P – 031 Low level of centromere-associated protein E promotes growth of hepatocellular carcinoma and is associated with adverse clinical features

Y Lin[1], P He[2], P Hu[3], H Chen[4], Y Chen[5], E McGowan[1]

[1]School of Life Sciences, University of Technology Sydney, Broadway, Australia, [2]General Hospital of Guangzhou Military Command, Guangzhou, China, [3]Affiliated Jiangmen Hospital of Sun Yat-sen University, Jiangmen, China, [4]Department of TCM, The Third Affiliated Hospital of Sun Yet-sen University, Guangzhou, China, [5]Department of TCM, Third Affiliated Hospital of Sun Yat-sen University, Guangdong Key Laboratory of Liver Disease Research, Guangzhou, China

Introduction: Human kinesin centromere-associated protein E (CENP-E), a spindle checkpoint protein, has been identified as a tumour suppressor. Although reduced CENP-E expression has been reported in human hepatocellular carcinoma (HCC) tissues, its role in hepatocarcinogenesis is unknown. To date, there is no evidence linking reduced CENP-E expression to HCC initiation and development, nor any evidence that low CENP-E in HCC has any clinical relevance. In this study, we investigated the contribution of reduced CENP-E on HCC development and the clinical relevance of low CENP-E in HCC patients.

Methods: HCC cell lines (SMMC7721 and QGY7701), animal xenograft models, and 90 human HCC tissues were used to investigate the importance of CENP-E as a tumour suppressor. CENP-E was silenced using-shRNAs and validated by western blotting and immunohistochemistry (IHC). In vitro effects were studied using cell proliferation, migration, colony forming, and wound closure assays. Cell-cycle and cell apoptosis were analysed by flow cytometry. The in vivo effect of down-regulated CENP-E on tumour growth was examined in a xenograft tumour model. CENP-E expression in HCC tissues was analysed by IHC. Analysis of patient survival was performed using Kaplan–Meier analysis and Cox regression analysis (SPSS).

Results: We demonstrated that down-regulation of CENP-E by CENP-E-silencing shRNAs significantly promoted HCC proliferation/growth both in vitro and in vivo. CENP-E suppressed the proliferation of HCC cells by halting cell cycle progression at the G1-S phase and accelerated cell apoptosis. Analyses of HCC patient samples/clinical data revealed that CENP-E was significantly down-regulated in HCC tissues and low CENP-E expression was significantly associated with patient adverse clinicopathological features including poor prognosis, advanced TNM stage, metastasis, and larger tumor size. Multivariate analysis indicated that CENP-E was an independent prognostic factor predicting outcomes of advanced HCC patients.

Conclusion: Our data suggest that loss of CENP-E contributes to HCC development and is strongly associated with the adverse clinical pathology of HCC. Thus CENP-E could be a novel target for new treatments and a useful prognostic biomarker for HCC patients.