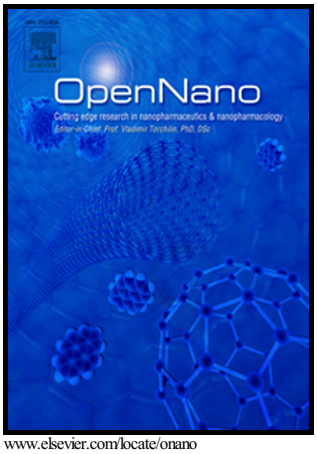

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Magnetotactic Bacterial Cages as Safe and Smart Gene Delivery Vehicles

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Abstract

In spite of the huge advances in the area of synthetic carriers, their efficiency still poorly compares to natural vectors. Herein, we report the use of unmodified magnetotactic bacteria as a guidable delivery vehicle for DNA functionalized gold nanoparticles (AuNPs). High cargo loading is established under anaerobic conditions (bacteria is alive) through endocytosis where AuNPs are employed as transmembrane proteins mimics (facilitate endocytosis) as well as imaging agents to verify and quantify loading and release. The naturally bio-mineralized magnetosomes, within the bacteria, induce heat generation inside bacteria through magnetic hyperthermia. Most importantly after exposing the system to air (bacteria is dead) the cell wall stays intact providing an efficient bacterial vessel. Upon incubation with THP-1 cells, the magnetotactic bacterial cages (MBCs) adhere to the cell wall and are directly engulfed through the phagocytic activity of these cells. Applying magnetic hyperthermia leads to the dissociation of the bacterial microcarrier and eventual release of cargo.

Key notes: magnetotactic bacteria; magnetosomes; microbots; hyperthermia.

1. Introduction

Designing synthetic carriers has been heavily pursued to resolve the intrinsic issues associated with bioactive molecules delivery such as hydrophobicity, unwanted toxicity, and most importantly poor stability. Despite numerous systems that have been fabricated based on polymeric vesicles (Uhrich et al. 1999; Gupta, Vermani, and Garg 2002; de Las Heras Alarcon, Pennadam, and Alexander 2005; Zhang et al. 2014), liposomes (Li et al. 2014; Yoshimoto, Kozono, and Tsubomura 2015; Bertrand et al. 2010), and mesoporous silica nanoparticles(Slowing et al. 2008; Gimenez et al. 2015; Cauda et al. 2009; Zhao et al. 2014), major limitations still exist. Reproducibility in the preparation of a synthetic carrier is key for eventual scale-up and commercialization and thus systems that require multi-step synthesis are not feasible. Moreover, the type and amount of agents that could be loaded is a crucial design requirement that synthetic carriers have mainly suffered from due to their variable loading efficiency and constriction on the size and charge of the loaded agent.

Natural carriers or vectors such as bacteria and viruses are very attractive, as they possess their own delivery mechanisms by which they induce disease. Copying nature's designs, researchers have produced many bioengineered and biomimetic drug delivery carriers (Yoo et al. 2011). Virus-like particles and virosomes based vaccines are already FDA approved and available commercially such as Gardasil (Merck)(Group 2007; Einstein et al. 2009), Cervarix (GlaxoSmithKline)(Paovonen et al. 2009; Boxus et al. 2014), and Epaxal (Crucell)(Bovier 2008a; D'Acremont, Herzog, and Genton 2006; Bovier 2008b). However, these systems are limited by their potential immunogenicity when used for non-vaccine delivery (Leroux-Roels 2010; Waelti et al. 2002; Datta et al. 2008; Wu et al. 2009). On the other hand, no successful bacterial candidate has made it to market so far. Bacterial carriers are divided into 3 major categories including recombinant bacteria (non-pathogenic bacteria that are genetically modified to produce and deliver biologically active proteins), microbots (bacteria that carry nanoparticles on their surface), and