allied academies

11th International Conference on
CANCER STEM CELLS AND ONCOLOGY RESEARCH

June 11-13, 2018 | Dublin, Ireland

hTERThigh NUMB-/LOW STATE ENRICHES A CASTRATION RESISTANT PROSTATE CANCER CELL SUBPOPULATION WITH TUMOR INITIATING CAPACITY

Helen He Zhu[1, 2]
[1]Ren Ji Hospital, School of Medicine, China
[2]Shanghai Jiao Tong University, China

Castration resistant prostate cancer (CRPC) remains one of the most deadly and incurable cancer types worldwide. Tumor cells in CRPC patient samples display tremendous heterogeneity. Cancer stem cells (CSCs) are proposed to be the driving force in cancer progression and recurrence. Identification of the CSC or prostate cancer cell sub-population with greater castration resistance is a key to the development of targeted anti-CRPC treatment strategies. We report that the hTERThigh PCa cells exhibit CSC properties including stem cell associated gene expression signature, long term tumor propagating capacity, and epithelial-to-mensenchymal transition. hTERThigh CSC cells display distinct cell division modes and can undergo both symmetric division and asymmetric division, as compared to hTERT-/low Pca cells. Numb, an evolutionarily conserved cell fate determinant, tends to segregate into the more differentiating daughter cell during symmetric division and asymmetric division of hTERThigh CSC cells. Further investigation revealed that Numb is down-regulated and negatively correlated with PCa advancement. Functionally, Numb exerted an inhibitory role in xenograft prostate tumor growth and CRPC development via suppression of Notch and Hedgehog signaling. Through a Numb promoter based lentiviral reporter system, we were able to separate Numb-/low Pca cells from Numbhigh cells. Numb-/low PCa cells are smaller and quiescent, preferentially express Notch and Hedgehog downstream and stem-cell-associated genes, and are associated with greater resistance to androgen deprivation therapy. Targeting Notch and Hedgehog signaling with inhibitors can effectively deplete the Numb-/low castration resistant PCa cells. Collectively, these findings provide novel insight into cellular and molecular mechanisms for the development of advanced CRPC and to the development of effective anti-CRPC treatment strategies.

Note:

BIOGRAPHY

Helen He Zhu received her Bachelor Degree from Fudan University, China. She performed her PhD study in Molecular Pathology at School of Medicine, University of California-San Diego and did her postdoctorate training in the Department of Biology, University of California-San Diego. In 2012, She relocated back to China and started to work as an Associate Professor then Professor in Ren Ji Stem Cell Research Center, Ren Ji Hospital at School of Medicine, Shanghai Jiao Tong University. Her current work focuses on 1) adult tissue stem cells from hematopoietic system and prostate in tissue development and tumorigenesis. 2) roles of prostate cancer stem cells in therapeutic resistance and tumor metastasis. Her publication includes first author and corresponding author papers in Blood, PNAS, Gastroenterology, Clinical Cancer Research, Cancer Research and etc.

zhuhecrane@shsmu.edu.cn