Biodistribution of polymer hydrogel capsules for the delivery of therapeutics

Tracey M. Hinton\textsuperscript{a,}\textsuperscript{*}, Paul Monaghan\textsuperscript{a}, Diane Green\textsuperscript{a}, Sander A.A. Kooijmans\textsuperscript{b}, Shuning Shi\textsuperscript{a}, Kerry Breheney\textsuperscript{c}, Mark Tizard\textsuperscript{d}, Joseph A. Nicolazzo\textsuperscript{b}, Alexander N. Zelikin\textsuperscript{d}, Kim Wark\textsuperscript{e}

\textsuperscript{a}CSIRO Livestock Industries, Australian Animal Health Laboratory, 5 Portarlington Road, East Geelong, Victoria 3219, Australia
\textsuperscript{b}Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University (Parkville Campus), 381 Royal Parade, Parkville, Victoria 3052, Australia
\textsuperscript{c}CSIRO Materials Science and Engineering, 343 Royal Parade, Parkville, Victoria 3220, Australia
\textsuperscript{d}Department of Chemistry and iNANO Interdisciplinary Nanoscience Centre, Aarhus University, Denmark
\textsuperscript{e}Victorian Cancer Agency, 12 Victoria Street, Carlton, Victoria 3053, Australia

\textsuperscript{*}Corresponding author. Tel.: +61 3 5227 5746; fax: +61 3 5227 5555. E-mail address: Tracey.Hinton@csiro.au (T.M. Hinton).

1. Introduction

The requirement for improved tissue and cell targeting of new therapeutics to minimize toxic side effects as seen with many anti-cancer agents has triggered an interest in the development of "smart" vehicles for targeted delivery of these next generation drugs [1]. Improving access to poorly accessible tissues such as organs, has wide-reaching implications for the treatment of cancer, genetic diseases and viral infections.

At present, many novel delivery systems for cancer treatment rely on a combination of targeted delivery to cancerous cells using ligands for receptors that are upregulated in these cells and the lea-

500 nm in diameter, were taken up into the cells in a time-dependent manner in all three cell lines. Capsules were observed in plasma membrane-derived vesicles within the cells. After 24 h a significant proportion of the capsules was observed in lysosomes. To understand the behaviour of the capsules in vivo, Alexa 488 labelled fluorescent capsules were intravenously injected into Sprague–Dawley rats and after 24 h the fate of the capsules in a number of organs was determined by flow cytometry and confocal microscopy. Capsules were detected in the spleen whilst similar numbers were found in the lung and liver. By confocal microscopy, the majority of the capsules were found in the lung and spleen with significantly less capsules in the liver, heart and kidney. Colocalization of capsules with cell-type specific markers indicated that in lung, heart and kidney, the majority of the capsules were located in endothelial cells. In the spleen ~50% of the capsules were found in CD163-positive cells, whereas in the liver, almost all capsules were located in CD163-positive cells, indicating uptake by Kupffer cells. Electron microscopy confirmed the presence of capsules within Kupffer cells.

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