A Novel siRNA-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 and synthesize an siRNA treatment for the knockdown of the CDK6 gene with high cancerous cell 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 and lipoplexes were prepared with the thin film rehydration method. After cells were at 80% confluency, they were transfected using the lipoplexes and a commercial transfection reagent. After 46 hours of incubation, cell viability was measured through an MTT assay. Two of the tested targeting sequences were successful in significantly reducing cancerous cell viability when transfected with a commercial reagent. The synthesized delivery vehicles were shown to exhibit significant toxicities and appeared to have a low transfection rate, so further modifications should be made to improve these characteristics. This could be achieved by altering the cationic and neutral lipid ratio. Future experimentation will also increase the sample size and incorporate RT-qPCR into testing to validate and quantify knockdown. Overall, the data appears promising and suggests the need for further experimentation to improve the compound.