an ideal carrier for drug and imaging probes. MRI contrast agent and anticancer drugs were further conjugated onto the zwitterionic PGD, and their contrast-enhanced MRI and anti-cancer study are under research.

Keywords: polyglycerol, dendrimer, non-fouling, MRI contrast agent, drug delivery

References

[1] M. Calderon, M.A. Quadir, S.K. Sharma, R. Haag, Dendritic polyglycerols for biomedical applications, Adv. Mater. 22 (2010) 190–218.
[2] R. Haag, A. Sunder, J.F. Stumbe, An approach to glycerol dendrimers and pseudo-dendritic polyglycerols, J. Am. Chem. Soc. 122 (2000) 2954–2955.

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pH-sensitive poly(peptide-*co*-β-amino ester)s micelles for enhanced cancer therapy

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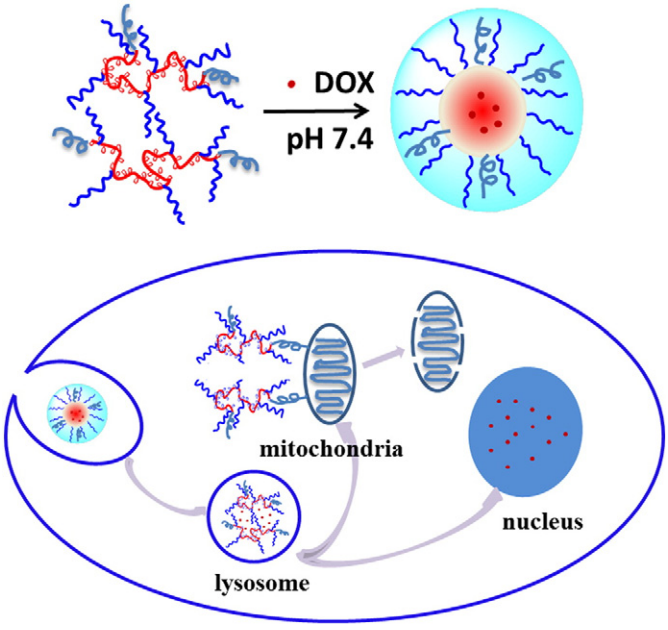
Peptide drugs, classified as biopharmaceuticals or biodrugs, comprise an increasing share of the pharmaceutical market. As anticancer drugs, peptides are readily synthesized, optimized and evaluated, do not cause serious immune responses, and accumulate in specific organs such as kidney and liver [1]. However, the peptide drugs have obvious disadvantages such as low bioavailability and limited chemical stability or half-life. In order to solve these problems, we developed peptide-loaded pH-sensitive polymers for enhanced cancer therapy. Poly(peptide-*co*-β-amino ester)s with targeted drug delivery have been prepared by the Michael addition method [2].



Scheme 1. Drug-encapsulated self-assembled poly(peptide-*co*-β-amino ester) copolymer micelles and their acid-triggered dissociation for efficient drug release.

Poly(peptide-*co*-β-amino ester)s graft copolymers with PEG side chains were synthesized by Michael addition. The end acrylate groups were conjugated by functional peptides such as therapeutic peptides and cell-penetrating peptides. The copolymers could form micelles with pH-sensitive cores and hydrophilic PEG shells, with hydrophobic peptide drugs loaded into the core of micelles. The micelles could effectively enter the cells by endocytosis, and the drugs were released at acidic condition in the lysosomes, resulting in effective death of cancer cells (Scheme 1).

Keywords: poly(β-amino ester)s, therapy peptide, cell-penetrating peptide, anticancer drug

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References

[1] Z. Antosova, M. Mackova, V. Kral, T. Macek, Therapeutic application of peptides and proteins: parenteral forever? Trends Biotechnol. 27 (2009) 628–635.
[2] Z.Y. Qiao, S.L. Qiao, G. Fan, Y.S. Fan, Y. Chen, H. Wang, One-pot synthesis of pH-sensitive poly(RGD-*co*-β-amino ester)s for targeted intracellular drug delivery, Polym. Chem. 5 (2014) 844–853.

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Co-administration of iRGD enhancing the anticancer efficacy of cisplatin-loaded polypeptide nanoparticles

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Nanoparticles mainly remain in the perivascular regions of solid tumors ($D_{mean} < 50\ \mu m$) after i.v. injection. Therefore, there is a low contact probability for nanoparticles to reach a majority of target cells within a solid tumor. As a result, the therapeutic efficacy of anticancer nanomedicines is limited [1]. iRGD can selectively enhance the vascular and tissue permeability of tumors overexpressing α_v integrins and neuropilin-1. Consequently, the co-administration of iRGD may have the possibility to enhance the efficacy of anticancer nanomedicine. Herein, we present the treatment of B16F1 melanoma with a combination of cisplatin-loaded poly(l-glutamic acid)-*g*-methoxy poly(ethylene glycol) nanoparticles (NP2) and iRGD [2].

A murine melanoma xenograft tumor model was generated by sc injection of B16F1 cells (1.0×10^6 cells) into the right flank of each C57BL/6 mouse. When the tumor volume was approximately 60 mm^3, the mice were injected intravenously (tail vein) with PBS (pH 7.4), NP2 nanoparticles (5 mg kg^{-1} on the basis of cisplatin), and NP2 nanoparticles + iRGD (5 mg kg^{-1} on the basis of cisplatin, 8 mg kg^{-1} on iRGD) by i.v. injection on days 0, 2 and 4.

