Bioactive Materials 15 (2022) 469–481

Contents lists available at ScienceDirect

Bioactive Materials

journal homepage: www.keaipublishing.com/en/journals/bioactive-materials

Augmented cellular uptake and homologous targeting of exosome-based drug loaded IOL for posterior capsular opacification prevention and biosafety improvement

Siqing Zhu, Huiying Huang, Dong Liu, Shimin Wen, Liangliang Shen, Quankui Lin *

Department of Biomaterials, School of Ophthalmology & Optometry, Eye Hospital, Wenzhou Medical University, Wenzhou, 325027, PR China

ARTICLE INFO

Keywords:
Exosome
Intraocular lens
Surface modification
Targeted therapy
Posterior capsular opacification

ABSTRACT

Posterior capsular opacification (PCO), the most common complication after cataract surgery, is caused by the proliferation, migration and differentiation of residual lens epithelial cells (LECs) on the surface of the intraocular lens (IOL). Although drug-loaded IOLs have been successfully developed, the PCO prevention efficacy is still limited due to the lack of targeting and low bioavailability. In this investigation, an exosome-functionalized drug-loaded IOL was successfully developed for effective PCO prevention utilizing the homologous targeting and high biocompatibility of exosome. The exosomes derived from LECs were collected to load the anti-proliferative drug doxorubicin (Dox) through electroporation and then immobilized on the aminated IOLs surface through electrostatic interaction. In vitro experiments showed that significantly improved cellular uptake of Dox@Exos by LECs was achieved due to the targeting ability of exosome, compared with free Dox, thus resulting in superior anti-proliferation effect. In vivo animal investigations indicated that Dox@Exos-IOLs effectively inhibited the development of PCO and showed excellent intraocular biocompatibility. We believe that this work will provide a targeting strategy for PCO prevention through exosome-functionalized IOL.

1. Introduction

Cataract, the opacity of lens, is still the leading cause of vision lost around the world. As the global population ages, the incidence of cataract is increasing [1–3]. Phacoemulsification combined with intraocular lens (IOL) implantation is the only effective treatment currently [4]. However, surgical wound healing and foreign body reactions often lead to multiple complications, among which posterior capsular opacification (PCO) is the most common complication of cataract surgery. It is reported that the incidence of PCO is 20–40% in adults and up to 100% in children within 2–5 years after surgery [5,6]. The main cause of PCO is the proliferation, migration and differentiation of residual lens epithelial cells (LECs) adhering to the IOL surface and posterior capsule [7,8]. At present, neodymium-doped yttrium aluminum garnet (Nd:YAG) laser capsulotomy is the most commonly used treatment for PCO, which, however, will cause a series of new complications, such as IOL injury and displacement, macular cystic edema and retinal detachment [9,10]. Therefore, it is of great significance to implement more efficient and safer PCO preventive measures.

At present, in addition to the optimization of IOL shape and development of novel IOL materials, IOL surface modification, which is easy to prepare and does not require extra intraocular surgery also contributes to PCO prevention [6,11–18]. In previous studies, researchers mainly focused on hydrophilic coating on the IOL surface to prevent the adhesion of LECs [19–22]. However, recent studies have shown that hydrophilic coating can only initially reduce LECs adhesion and proliferation on the surface but do not inhibit PCO in the long term [23]. As a result, drug loaded coating modified IOL implantations as potential treatments for posterior cataract have attracted wide attention [17,24–27]. For example, in our previous studies, drug loaded IOLs were prepared by layer-by-layer assembly or surface-initiated reversible addition-breaking chain transfer (SI-RAFT) polymerization to prevent PCO [19,28]. In vivo experiments showed that the coating can effectively inhibit the proliferation of LECs. However, due to lack of targeting and poor bioavailability, the released drugs may potentially toxic to the surrounding intraocular tissues. Therefore, targeted drug delivery systems are urgently needed.

Exosomes are nanoscale extracellular vesicles secreted by cells with a

Peer review under responsibility of KeAi Communications Co., Ltd.
* Corresponding author.
E-mail address: linqk@wmu.edu.cn (Q. Lin).

https://doi.org/10.1016/j.bioactmat.2022.02.019
Received 29 November 2021; Received in revised form 16 February 2022; Accepted 16 February 2022
Available online 26 February 2022