Editorial

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Lipid bilayer nanoparticle-based drug delivery systems in the treatment of rheumatoid arthritis: a glance at liposomes and exosomes

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease leading to joint destruction, with its pathogenesis still not fully understood and currently no cure available [1,2]. Treatment of RA usually focuses on symptomatic relief by employing various therapeutics, such as non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), glucocorticoids and biologics (i.e. cytokine targeting biological agents) [3]. High systemic drug doses are usually required for RA treatment due to their relatively low bioavailability and/or poor selectivity, which entail side effects and toxicity, especially at repeated administrations that are required for the chronic disease [2,4]. Thus, to improve the therapy outcome of RA, appropriate drug delivery systems capable of enhancing treatment efficacy, reducing off-target toxicity and providing sustained release are on demand, for instance, nanodelivery systems.

Nanotechnologies have shown significant advances in designing and fabricating various nanomaterials for a wide variety of medical applications [5-7]. Lipid bilayer nanoparticles as zero-dimensional materials are widely explored as delivery systems for therapeutics, due to their membrane-like structure, low toxicity, passive targeting, good biocompatibility and sustained release to name a few [8]. In particular, liposomes and exosomes representing artificial and natural lipid bilayer nanoparticle-based drug delivery systems, respectively, have sparked great interest in their applications for the treatment of RA, especially when considering the characteristics of RA and the shortcomings of conventional drug administration techniques [4].

Liposomes have been reported as effective nanocarriers for drug delivery, with many liposome-based drug formulations studied in clinical trials of which some are FDA-approved and marketed [9,10]. In RA, the enhanced vascular permeability leads to enhanced permeation and retention (EPR) effect, which allows liposomal passive targeting for specific accumulation at inflamed sites even upon systemic administration. On the other hand, local administration of large-sized liposomal formulations in inflamed joints significantly promotes the retention of liposome-encapsulated drugs [11,12]. It is believed that liposomes exhibit good skin penetration, which may increase the efficacy of local transdermal administration [13]. Due to their artificial nature, liposomes can be manipulated, e.g. by grafting targeting elements (i.e., antibodies or aptamers capable of specific binding) onto the liposome surface, in order to enable specific and selective RA therapy [14,15]. Other benefits of liposomes include loading of hydrophobic drugs and stabilization of encapsulated drugs [16]. All these characteristics have resulted in a substantial body of data on liposomes as superior drug delivery systems for RA management. Accordingly, liposomes are credited for enhancing therapeutic efficacy, reducing systemic toxicity and prolonging release time [4,12,17]. However, it is worth noting that the current marketed liposomal drug formulations mainly concentrate on cancer therapy, and liposomal preparations still face the problems like drug leakage [9,10]. Further efforts are still in need to advance the development of liposomal preparations in clinical trials and marketing in the field of RA therapy.

Exosomes are cell-derived extracellular nanovesicles playing important roles in intercellular communication and biomolecule

delivery, which have aroused extensive attention in the past two decades [18]. With similar vesicle size and lipid bilayer structure to liposomes, exosomes not only display the advantages of liposomes, but exhibit additional benefits due to their cellular origin, such as good biocompatibility, natural protein decoration and immunoregulatory activity, which may be valuable features for the rational design of exosome-based drug delivery systems for RA treatment [18-21]. As a young and developing field, exosomes have been employed for drug delivery in the treatment of inflammatory and other diseases, but their application as drug carriers for RA therapy is largely unexplored [22-24]. Considering the exciting results of liposomes in RA therapy and the unique properties of exosomes, exosomes have a real potential to become powerful drug delivery systems for the treatment of RA. Furthermore, the fusion of exosomes and liposomes may create attractive novel delivery systems, merging the advantages of natural and synthetic lipid bilayer-based compositions.

We hope this brief overview of liposomes and exosomes and their potential in the treatment of RA can provide a better understanding on lipid bilayer nanoparticle-based drug delivery systems for RA therapy, and inspire new therapeutic approaches.

Conflict of interest

The authors report no declarations for conflict of interest.

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