



AB033. P-01. Andrographolide (AP1) inhibits cholangiocarcinoma cell invasion *in vitro* model

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Background: In Thailand, there has been an intensive pursuit for new treatment derived from herbal medicine. Andrographolide (AP1) is one of the major diterpene lactones that considered being the most active and important constituent of *Andrographis paniculata*, a medicinal plant that is included in “the National List of Essential Drugs: List of Herbal Medicinal Products”. AP1 has several therapeutic effects including hepatoprotective effects, promotes bile flow, potent anti-angiogenic, and anti-cancer properties. Treatment with AP1 blocks numerous signaling pathways as well as promoting apoptosis and inhibiting cell cycle proteins. Proline-rich homeodomain protein/haematopoietically expressed homeobox (PRH/HHEX) is a transcription factor that regulates cell

proliferation, migration, and differentiation in multiple tissues. PRH is essential for embryonic development of the liver and bile ducts and has tumour suppressor activity in hepatocellular carcinoma (HCC). Misregulation of PRH is associated with several cancers including HCC, breast cancer, prostate cancer, and leukaemia. Our objective is to examine the association between AP1 and PRH and its role in cholangiocarcinoma (CCA) invasion.

Methods: Knockdown of PRH was achieved by stable and transient expression of PRH shRNA and PRH siRNA. Cell proliferation was measured by BrdU incorporation. Cell invasion was examined using transwell matrigel invasion assay. Western blotting was used to examine the expression of PRH and the corresponding proteins in CCA.

Results: Western blotting reveals that high PRH expression is associated with highly invasive CCA cell lines. PRH KD decreases the proliferation and invasion of CCLP-1, HuCCA-1, KKKU-M213 CCA cell lines and alters the epithelial-mesenchymal transition (EMT)-related proteins. Low dose AP1 inhibits the invasive properties of CCLP-1, HuCCA-1, KKKU-M213 CCA cell lines. Interestingly treatment of CCA cells with AP1 decreases the PRH/HHEX protein levels.

Conclusions: Our data suggest that AP1 down-regulates PRH expression (at least in part) and that this blocks CCA invasion.

Keywords: *Andrographis paniculata*; andrographolide; proline-rich homeodomain protein (PRH); cholangiocarcinoma (CCA); bile duct cancer; invasion

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