inner lipid-shell was labeled with rhodamine-PE. Nile Red-loaded FLPNPs showed higher efficient endocytosis abilities in FR-overexpressing EMT6 cells when compared to nontargeted LPNPs. In BALB/c mice bearing EMT6 tumors, PTX-loaded FLPNPs showed similar antitumor efficacy but low toxicity compared to Taxol® *via*intratumoral chemotherapy. More importantly, PTX-loaded FLPNPs exhibited superior therapeutic efficiency than the PTX-loaded LPNPs, confirming the effective cellular accumulation and anticancer activity of folate targeted NPs *via* receptor-mediated endocytosis. These findings indicated that the PTX loaded-FLPNPs with mixed lipid monolayer shell and biodegradable polymer core would be a promising nanosized drug formulation for tumor-targeted therapy.

Keywords: lipid-polymer hybrid nanoparticles, paclitaxel, drug delivery, PCL-PEG-PCL, folate

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An agarose-PEI-HA copolymer as tumor-targeted gene vector with high efficiency and low toxicity

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Development of effective gene vectors is critical to the success of gene therapy [1]. Up-to-date, readily-available gene vectors are limited due to their inefficiency, cytotoxicity and poor targeting capability [2]. It is still a major task to find an ideal gene vector with high transfection efficiency, improved specific targeting capability and better safety *in vitro* and *in vivo* [3]. In this work, a novel ternary copolymer Agarose-PEI-HA was designed and synthesized for tumor-targeted gene delivery. The three components in the copolymer were expected to synergistically function to realize tumor targeted and efficient gene transfection (Fig. 1). Abundant hydroxyl groups in agarose chains could provide attachment sites for conjugating with low molecule PEI for loading DNA. The gelling property of agarose could promote complexation with genes. The HA could target to HA receptors on cancer cells and promote transfect efficiency. The results showed that this copolymer Agarose-PEI-HA was able to condense pDNA into spherical nanoparticles with a diameter about 200 nm which is suitable for cell uptake. *In vitro* transfection efficiency of Agarose-PEI-HA showed a much improved performance than Lipo2000 in Hela cells. Due to the targeting effect of high density of HA, remarkable tumor cellular uptake was observed. Moreover, *in vivo* studies indicated that the polyplexes had remarkable blood circulation time and could target specifically to tumor tissues in mice. Our results revealed the great potential of this copolymer as an advanced gene delivery system with features including low cytotoxicity, biodegradability, high transgene transfection activity, tumor targetability and long circulation *in vivo*.

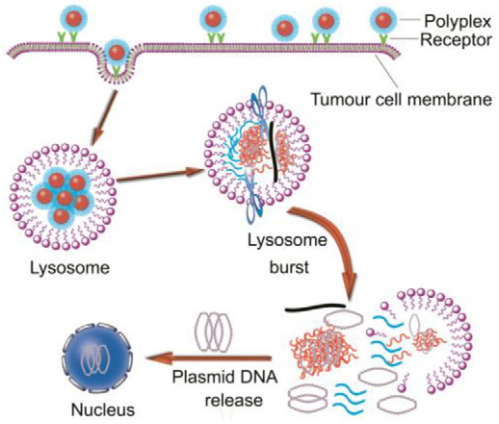

Fig. 1. The proposal process of the internalization and fate of AG-PEI-HA/pDNA polyplexes.

Keywords: gene delivery, gene expression, polyethyleneimine, tumor targeting

Acknowledgements

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Fabrication and characterization of compound vitamin B/silk fibroin nanofibrous matrices

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Silk fibroin from silk worms (*B. mori*) is a naturally-rich protein polymer at a low cost. With intrinsic unique properties, it has been widely explored as various kinds of biomedical materials for cell culture and tissue regeneration. In particular, nanofibrous silk fibroin constructs are favoured by cells and tissues due to their similarity to natural extracellular matrices [1]. However, some capabilities or capacities still need improving toward increasing demand of practical application. One of good strategies is to include active ingredients or factors in fibrous matrices. Our previous study has found the incorporation of pantothenic acid improves the capability of regenerated silk fibroin nanofibrous matrices for supporting a high level of cell viability in a long culture period [2].

