



Article

Investigations on Cellular Uptake Mechanisms and Immunogenicity Profile of Novel Bio-Hybrid Nanovesicles

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Abstract: In drug delivery, the development of nanovesicles that combine both synthetic and cellular components provides added biocompatibility and targeting specificity in comparison to conventional synthetic carriers such as liposomes. Produced through the fusion of U937 monocytes' membranes and synthetic lipids, our nano-cell vesicle technology systems (nCVTs) showed promising results as targeted cancer treatment. However, no investigation has been conducted yet on the immunogenic profile and the uptake mechanisms of nCVTs. Hence, this study was aimed at exploring the potential cytotoxicity and immune cells' activation by nCVTs, as well as the routes through which cells internalize these biohybrid systems. The endocytic pathways were selectively inhibited to establish if the presence of cellular components in nCVTs affected the internalization route in comparison to both liposomes (made up of synthetic lipids only) and nano-cellular membranes (made up of biological material only). As a result, nCVTs showed an 8-to-40-fold higher cellular internalization than liposomes within the first hour, mainly through receptor-mediated processes (i.e., clathrin- and caveolae-mediated endocytosis), and low immunostimulatory potential (as indicated by the level of IL-1 α , IL-6, and TNF- α cytokines) both in vitro and in vivo. These data confirmed that nCVTs preserved surface cues from their parent U937 cells and can be rationally engineered to incorporate ligands that enhance the selective uptake and delivery toward target cells and tissues.

Keywords: cellular uptake; endocytosis; immunogenicity; pro-inflammatory cytokines; bio-hybrids

1. Introduction

In recent years, cell-based therapy has gained popularity as a promising approach for various diseases [1,2]; however, carcinogenic risk and immunogenicity are still major concerns when using any cell-based product as a therapeutic agent. Particular concerns have been surrounding the use of therapeutic cells (i.e., stem cells and immune cells), as cells can actively proliferate, and this unregulated cell division and growth can cause tumor formation [3]. Moreover, depending on the cell types, the unregulated paracrine signaling may also participate in unwanted side effects [4], such as activation of the immune system

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web wolverine video oyunu 1991 x men başlangıç wolverine 2009 yapımı film x men origins wolverine video oyunu filminden

uyarlanan video oyunu wolverine film 2013 yapımı film wolverine marvel anime dizisinin bir bölümü x 23 wolverine adını kullanan marvel comics karakteri