Evaluating innate immune immunotoxicity of a novel therapeutic delivery system: Assessing immunotoxicity of extracellular vesicles in human monocyctic cell lines

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ABSTRACT

There is an increasing number of array of therapeutics which specifically or non-specifically target immune cells. Current immunotoxicologic evaluations for novel therapeutic delivery systems (i.e. TiO₂) often include changes in innate immune cells. However, changes in innate immune cells (e.g. myelomonocytic) have far-reaching effects on both innate and adaptive immune responses. Monocytes and monocyte-derived cells (like macrophages) can differentiate into macrophages or dendritic cells. Agents affecting monocyte survival or function can dramatically impact both innate and adaptive immune responses. Extracellular vesicles (EV) are a promising novel therapeutic delivery system that target specific cells to deliver a therapeutic payload. These EVs are produced by cultured cells and can be isolated from culture medium or other sources of the immune system. This study evaluated the potential immunotoxic effects of HED293T-Derived EV on the two human monocytic cell line THP-1 and U937 by evaluating the cytotoxicity (apoptosis versus necrosis) and cell function (phagocytosis) by flow cytometry. Results: Human monocytes are highly permeable to EV entry in a dose-dependent manner by flow cytometry. EV ingestion in cell culture was not affected by the membrane levels of Annexin V or Calcein-AM. Although lower doses of EV increased phagocytic capacity in both cell lines, phagocytic efficiency of individual cells was not affected by EV exposure at any of the doses evaluated. The study demonstrates the application of a dose-innate immunotoxicity assessment of innate immune cells in human monocytic cells to deliver a therapeutic payload. Evaluating innate immune endpoints are an additional traditional innate immune immunotoxicity assessment.

INTRODUCTION

Extracellular vesicles (EV) are naturally occurring nanosized lipid vesicles are involved in many biological processes. EVs and their function are important for maintaining endogenous homeostasis. Extracellular vesicles (EV) are produced by cultured cells and can be isolated from culture medium or other sources of the immune system. This study evaluated the potential immunotoxic effects of HED293T-Derived EV on the two human monocytic cell line THP-1 and U937 by evaluating the cytotoxicity (apoptosis versus necrosis) and cell function (phagocytosis) by flow cytometry. Results: Human monocytes are highly permeable to EV entry in a dose-dependent manner by flow cytometry. EV ingestion in cell culture was not affected by the membrane levels of Annexin V or Calcein-AM. Although lower doses of EV increased phagocytic capacity in both cell lines, phagocytic efficiency of individual cells was not affected by EV exposure at any of the doses evaluated. The study demonstrates the application of a dose-innate immunotoxicity assessment of innate immune cells in human monocytic cells to deliver a therapeutic payload. Evaluating innate immune endpoints are an additional traditional innate immune immunotoxicity assessment.

MATERIALS AND METHODS

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