EMT) and overexpression of CD133 through upregulation micro-RNA 21, and ERK phosphorylations. Knockdown of miR-21 in PA1 cells attenuated whereas overexpression of miR-21 promoted cell growth. Moreover, knockdown of miR-21 resulted in a marked reduction in the CD133+ population and sphere formation of CSPCs. In contrast, overexpression of miR-21 resulted in a marked increase in the population of CD133+ cells and sphere formation of CSPCs. Furthermore, E2/ERα signals trigger a positive feedback regulatory loop within miR21 and ERK. At last, cytosolic ERα, CD133, and EMT markers, but not epithelial cell markers, in IOT tissue samples were co-expressed. In conclusion, estrogenic signals exert malignant transformation capacity of cancer cells, exclusively through non-genomic regulation in female germ cell tumors.

Biography

Wen-Lung Ma received Ph.D. degree from University of Rochester in 2009. After 18 months post-doctorate training in Wilmot Cancer Center, University of Rochester Medical Center, he promoted to Assistant Professor in China Medical University in 2011. He published total 20 papers with 5 major in the Gastroenterology field of highest profile journals during his PhD and post-doc training period. He then demonstrated his independency with three published papers in cancer stem cell/GYN cancer field this year. He also received long term supports for conducting his study of interests since 2010 from National Science Council, Taiwan.