World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:8, No:05, 2014

Initiation of Paraptosis-Like PCD Pathway in Hepatocellular Carcinoma Cell Line by Hep88 mAb through the Binding of Mortalin (HSPA9) and Alpha-Enolase

Authors : Panadda Rojpibulstit, Suthathip Kittisenachai, Songchan Puthong, Sirikul Manochantr, Pornpen Gamnarai, Sasichai Kangsadalampai, Sittiruk Roytrakul

Abstract : Hepatocellular carcinoma (HCC) is the most primary hepatic cancer worldwide. Nowadays a targeted therapy via monoclonal antibodies (mAbs) specific to tumor-associated antigen is continually developed in HCC treatment. In this regard, after establishing and consequently exploring Hep88 mAb's tumoricidal effect on hepatocellular carcinoma cell line (HepG2 cell line), the Hep88 mAb's specific Ag from both membrane and cytoplasmic fractions of HepG2 cell line was identified by 2-D gel electrophoresis and western blot analysis. After in-gel digestion and subsequent analysis by liquid chromatography-mass spectrometry (LC-MS), mortalin (HSPA9) and alpha-enolase were identified. The recombinant proteins specific to Hep88 mAb were cloned and expressed in E.coli BL21 (DE3). Moreover, alteration of HepG2 and Chang liver cell line after being induced by Hep88 mAb for 1-3 days was investigated using a transmission electron microscope. The result demonstrated that Hep88 mAb can bind to the recombinant mortalin (HSPA9) andalpha-enolase. In addition, gradual appearance of mitochondria vacuolization and endoplasmic reticulum dilatation were observed. Taken together, paraptosis-like programmed cell death (PCD) of HepG2 is induced by binding of mortalin (HSPA9) and alpha-enolase to Hep88 mAb. Mortalin depletion by formation of Hep88 mAb-mortalin (HSPA9) complex might initiate transcription-independent of p53-mediated apoptosis. Additionally, Hep88 mAb-alpha-enolase complex might initiate HepG2 cells energy exhaustion by glycolysis pathway obstruction. These results imply that Hep88 mAb might be a promising tool for development of an effective treatment of HCC in the next decade.

Keywords : Hepatocellular carcinoma, Monoclonal antibody, Paraptosis-like program cell death, Transmission electron microscopy, mortalin (HSPA9),alpha-enolase
Conference Title : ICMBBE 2014 : International Conference on Molecular Biochemistry and Biological Engineering
Conference Location : Tokyo, Japan
Conference Dates : May 29-30, 2014