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IL-13-functionalized Liposomes Loaded with Prednisolone for Active Targeting of Melanoma Microenvironment †

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Abstract: The complex cell interactions within the tumor microenvironment (TME) play a very important role in cancer cell survival, proliferation, and metastasis. Our previous studies highlighted the unique advantage of exploiting such interactions for melanoma therapy by using long-circulating liposomes encapsulating prednisolone phosphate (LCL-PLP). In the current study, we aimed to increase the antitumor activity of PLP via its loading into IL-13- conjugated liposomes (IL-13-LCL-PLP), which offers the advantage of active TME targeting. The maleimide functionalized LCL-PLP was prepared by lipid film hydration method, and IL-13-LCL-PLP was obtained by covalent attachment of thiolated IL-13. Liposomes were characterized in terms of size, PdI, zeta potential, and stability in biological fluids by DLS. Hemolytic potential and cellular uptake in murine macrophages and melanoma cells were also determined. The antitumor activity of IL-13-LCL-PLP was investigated using C57BL6 melanoma-bearing mice. Molecular parameters linked with various tumor processes, such as oxidative stress, apoptosis, angiogenesis, and inflammation, were assessed by HPLC, western blot, and protein arrays. Our results showed that IL-13-LCL-PLP had a mean particle size <200 nm, a narrow size distribution, good stability in biological fluids, and low hemolytic potential. Importantly, IL-13-LCL-PLP exhibited higher uptake by macrophages compared with LCL-PLP. Moreover, mice treated with IL-13-LCL-PLP had a significantly decreased tumor volume compared with that of the mice receiving either LCL-PLP or PBS. This beneficial therapeutic effect resulted from the alteration of tumor-associated oxidative stress, inflammation/angiogenic, apoptosis, and invasion markers, by the new PLP-liposomal formulation. These findings imply that IL-13-LCL-PLP specifically targets the crosstalk of cells in TME that drive tumor growth and might be promising nanoplatforms for the delivery of melanoma chemotherapy.

Keywords: active tumor targeting; melanoma; tumor microenvironment; liposomes

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Conflicts of Interest

The authors declare no conflict of interest.