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Current Opinion in Pharmacology

Nano-labelled cells — a functional tool in biomedical applications

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Nanotechnology offers an unprecedented number of opportunities for biomedical research, utilizing the unusual functionalities of nanosized materials. Here we describe the recent advances in fabrication and utilization of nanoparticle-labelled cells. We present a brief overview of the most promising techniques, namely layer-by-layer polyelectrolyte assembly on cells and intracellular and extracellular labelling with magnetic nanoparticles. Several important practical application of nanofucntionalized cells, including tissue engineering and tumour therapy, are reviewed.

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Current Opinion in Pharmacology 2014, **18**:84–90

This review comes from a themed issue on **New technologies**

Edited by **Gleb B Sukhorukov**

For a complete overview see the Issue and the Editorial

Available online 29th September 2014

http://dx.doi.org/10.1016/j.coph.2014.09.009

Introduction

Nanosized particles of various morphologies and functionalities have been extensively employed in biomedical research and clinical applications [1]. Particularly, nanoparticles are regarded as promising drug delivery vehicles [2]. Among other strategies, labelling of cells with various nanomaterials, attracts the attention of researchers worldwide. The potential of cell labelling with nanoparticles is secured by the novel functionalities which nanoparticles render to the cells. This paper is aimed to briefly overview of the current progress within this novel and vibrant area of research.

The layer-by-layer (LbL) polyelectrolyte deposition [3,4], originally designed primarily for the fabrication of and colloidal microcapsules, has been successfully applied to modify and functionalize surfaces of biological cells [5] and since has been utilized in a number of biomedical applications [6]. First reports were focused on applying LbL assembly technique for the deposition of oppositely charged polymer thin films to modify surfaces of microbial and mammalian cells in order to fabricate polyelectrolyte microcapsules imitating the geometries of biological cells. The pioneering paper by Neu *et al.* demonstrated the polyelectrolyte LbL assembly for the effective fabrication of micron-sized multilayered polymer capsules template on red blood cells and bacteria [7]. Cells as templates are attractive as their morphology, if repeated by the resulting microcapsules, allows for the higher biocompatibility. The typical procedure of cell surface modification with polyelectrolytes is based on the sequential deposition of oppositely charged polymers onto cells, additionally, various nanomaterials, such as nanoparticles, nanotubes and nanosheets can be deposited between the polyelectrolyte layers [8]. Alternatively, several reports demonstrate the direct, single-step deposition of polymer-functionalized nanoparticles onto living cells [9,10]. These modifications can be performed using both viable and non-viable cells. Most of the researchers concentrated on fabrication of functional nanocoatings on viable cells, allowing for attenuation of functional properties of cells [11•]. Typically, the recent reports on LbL assembly of polymer shells on cells utilize the surface modification of microorganisms [5], while others are trying to investigate the toxicity of polymer shells towards the mammalian cells [12]. The toxic effects of the surface modification of mammalian cells are attributed to the impact of positively charged polyelectrolytes [13]. Nevertheless, several reports demonstrate the successful use of surface modification of mammalian cells with LbL nanofilms for the biomedical applications [14,15].

However, the current methodology of cells nanolabelling is not limited to the LbL modification. The other approaches include, but are not limited to the direct deposition of nanomaterials, based on fabrication of the layers of magnetic nanoparticles [10] or 'hard' mineral shells [16] on cells. In addition, the intracellular labelling of cells with nanoparticles (i.e. magnetic nanoparticles) is another promising way to functionalize the cells.

Layer-by-layer (LbL) cell surface modification for tissue engineering

Arguably, the most promising applications of LbL-based cell surface modification are attributed to tissue engineering, a novel therapy technique where the cells are controllably assembled in multi-layered tissue-like structures.