

Impact of FOXP3 in Hepatocellular Carcinoma

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Transcription factor FOXP3, a biomarker for regulatory T cells, can also express in several types of cancers but its function is debatable. The role of hepatocyte-expressed FOXP3 in hepatocellular carcinoma (HCC) has not been studied. In this study, the tumor samples and clinical information were collected from 115 HCC patients. 5 human cancer cell lines were used for various experiments. The sequence of FOXP3 was examined for mutation and the promoter activity was checked by luciferase assay. Mouse tumor model was employed to confirm in vitro results. We found that mutations in FKH domain of FOXP3 mRNA were detected in 33% HCC tumor tissues but none of the adjacent non-tumorous tissues. No prevalent mutations were identified at high frequency in the samples, indicating the mutations occurred randomly. Moreover, the mutations were not detected in corresponding regions of genomic DNA. Many mutations resulted in amino acid substitutions in FKH region, which could subsequently cause changes of FOXP3 subcellular localization. The delocalization of FOXP3 from nucleus to cytoplasm caused loss of its transcription regulation and xenograft tumor-suppressor capabilities and different cellular responses to HDAC inhibitors. In addition, more complicated FKH mutations appeared to be associated with worse prognosis in HCC patients. Collectively, mutations in FKH domain of FOXP3 mRNA frequently occurred in HCC. The mutations were most possibly caused by transcription errors but not derived from genomic DNA mutations. Our results have suggested for the first time that transcriptional mutagenesis of FOXP3 plays a suppressive role in HCC. (Supported by NSFC No.81472339)

Biography:

George G Chen is an Emeritus Professor in the Department of Surgery, and Senior Research Fellow, Department of Otorhinolaryngology, Head and Neck Faculty of Medicine, the Chinese University of Hong Kong, China. He has extensive experience in cancer research. He has authored or co-authored 230 papers and has written a number of books or book chapters, with h-index: 45.