J Cancer Sci Ther 2016, 8:6 (Suppl)
http://dx.doi.org/10.4172/1948-5956.C1.070

Valproic Acid (VPA) inhibits the epithelial-mesenchymal transition in prostate carcinoma via the dual suppression of SMAD4

Qinghua Xia[1], Xiaopeng Lan[1], Guoliang Lu[1], Chuanwei Yuan[1], Shaowei Mao[1], Wei Jiang[2], Yougen Chen[1] and **Xunbo Jin[1]**
[1]Provincial Hospital, China
[2]Dongying People`s Hospital, China

The epithelial-mesenchymal transition (EMT) plays an important role in cancer metastasis. Previous studies have reported that Valproic Acid (VPA) suppresses prostate carcinoma (PCa) cell metastasis and down-regulates SMAD4 protein levels, which is the key molecule in TGF-β-induced EMT. However, the correlation between VPA and the EMT in PCa remains uncertain. Markers of the EMT in PCa cells and xenografts were molecularly assessed after VPA treatment. The expression and mono-ubiquitination of SMAD4 were also analyzed. After transfection with plasmids that express SMAD4 or short hairpin RNA (shRNA) for SMAD4 down-regulation, markers of EMT were examined to confirm whether VPA inhibits the EMT of PCa cells through the suppression of SMAD4. VPA induced the increase in E-cadherin ($p<0.05$), and the decrease in N-cadherin ($p<0.05$) and Vimentin ($p<0.05$), in PCa cells and xenografts. SMAD4 mRNA and protein levels were repressed by VPA ($p<0.05$), whereas the level of mono-ubiquitinated SMAD4 was increased ($p<0.05$). SMAD4 knockdown significantly increased E-cadherin expression in PC3 cells, but SMAD4 over-expression abolished the VPA-mediated EMT-inhibitory effect. VPA inhibits the EMT in PCa cells via the inhibition of SMAD4 expression and the mono-ubiquitination of SMAD4. VPA could serve as a promising agent in PCa treatment, with new strategies based on its diverse effects on post-transcriptional regulation.

xqhgege@hotmail.com

Animal and cellular models of hepatocellular carcinoma bone metastasis: Establishment and characterization

Rui Hou
Peking Union Medical College Hospital, China

An increasingly high occurrence of bone metastases in Hepatocellular Carcinoma (HCC) patients highlights the importance of fundamental research on HCC bone metastasis, which has been limited in its success due to the lack of a model system. We successfully established a nude mouse model of HCC bone metastasis using the HCC cell lines HCCLM3 and MHCC97H via intracardiac injection. Injected tumour cells formed metastases in skull, spine, hind limbs, and sternum, causing osteolytic lesions via MMP-1 and recruitment of osteoclasts. Four bone metastatic cell lines (BM1) were extracted from HCCLM3-inoculated mice and were demonstrated to exhibit a much stronger ability to form bone metastases as well as other phenotypes, including enhanced *in vitro* migration/invasion and colony formation. Moreover, the expression of PTHrP, MMP-1, and CTGF was significantly elevated in bone metastatic cells compared to parental cells. In conclusion, the nude mouse model and bone metastatic cell lines (BM1) together provide an effective simulation of HCC bone metastasis. These model systems will become powerful tools with which to explore the mechanisms and therapies of HCC bone metastasis. Additionally, PTHrP, MMP-1, and CTGF are candidate genes related to HCC bone metastasis.

henrequelme@aliyun.com