

2nd International Summit on **Integrative Biology**

August 04-05, 2014 Hilton-Chicago/Northbrook, Chicago, USA

A novel nano-gene therapy to specifically target human hepatocellular carcinoma

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Except surgical resection of cancer, no effective therapy is available for human hepatocellular carcinoma (HCC). Moreover, the majority of HCC patients are not qualified for the surgical resection because of the late stage of the disease at the diagnosis. Therefore, there is an urgent need to develop new and effective treatments for HCC. Among various developments, the gene therapy is one of potential options. We have found that single-nucleotide polymorphisms (SNPs) in human alpha-fetoprotein (AFP) promoter are associated with HCC serum AFP, the well-known biomarker for HCC, suggesting that AFP promoter variants may generate better transcriptional activities while retaining high specificity to AFP-producing cells. We thus sequenced human AFP promoters, cloned 15 different genotype promoters and tested their reporter activity in AFP-producing and non-producing cells. AFP promoter variant EA4D that is with the highest activity was fused with tBid and coupled with nano-particle vector (H1) to form pGL3-EA4D-tBid whose therapeutic efficiency was tested *in vitro* and *in vivo*. Among various AFP variant fragments tested, EA4D exhibited the highest reporter activity. When coupled with H1, pGL3-EA4D-tBid could express a high level of tBid while retaining the specificity to AFP-producing cells. Application of pGL3-EA4D-tBid/H1 in a HCC tumor model significantly inhibited the growth of AFP-producing-implanted tumors with minimal side-effects, but not non-AFP-producing tumors. In conclusion, pGL3-EA4D-tBid/H1, a nano-construct with the AFP promoter EA4D and the novel H1 delivery system can specifically target and effectively suppress the AFP-producing HCC. This new therapeutic tool shows little toxicity *in vitro* and *in vivo* and it should thus be safe for further clinical tests.

Biography

George G Chen is a Professor in the Department of Surgery, Director of Surgical Research Laboratories, the Chinese University of Hong Kong, Hong Kong, China. He is also served as a principle investigator at the Hong Kong Cancer Institute. He has extensive experience in cancer research, particularly in the area of apoptosis in hepatocellular carcinoma, lung cancer and thyroid cancer. He has authored or co-authored 178 papers and has written a number of books or book chapters. He is currently a member of editorial boards or a guest editor of a number of scientific journals and a regular peer-reviewer for several grant agents.

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