Biomaterials 33 (2012) 5798–5802

Contents lists available at SciVerse ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Role of physicochemical properties of coating ligands in receptor-mediated endocytosis of nanoparticles

Hong-ming Ding [a], Yu-qiang Ma [a,b,*]

[a] National Laboratory of Solid State Microstructures and Department of Physics, Nanjing University, Nanjing 210093, China
[b] Center for Soft Condensed Matter Physics and Interdisciplinary Research, Soochow University, Suzhou 215006, China

ARTICLE INFO

Article history:
Received 16 April 2012
Accepted 23 April 2012
Available online 16 May 2012

Keywords:
Nanoparticles
Endocytosis
Membrane
Molecular modelling

ABSTRACT

A fundamental understanding of the receptor-mediated endocytosis is of great importance in biomedicine. In this paper, we systematically investigate the effect of the properties of coating ligands on the cellular uptake of nanoparticles by using dissipative particle dynamics, and find that the strength of the receptor-ligand interaction, the ligand density and length as well as its rigidity can strongly affect the final equilibrium in the receptor-mediated endocytosis. Interestingly, it is found that the particle decorated with longer ligands is more likely to attach to the membrane, while it is harder to be totally engulfed. Increasing the ligand density and rigidity which enhances the uniform distribution of ligands on the particle may lead to the total engulfment. Further, we also show that the particle can be totally engulfed if one can reasonably design the hydrophobic/lipophobic properties of ligands. The present study shows that not only the chemical but also the physical parameters of ligands can govern the nanoparticle–cell interaction, which may give some significant insights into future nanoparticle design in drug delivery.

1. Introduction

Recently, nanoparticles have been widely used in biomedicine because they can be taken as carriers to translocate drug molecules into cell interiors [1–5]. A good understanding of the interactions between nanoparticles and membranes that act as the selected barrier of cells is of great importance in their potential applications [6–9]. It is now realized that receptor-mediated endocytosis (RME) and direct penetration (diffusion) are two main passive ways (i.e., not involving the cell machinery) [10] by which extracellular materials like nanoparticles and bio-macromolecules enter into the cell interiors [8,9]. Compared to the direct penetration, the size range of the RME is much wider, and therefore the RME may become a more general way [11–14].

The RME process can be generally divided into three stages: first particles sticking to the membrane, second the membrane wrapping the particle and finally the pinch-off (particle–lipids complex detaching from the membrane) [9,12,14]. Previous studies have shown that the chemical/physical properties of nanoparticles can have important impacts on the RME [7,8,15,16], i.e., besides the type of the nanoparticle itself (e.g., the organic and inorganic particles) which may show different behavior when interacting with membranes [5,11], the particle size, shape and surface texture can also affect the RME obviously [17–21]. Further, it is found that the mechanics of particles can also be very crucial, for example, the soft particles which tend to spread along the membrane may become difficult to be totally engulfed by cells [22,23].

However, previous studies mainly focused on the design of particle itself [20,24,25]. Though some experimental studies have shown that different types of ligands may affect the RME [21,26,27], the underlying mechanism is still largely unknown. For example, except for the chemical properties, does the physical properties of ligands coated on the particles matter? The purpose of the present paper is to apply the dissipative particle dynamics (DPD) to study the effect of the chemical properties (e.g., ligand hydrophobicity) as well as physical properties (e.g., ligand length and rigidity) of ligands on the RME.

2. Model and methods

Fig. 1 shows the coarse-grain models of different components in our simulations. Each amphiphilic lipid consists of a headgroup containing three connected hydrophilic beads (H) and two tails with respective three hydrophobic beads (T) [28–30]. The receptor molecule has the same conformation of lipid molecules, but its head bead (R) is different from the head bead of lipids (H) [20]. The nanoparticle is fabricated by arranging the hydrophilic DPD beads (P) on a fcc lattice with lattice constant $\alpha = 0.5$ nm into a desired geometry shape and volume, and all beads comprising a nanoparticle move as a rigid body [31]. The ligands decorated on the

* Corresponding author. National Laboratory of Solid State Microstructures and Department of Physics, Nanjing University, Nanjing 210093, China.
E-mail address: myqiang@nju.edu.cn (Y.-q. Ma).

0142-9612/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2012.04.055