The IC_{50} of NP2 to B16F1 is 28.8 mg L^{-1}. The co-administration of iRGD enhances the tumor growth suppression rate from 49% (NP2) to 76% (NP2 + iRGD) (Fig. 1A). The mice of NP2 nanoparticles + iRGD group loses 11.0% of body weight after three times of drug administration, indicating that the use of iRGD may bring about side effects. Fig. 1B gives the survival rates of mice of each group. Longest survival time is achieved by combination of NP2 nanoparticles + iRGD. In conclusion,

co-administration of iRGD can significantly enhance the anticancer efficacy of cisplatin-loaded polypeptide nanoparticles.

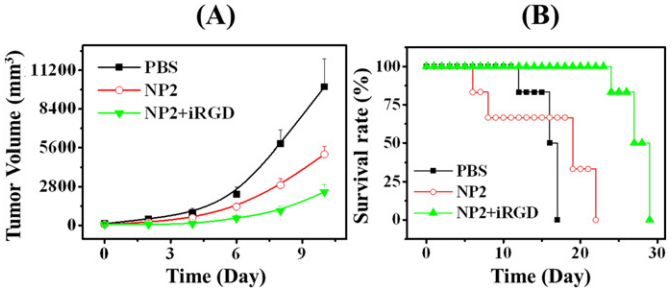

Fig. 1. Tumor volume growth curve (A) and survival rate with time (B).

Keywords: nanoparticles, iRGD, cisplatin, glutamic acid, co-administration

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References

[1] J.W. Nichols, Y.H. Bae, EPR: evidence and fallacy, J. Control. Release 190 (2014) 451–464.
[2] H. Yu, Z. Tang, M. Li, W. Song, D. Zhang, Y. Zhang, Y. Yang, H. Sun, M. Deng, X. Chen, Cisplatin loaded poly(L-glutamic acid)-*g*-methoxy poly(ethylene glycol) complex nanoparticles for potential cancer therapy: preparation, *in vitro* and *in vivo* evaluation, J. Biomed. Nanotechnol. 11 (2015) 1–10.

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Electrospun attapulgite-doped poly(lactic-*co*-glycolic acid) nanofibers for osteogenic differentiation of human mesenchymal stem cells

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The extracellular matrix (ECM) mimicking properties of electrospun polymer nanofibers afford their use as an ideal scaffold material for differentiation of human mesenchymal stem cells (hMSCs), which is important for various tissue engineering applications [1]. The incorporation of clay materials within polymer nanofibers is able to improve the mechanical durability and cytocompatibility of the nanofibers [2], thereby making the formed hybrid nanofibers attractive for stem cell differentiation.

Here, we report the fabrication of electrospun poly(lactic-*co*-glycolic acid) (PLGA) nanofibers with incorporated attapulgite (ATT) nanorods, a clay material for osteogenic differentiation of human mesenchymal stem cells (hMSCs). We show that the incorporation of ATT nanorods does not significantly change the uniform morphology (Fig. 1a) and the hemocompatibility of the PLGA nanofibers; instead the surface hydrophilicity and cytocompatibility of the hybrid nanofibers slightly increase after doping with ATT. Alkaline phosphatase activity, osteocalcin secretion, calcium content (Fig. 1b), and histochemical assays reveal that hMSCs are able to be differentiated to form osteoblasts onto both PLGA and PLGA–ATT composite nanofibers in osteogenic medium. Most strikingly, the PLGA nanofibers doped with ATT are able to induce osteoblast differentiation of hMSCs in growth medium without any inducing factors (Fig. 1b). The fabricated organic/inorganic hybrid ATT-doped PLGA nanofibers may find many applications in the field of tissue engineering and regenerative medicine.

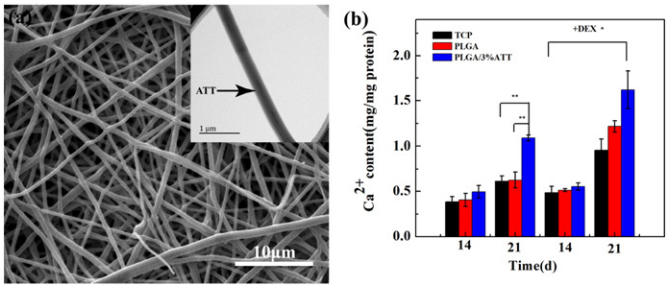

Fig. 1. (a) SEM micrographs of ATT-doped electrospun PLGA nanofibers; (b) calcium content assay of hMSCs cultured onto TCP, PLGA and PLGA/ATT (3% ATT in PLGA) nanofibers in growth medium without inducing factors and osteogenic medium at different culture time periods, respectively.

Keywords: nanofibers, attapulgite, cytocompatibility, stem cells, osteogenic differentiation

Acknowledgements

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References

[1] S. Wang, R. Castro, X. An, C. Song, Y. Luo, M. Shen, H. Tomás, M. Zhu, X. Shi, Electrospun laponite-doped poly (lactic-*co*-glycolic acid) nanofibers for osteogenic differentiation of human mesenchymal stem cells, J. Mater. Chem. 22 (2012) 23357–23367.
[2] F. Zheng, S. Wang, S. Wen, M. Shen, M. Zhu, X. Shi, Characterization and antibacterial activity of amoxicillin-loaded electrospun nano-hydroxyapatite/poly(lactic-*co*-glycolic acid) composite nanofibers, Biomaterials 34 (2013) 1402–1412.

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Hydrophobic *N*-acetyl-l-leucine grafted polyethylenimine as an efficient carrier for DNAzyme delivery

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Aurora kinase A has been demonstrated to be involved in the malignant progression of many types of cancer, as its amplification and up-regulation could induce the chromosomal instability [1]. Thus, it could be used as a good target for cancer therapy, especially decreasing its expression level through oligonucleotide technology. Among the oligonucleotides, DNAzyme is an attractive therapeutic