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Therapeutic effect of polymer nanoparticle-conjugated microRNA-145 on a murine model of hepa-tocellular carcinoma

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Several studies revealed specific miRNA signatures in hepatocellular carcinoma (HCC) that could be exploited as potential therapeutic targets. Among these miRNAs, miR-145, which is found to be associated with the clinicopathological features, histological grade, and prognosis of the disease. So, this study was designed to study the therapeutic effect of miR-145 alone and in conjugation with polymer nanoparticles, to extend miRNA circulating time and its stability, on an experimental model of HCC. Four groups of mice were utilized; a control group and three other groups injected with diethylnitrosamine (DEN) once/week for 12 weeks to induce HCC. Then, the 1st HCC group served as a pathological control, the 2nd HCC group was injected with free miRNA-145, at a dose of 100 ul i.v. once/week for 4 weeks, and the 3rd HCC group was injected with polymer nanoparticle-conjugated miRNA-145, at a dose of 100 ul i.v. once/week for 4 weeks. At the 12th and 16th weeks, HCC-associated biomarkers were assessed in the serum of mice. Also, hepatic specimens were examined histopathologically. The results showed that AFP, VEGF, and TNF-α decreased significantly, in the free and the nanoconjugated-miRNA-145-treated group, in comparison to the DEN-injected group. Similarly, the histopathological changes improved significantly in in the free and the nanoconjugated-miRNA-145-treated group, in comparison to the pathological group. In conclusion, administration of miRNA-145, either in a free form or in conjugation with nanoparticles, is a potential therapeutic agent against HCC.

Keywords: Diethylnitrosamine; hepatocellular carcinoma; miRNA-145, polymer nanoparticles

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