To investigate the role of cofilin in Apicidin-induced chemical resistance HA22T Hepatocellular carcinoma cells

Po-Hsiang Liao¹., Wei- Wen Kuo³., Chih Yang Huang. ^{1,2}

¹Graduate Institute of Basic Medical Science, China Medical University, Taichung

² Department of Biological technology, Asia University, Taichung

³Department of Biological Science and Technology, China Medical University, Taichung

E-mail: robert750927@hotmail.com

Abstract

Hepatocellular carcinoma (HCC) is the most common primary tumor of the liver. Chemoresistance is the major issue in HCC therapy. In our previous study indicated that β -catenin play a important role in metastasis in HA22T HCC cell line and HCC patients. Apicidin is a novel HDAC inhibitor, derived from a fungal metabolite, and it's treatment resistant in HCC remains to be elucidated. To establish a stable HA22T HCC cell line chronically resistant to apicidin, HA22T cells were exposed to gradually increasing concentrations of apicidin. We observed that Apicidin-resistant HA22T (Apicidin-R) cells were highly increased highly potentiate metastasis and pro- survival effect and discovered several proteins highly expression in Apicidini-R cell by 2-dimensional gel electrophoresis (2-DE). In this study, we demonstrated that the protein, phosphorylated cofilin 1 (p-CFL1) correlates with Apicidin resistance in HCC cells. Some protein spots between HA22T and Apicidin-R cells were revealed to be significantly different in spot intensity by statistical analysis, Cofilin 1 (CFL1) was selected as a candidate which may play an important role in Apicidin resistance. Higher expression levels of p-CFL1 in Apicidin-R cells were demonstrated. Furthermore, other studies indicated overexpression of CFL1 or phosphorylation of cofilin correlated with tumor metastasis, but we observed that Apicidin-R cells decrease ROS induce mitochondria-dependent apoptosis via phosphorylation of cofilin.