Here, we report the development of compound vitamin B (nicotinic acid and pantothenic acid)/silk fibroin nanofibrous matrices for wound healing and personal skin care. In this work, we produced compound vitamins/silk fibroin nanofibers using a green electrospinning technology developed in our previous study [2]. The incorporation of nicotinic acid significantly decreases the width of pure silk fibroin nanofibers and pantothenic acid/silk fibroin composite nanofibers. Furthermore, the resulting matrices show more cross-linked sites of nanofibers from compound vitamin B/silk fibroin compared with those from pure silk fibroin or pantothenic acid/silk fibroin. As-prepared nanofibrous matrices become water-insoluble after exposure to 75% (v/v) ethanol vapour due to the structure transformation of silk fibroin from random-coil-dominant silk I to β-sheet-dominant silk II structure. Interestingly, compound vitamins/silk fibroin nanofibrous matrices support a higher proliferation viability of fibroblast cells. Our work could be an inspiring study for developing multifunctional nanofibrous matrices of compound vitamins/silk fibroin for various applications.

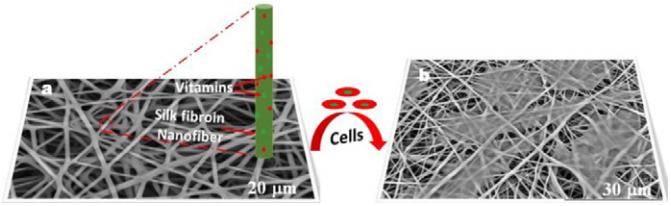

Fig. 1. SEM images of vitamins/silk fibroin nanofibers (a) and fibroblasts growing on nanofibers (b).

Keywords: silk fibers, nicotinic acid, pantothenic acid, compound vitamin B, green electrospinning

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pH-Sensitive degradable polymeric micelles for bio-triggered targeted anti-tumor drug delivery

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Ortho ester-based pH-responsive polymeric micelles have drawn much interest for delivery of antitumor drugs due to the pH gradients in tumor microenvironment and organelles [1]. However, the main weakness of these micelles is lack of the tumor specific targeting. Hyaluronic acid (HA) is a super-efficient targeting molecule which can be specifically recognized by the CD44 receptors overexpressed in many tumor cells [2]. Herein, we synthesized an acid degradable compound 2-(octadecyloxy)-1,3-dioxan-5-amine (OD) containing an ortho ester group, and then conjugated OD to HA backbone, thus obtaining pH-responsive and tumor-targeted polymer hyaluronic acid-g-2-(octadecyloxy)-1,3-dioxan-5-amine (HOD), which could self assemble into drug loaded micelles for the intracellular delivery of doxorubicin (DOX) (Fig. 1). The DOX/HOD micelles, with a narrow size distribution, were stable under physiological conditions, but the drug was released quickly in the tumor acidic microenvironment. *In vitro* cell tests proved that the pH-sensitive DOX/HOD micelles had enhanced cytotoxicity, effective internalization and promptly pH-triggered release compared to free DOX and DOX/HOD micelles. Moreover, endocytosis inhibition studies revealed that DOX/HOD micelles were internalized mainly via caveolae/clathrin-mediated endocytosis pathway. These results demonstrate that HOD conjugates can be used as biocompatible, pH-sensitive and tumor-targeting nanocarriers for efficient delivery of hydrophobic anticancer drugs.

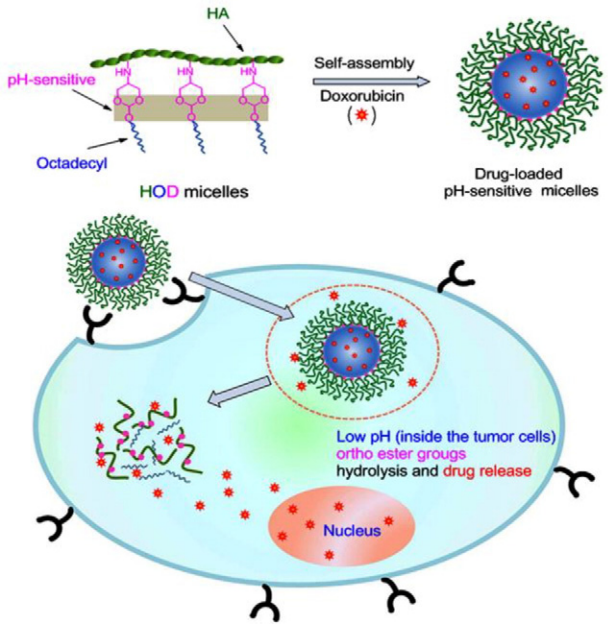

Fig. 1. Illustration of self-assembly process and intracellular uptake of DOX/HOD micelles.

Keywords: pH-responsive; hyaluronic acid; doxorubicin; self-assembled micelles