

A Novel RNAi-Based Drug for the Treatment of Hepatocellular Carcinoma

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As the prevalence of obesity and other chronic diseases continue to increase, so do the cases of hepatocellular carcinoma (HCC). Despite the development of new treatments, HCC remains difficult to treat. Research has found the Cdk6 protein to play a role in HCC development. However, due to its high homology to the Cdk4 protein, traditional Cdk6 inhibitors may be toxic to patients. An RNA interference based treatment allows for selective targeting, so the purpose of this experiment was to design an siRNA treatment for the knockdown of the CDK6 gene with high gene specificity, maximum efficacy, and minimum side effects. siRNA sequences were designed using the GenScript and Eurofins Genomics siRNA design tools and synthesized by transcribing DNA oligonucleotides. Liposomes were prepared with the direct rehydration method. Resuspended lipids were used to make lipoplexes. Two days after the culture was split, cells were transfected using the lipoplexes and a commercial transfection reagent. After 46 hours of incubation, cell viability was measured through an MTT assay. Several of the tested sequences were effective in reducing cancer cell viability. However, the non-targeting sequence may have induced an intracellular immune response in the cells, decreasing their viability. Therefore, future experiments should perform further RNA purification and explore applications of this immune response in cancer therapy. The liposomes used were shown to be cytotoxic, so new liposomes with a lower cationic lipid ratio were formulated for later testing. Overall, the data appears promising and suggests the need for further experimentation to improve the treatment.