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Collagen IV-Targeted Nanoparticles for Cardiac Tumor Drug Delivery

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Abstract

Patients with cardiac tumors have a limited prognosis and the only available treatments are tumor resection surgery, radiation and chemotherapy, with poor expected outcomes. Therefore, it is necessary to identify promising therapeutical strategies for targeting dysregulated molecules in the extracellular matrix characteristic of cardiac tumors. Collagen IV is a promising target for cardiac tumor treatment, due to its high expression in cardiac vasculature, fibrotic cardiac tissue, and the tumor stroma. We aim to synthesize collagen IV-targeted nanoparticles (Col-NPs) as a novel drug delivery system in cardiac tumors. Lipid NPs containing the phospholipids DOPG, POPC and Mal-PEG-DSPE were synthesized using the reverse-phase evaporation technique. The obtained lipid NPs were coupled on their surface with collagen IV-binding peptides via a maleimide-cysteine bond. Col-NPs were characterized for their hydrodynamic diameter and Zeta potential. The biocompatibility and accumulation of Col-NPs in the heart were assessed in a mouse model with increased collagen IV expression in cardiac tissue. The mice were injected intravenously with fluorescently labeled Col-NPs to investigate their localization in organs using an IVIS Spectrum Caliper 200 Imaging System. For the safety evaluation of Col-NPs, biochemical plasma parameters (cholesterol, triglycerides, urea, creatinine, transaminases) were assessed with commercial kits. Organ tissues were analyzed histopathologically using hematoxylin-eosin staining. Col-NPs have a hydrodynamic diameter of ~ 140 nm and a Zeta potential of ~ -35 mV. After intravenous administration, both Col-NPs and untargeted NPs (Scr-NPs) primarily accumulated in the liver and spleen of the mice. When examining the hearts of mice, a greater accumulation of Col-NPs compared to Scr-NPs was observed. There was no evidence of renal or hepatic toxicity, and Col-NPs were found to be biocompatible. Additionally, no pathological lesions were detected in the liver, lung, spleen, and kidney of mice injected with Col-NPs. This targeted approach has the potential to not only improve therapeutic efficacy by facilitating the accumulation of the drug at the tumor site in sufficient concentrations to exert its effects but also to reduce the required dosage, thereby minimizing systemic toxicity.