ADVANCED TISSUE ENGINEERING SCAFFOLDS FOR POSTOPERATIVE CANCER PATIENTS

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INTRODUCTION: Cancers are major threats to human lives. Surgical removal of tumors is currently the main cancer treatment. But the surgery may result in post-operation tissue dysfunction. The risk of cancer recurrence in patients is also a major problem. It is important to develop new approaches for regenerating tissues at surgical site and at the same time preventing cancer recurrence. In scaffold-based tissue engineering, electrospun scaffolds possess desirable properties for promoting the regeneration of human tissues [1]. And Au nanoparticle (AuNP)-based theranostics are investigated as novel tools for early cancer detection and cancer treatment [2]. This study investigated the fabrication and properties of novel nanofibrous scaffolds incorporated with theranostics for cancer patients.

MATERIALS AND METHODS: Folic acid-chitosan-capped gold (Au@CS-FA) NPs with highly branched AuNP core were made via one-pot synthesis [3]. CS-FA conjugate was the shell on NPs and FA would provide high tumor targeting ability. For cancer detection, R6G was embedded in theranostics for generating SERS signals. Coaxial electrospray [4] was used to encapsulate theranostics in core-shell structured PLGA microspheres. Multifunctional scaffolds were fabricated using the novel dual-source dual-power electrospinning and coaxial electrospray technique, with electrospinning producing nanofibrous PLGA (LA:GA=75:25) scaffolds and coaxial electrospray forming theranostic-containing PLGA (LA:GA=50:50) microspheres. The structure and properties of theranostics, theranostic-containing microspheres, and complex scaffolds were then studied.

RESULTS AND DISCUSSION: Microspheres containing Au@CS-FA theranostics in the aqueous core could be made via coaxial electrospray (Fig.1a) and nanofibrous PLGA

scaffolds could be produced via electrospinning (Fig.1c). Using dual-source dual-power electrospinning and coaxial electrospray and adjusting process parameters, multifunctional scaffolds containing theranostic-encapsulated polymer microspheres were fabricated (Fig.1b). Microspheres were randomly distributed in nanofibrous scaffolds, and the core-shell structure of microspheres embedded in scaffolds was clearly seen under TEM. Immersion tests in PBS were conducted and after 21-day degradation in PBS, PLGA shell of microspheres was broken down (Fig.2a) and theranostics were released (Fig.2b). As nanofibers in scaffolds were made of PLGA 75/25, they degraded faster than PLGA 50/50 microspheres and hence tissue regeneration would occur first in the surgical site of patients. Theranostics were studied before encapsulation in microspheres and after release in scaffolds. The released Au@CS-FA theranostics were found to retain the structure and morphology of original theranostics, still exhibiting highly branched AuNP core with many irregular tips. Strong SERS signals were seen from Au@CS-FA theranostics after their release in scaffolds (Fig.2c), indicating their ability for cancer detection.

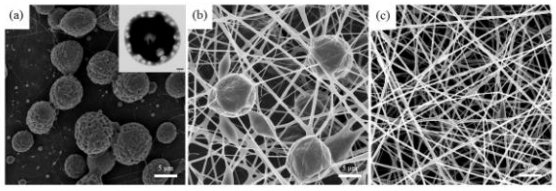

Fig. 1. (a) Theranostic-encapsulated PLGA microspheres made by coaxial electrospray; (b) Multifunctional scaffolds embedded with theranostic-encapsulated microspheres; (c) Nanofibrous PLGA scaffolds produced by electrospinning.

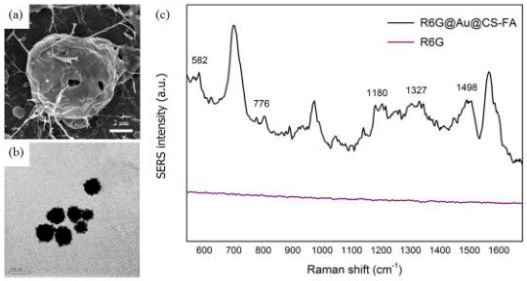

Fig. 2. (a) Breakdown of the shell of PLGA microspheres; (b) theranostics released in scaffolds; (c) SERS spectra obtained from pure R6G and released Au@CS-FA theranostics.

CONCLUSION: Using the novel fabrication technique, multifunctional scaffolds could be made for cancer patients for tissue regeneration at the surgical site and for detecting and treating cancer recurrence. The Au@CS-FA theranostics could be released in

nanofibrous scaffolds after the shell of polymer microspheres had degraded. The released theranostics gave strong SERS signals, indicating their potential for cancer cell detection.

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