Hepatic Stellate Cell-Targeting Nanoparticles for Hepatocellular Carcinoma Chemoprevention

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Hepatocellular Carcinoma (HCC) is the second leading cause of cancer death worldwide, and cirrhosis underlies 80-90% of HCC. Cirrhosis is initiated and advanced due to the activation of hepatic stellate cells (HSCs) which secrete collagen and fibrosis that impair the liver function by changing the hepatic architecture. In a previous study, treatment by erlotinib inhibited the epidermal growth factor pathway in HSCs in a diethylnitrosamine (DEN) induced HCC rat cirrhosis model, and prevented progression of cirrhosis to HCC, although the known toxicities of erlotinib limit its use for still cancer free, asymptomatic patients. To develop effective, but non-toxic HCC chemoprevention therapy, HSC-targeted delivery system for erlotinib was developed utilizing mesoporous silica-based nanoparticles (NPs) with a peptide binding platelet-derived growth factor beta receptor (PDGFRβ) specifically expressed on HSCs. The NPs were tested in the DEN rat model. Pre-neoplastic foci in the liver were determined by GSTP1 staining, and liver fibrosis was quantified by Sirius red staining. In an interim analysis of 32 rats, GSTP1-positive foci were reduced by 40% and liver fibrosis was reduced by 30%. These results suggest that less toxic molecular targeted cancer chemoprevention is feasible by using cell type-specific NPs.

Awards Won:

Third Award of $1,000