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Advanced Drug Delivery Reviews 57 (2005) 63–78

Advanced DRUG DELIVERY Reviews

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Real-time multiple-particle tracking: applications to drug and gene delivery

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Received 12 May 2004; accepted 5 August 2004

Abstract

Complex biological environments, such as the cell cytoplasm or the mucus lining the airways of the lungs, can pose significant barriers to efficient therapeutic drug and gene delivery. Biological barriers are particularly important in controlled drug delivery applications that utilize a large carrier particle, such as a liposome or a polymer micro- or nanosphere. The dynamic transport of particulate drug and gene delivery vehicles through these barriers is poorly understood, having been primarily studied with static methods in the past. Recently, the transport of synthetic drug and gene carriers has been investigated quantitatively with real-time particle tracking technology, providing new insight into particle behavior in complex biological environments that is guiding rational improvements in particle design. This review briefly highlights basic principles of particle tracking and its application to elucidate important phenomena that limit effective particulate drug and gene delivery.

Keywords: Drug delivery; Gene delivery; Multiple-particle tracking; Intracellular; Mucus; Diffusion; Transport; Rheology

Contents

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doi:10.1016/j.addr.2004.06.001

1. Introduction

Effective drug and gene delivery to target cells is often limited by inefficient particle transport through complex extra- and intracellular biological environments [1]. For example, drug/gene particulate carriers delivered to the gastrointestinal (GI) tract or to the lungs via inhalation must be capable of traversing mucus barriers designed to trap foreign particulates and prevent their transport to underlying cell surfaces [2,3]. Mucus depletion of cell monolayers typically dramatically improves gene transfection of cells with nonviral vectors [4], underscoring the importance of the mucus barrier. Once in cells, gene vectors must traverse the highly crowded cytoplasm, congested with macromolecules and organelles, to reach the nucleus [5]. The sparse quantitative investigations of these barriers have focused largely on bulk particle transport properties. In these studies, individual particle interactions with their biological environment remain a black box. Additionally, the dynamic interaction of drug/gene delivery vectors with components in the extra- and intracellular environments have often been overlooked. Limited understanding of barriers to efficient delivery hampers the rational design of improved vectors.

To address these issues, real-time multiple-particle tracking (MPT) technology has recently been applied to the study of drug and gene carrier delivery through biological environments [2,3,5,6]. As the name implies, multiple-particle tracking involves tracking the microscopic motion of tens of individual particles simultaneously in real-time using video microscopy. Particle tracking technology is valuable in obtaining information on how, and how fast, particles move in various environments. Data obtained at the individual particle level can be