CPAP promotes HCC angiogenesis and metastasis via interacting with and enhancing STAT3 signaling

Ruo-Yu Chen¹, Chia-Jui Yen³, Yao-Wen Liu⁵, Chun-Guo Guo², Chieh-Yu Weng², Yih-Jyh Lin⁴, and Liang-Yi Hung¹,²,*

¹Department of Biotechnology and Bioindustry Sciences, ²Institute of Bioinformatics and Biosignal Transduction, College of Bioscience and Biotechnology; National Cheng Kung University, Tainan 70101, Taiwan
³Division of Hematology-Oncology, Department of Internal Medicine, ⁴Department of Surgery, College of Medicine, National Cheng Kung University Hospital, Tainan 70403, Taiwan
⁵Department of Clinical Pathology, Kuo General Hospital, Tainan 70054, Taiwan

Centrosomal P4.1-associated protein (CPAP) is a centrosomal protein and can as a transcriptional coactivator of STAT5 and NF-κB in cancer. Our previous studies indicated that CPAP is overexpressed in tumor tissue and can increase TNFα-mediated NF-κB activation in HCC. Here, we demonstrated that overexpressed CPAP increases tumor growth, angiogenesis, as well as metastasis ex vivo and in vivo. We found that CPAP increases these malignant abilities of tumor cells are through IL-6/STAT3 signaling. We demonstrated that CPAP directly interacts with C-terminal domain of STAT3 to increase STAT3 activity. Overexpression of CPAP enhances IL-6/STAT3/IL-8-mediated angiogenesis and other metastatic genes expression such as CD44 and MCAM. These results indicated that CPAP leads to HCC malignancy and metastasis by increasing STAT3 activity through directly interaction. Clinically, CPAP positively correlates with IL-8 in HCC with vascular invasion; and also positively correlates with CD44 and MCAM in HCC tissues. In summary, our findings shed light on the importance of CPAP to act as a potential therapeutic target for inhibiting the IL-6/STAT3-mediated angiogenesis pathway and treating metastatic HCC.