

AB036. P-04. The upregulation of Oct4 in acidic extracellular pH is associated with gemcitabine resistance in cholangiocarcinoma cell lines

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Background: Cholangiocarcinoma (CCA), although is an uncommon liver cancer originating from bile duct epithelial cells, is one of the top 10 most fatal cancers. Chemoresistance is an unmet need always found in CCA patients. Tumor microenvironment conditions such as

hypoxia, nutrient starvation and acidic extracellular pH play critical roles in cancer progression. However, the role of acidic extracellular pH in chemoresistance in CCA has not been studied.

Methods: Human CCA cell lines (KKU-100, KKU-M055 and KKU-M213) were cultured under acidic (pH 6.5) or non-acidic (pH 7.4) condition. After that we measured doubling times, drug sensitivity and gene expression.

Results: Here, we demonstrated that extracellular acidic pH (pH 6.5) significantly increased doubling times of CCA cell lines compared with non-acidic condition (pH 7.4). Interestingly, extracellular acid condition induced chemoresistance in CCA cell lines. We showed that octamer-binding transcription factor 4 (Oct4) was up-regulated in these cell lines under extracellular acid condition.

Conclusions: Our findings suggest that Oct4 may be a key transcriptional regulator which mediates chemoresistance in response to extracellular acidic pH.

Keywords: Chemoresistance; tumor microenvironment; octamer-binding transcription factor 4 (Oct4); liver cancer; cancer stem cell-like cell

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