Induction of Human Mesenchymal Stem Cells Osteogenesis by Bioactive Agent-Releasing Liposomes

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Abstract

Stem cell therapy is a rapidly evolving area of research in regenerative medicine. Mesenchymal stem cells (MSCs) have received considerable attention by the scientific community because of their potential of expansion and the ability to differentiate into various mesodermal tissues. Liposomes are well-established non-viral carrier systems, presenting significant advantages over other nanoparticle-based drug delivery systems, namely a high load carrying capacity, a relative safety and an ease of large-scale production, as well as a versatile nature in terms of possible formulation and functionalization. The objectives of the present study were to evaluate the efficacy of growth differentiation factor-releasing liposomes on the induction of MSCs osteogenesis. For that, dexamethasone (Dex) was encapsulated within the liposome bilayer at different lipid formulations. The obtained liposomes showed a monodisperse distribution of particles size, and an increased ζ- potential for the PEGylated liposomes. Dex encapsulation studies demonstrate that the presence of cholesterol (Chol) decreases the Dex loading capacity of the liposome bilayer. The different stabilizing effect of Chol and Dex on the liposomes is due to differences in their interaction with phospholipid molecules. Highly lipophilic Chol gets incorporated between the acyl chains and reduces chain movement increasing rigidity and stabilization the membrane. Dex, being more hydrophilic, interacts differently with phospholipid acyl chains and head groups and destabilizes the membrane. *In vitro* release study demonstrated an initial burst release within an initial timeframe of 24 hours. Following the initial release, a slower release was observed until 6 days. Afterwards, Dex continues to be released at a slower but steady rate until day 21. The effect of Dex-loaded liposomes on viability, proliferation and osteogenic differentiation of human bone marrow-derived mesenchymal stem cells (hBMSCs) was assessed. The results of the biological activity showed that the Dex-loaded liposomes do not have any cytotoxic effect and, more importantly, were able to promote an earlier induction of hBMSCs differentiation into the osteogenic lineage, as demonstrated by the expression of osteoblastic markers at the

phenotypic and the genotypic levels. Concluding, Dex-loaded liposomes represent a novel biological or nature-inspired nanoparticle strategy for tissue engineering and regenerative medicine applications.