Biomaterials 33 (2012) 5650–5657

Contents lists available at SciVerse ScienceDirect

Biomaterials

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

# Cell response induced by internalized bacterial magnetic nanoparticles under an external static magnetic field

Jaeha Shin [a], Chang-Hyuk Yoo [b], Junghoon Lee [a,b,c], Misun Cha [c,*]

[a] School of Mechanical and Aerospace Engineering, Seoul National University, Seoul 151-744, South Korea
[b] Division of WCU Multiscale Mechanical Design, School of Mechanical and Aerospace Engineering, Seoul National University, Seoul 151-744, South Korea
[c] Inter-university Semiconductor Research Center, Seoul National University, Seoul, 151-744, South Korea

ARTICLE INFO

*Article history:*
Received 10 February 2012
Accepted 12 April 2012
Available online 8 May 2012

*Keywords:*
Bacterial magnetic nanoparticles (BMPs)
Magnetic field
Proliferation
Antiapoptosis
Microarray

ABSTRACT

Magnetic nanoparticles are widely used in bioapplications such as imaging and targeting tool. Their magnetic nature allows for the more efficient bioapplications by an external field gradient. However their combined effects have not yet been extensively characterized. Herein, we first demonstrate the biological effects of the communications between internalized bacterial magnetic nanoparticles (BMPs) and an external static magnetic field (SMF) on a standard human cell line. Combination of the BMPs and SMF act as the key factor leading to the alteration of cell structure and the enhanced cell growth. Also, their interaction reduced the apoptotic efficiency of human tumor cells induced by anticancer drugs. Microarray analysis suggests that these phenomena were caused by the alterations of GPCRs-mediated signal transduction originated in the interaction of internalized BMPs and the external SMF. Our findings may offer new approach for targeted cell therapy with the advantage of controlling cell viability by magnetic stimulation.



## 1. Introduction

Magnetic nanoparticles (MNPs) are primarily used for the diagnosis and treatment of diseases, especially in applications such as magnetic resonance imaging, drug delivery, and magnetic hyperthermia [1–4]. Delivery of MNPs to a target site and duration in the site are crucial steps for efficient therapy, which is controlled by the regulation of exposure to a magnetic field (MF) [5]. Thus it is of prime importance to understand the effect of MF on biological environments. “MFs are widely distributed in any biological systems; for example, small fields strengths (under 1T) may influence cells in terms of F-actin arrangement, cell alignment, and intracellular ion fluctuations, leading to changes in signaling pathways [6]. An external MF alone, however, has no or extremely small effects on the cell growth and survival under normal culture conditions, regardless of the strength of the MF [7–9]. On the other hand, MNPs can produce their own MF and influence the local tissue area around them through more intensive interactions or biophysical effects, which is often multiplied by the presence of an external MF. Therefore, when MNPs are used for biological applications under an MF, the multiple interactions between the MNPs and the MF may affect the cell system in an unexpected manner. Nevertheless, few studies have been reported regarding the combined effects of the MNPs and the MF on the cells exposed to them.

Herein we report on the biological effects of bacterial magnetic nanoparticles (BMPs) originated from *Magnetospirillum* sp. AMB-1 on a standard human cell line under an external MF. Human derived cells provide better prediction of human applications. BMPs used in our approach are ferromagnetic in nature, with high magnetic susceptibility, several orders of magnitude greater than that of paramagnetic particles [10–12]. In addition, the BMPs are inherently biocompatible, effectively conjugating with other biomolecules, and disperse well in aqueous solutions [13,14]. Some studies revealed that BMPs have considerable potential for biological applications [15,16]. In this study, we focus on synergetic effect caused by the reciprocal interaction between the internalized BMPs and exposure to an external static MF (SMF). Cell response induced by the internalized BMPs and the external SMF were assessed by analysis of the cell growth and changes in microtubule organization. We also examined how the signaling pathway was modulated by the internalized BMPs interacted with the external SMF.

## 2. Materials and methods

### 2.1. Preparation of BMP

BMPs were obtained from *Magnetospirillum* sp. AMB-1 (ATCC® 700264) which was cultured in magnetic spirillum growth medium (MSGM) for 5 days in shaking

* Corresponding author. Tel.: +82 2 880 9101; fax: +82 2 877 9104.
*E-mail address:* cmsbest@snu.ac.kr (M. Cha).

0142-9612/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2012.04.033