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Study of Programmed Co-axial Electrospun Injectable Nanofibers for Sequential Anti-tumor Treatment

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Maintaining the effective range, time, dose of the local chemotherapy drugs, and achieving minimally invasive and sequential therapy, are the focus of current research for drug delivery systems. In this study, an injectable nanofiber with a core-shell structure, constructed by coaxial electrospinning technology and ultrasonic oscillation technology, has different sequential releasing effects of hydroxycamptothecin (HCPT)and doxorubicin (DOX) for the local treatment of human lung cancer and salivary adenoid cystic carcinoma. Two kinds of programmed co-axial electrospun injectable nanofiber with a length of 10μm, a diameter of 552nm±44.5nm, and core-shell structure, were obtained as SF-HCPT/DOX (short fragment, core-DOX， shell-HCPT) and SF-DOX/HCPT (short fragment, core-HCPT， shell-DOX), of which the drug in shell layer would be released quickly in the first five days and the drug in core layer would be released stably. The different programmed co-axial electrospun injectable nanofibers had different therapeutic effects for different tumors. In vitro, the obviously inhibitory effect of human adenoid cystic cancer cells appeared in 2μg/ml SF-DOX/HCPT, with smaller half inhibitory concentration. In vivo, similar therapeutic effect of SF-DOX/HCPT was observed on human adenoid cystic carcinoma. On contrary, the better efficacy of human lung cancer cells appeared in SF-HCPT/DOX.

Utilizing co-axial electrospinning and ultrasonic oscillation methods, the programmed co-axial electrospun injectable nanofibers, micro/nano structured, were obtained with different sequentially releasing effects. The different sequentially releasing injectable nanofibers, carried chemotherapeutic drugs – HCPT and DOX, had different tumor inhibitory effects, suggesting that the injectable fibers obtained in this study can be used as an injectable drug delivery system for local sequence therapy of malignant tumors.

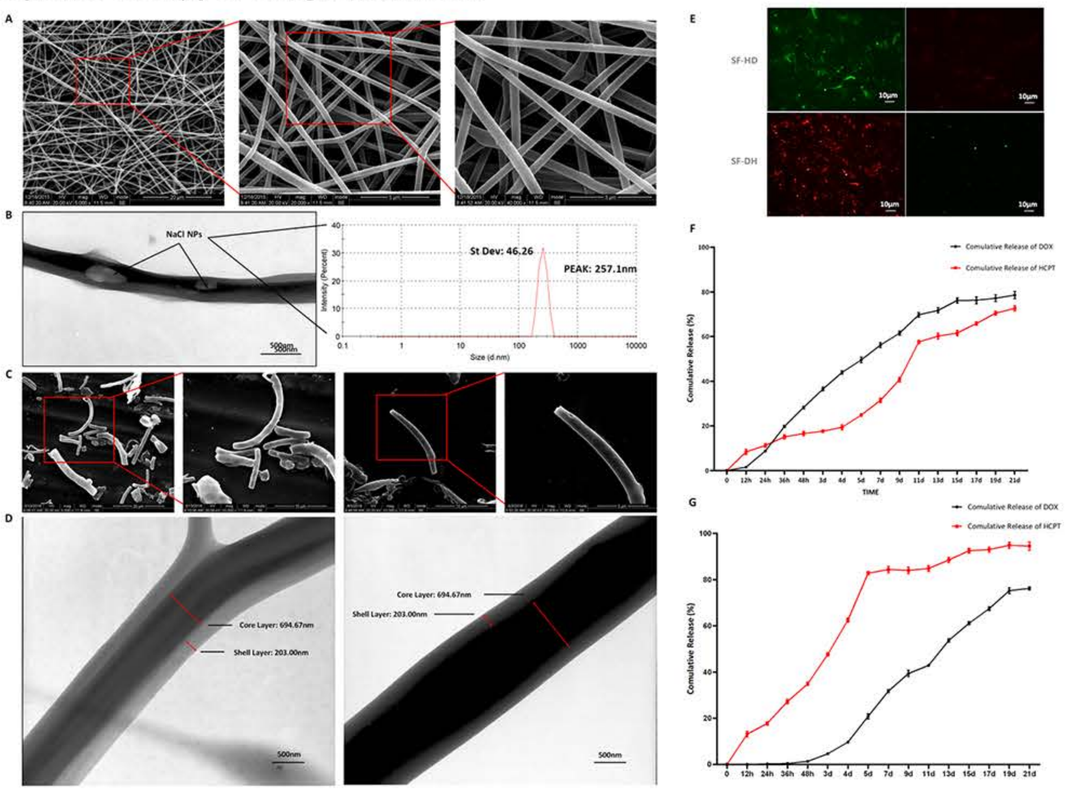

Fig1. A&C. The programmed co-axial electrospun injectable nanofiber with a length of 10μm, a diameter of 552nm±44.5nm, and core-shell structure by Scanning Electron Microscope (SEM). B. The injectable nanofiber with a core-shell structure, constructed by coaxial electrospinning technology and ultrasonic oscillation technology with NaCl NPs (257.1±46.26nm) via Transmission Electron Microscope (TEM). D&E. The core and shell structures shown via TEM. F. The different sequential releasing effects of hydroxycamptothecin (HCPT)and doxorubicin (DOX) were obtained as SF-HCPT/DOX (short fragment, core-DOX， shell-HCPT) and SF-DOX/HCPT (short fragment, core-HCPT， shell-DOX).

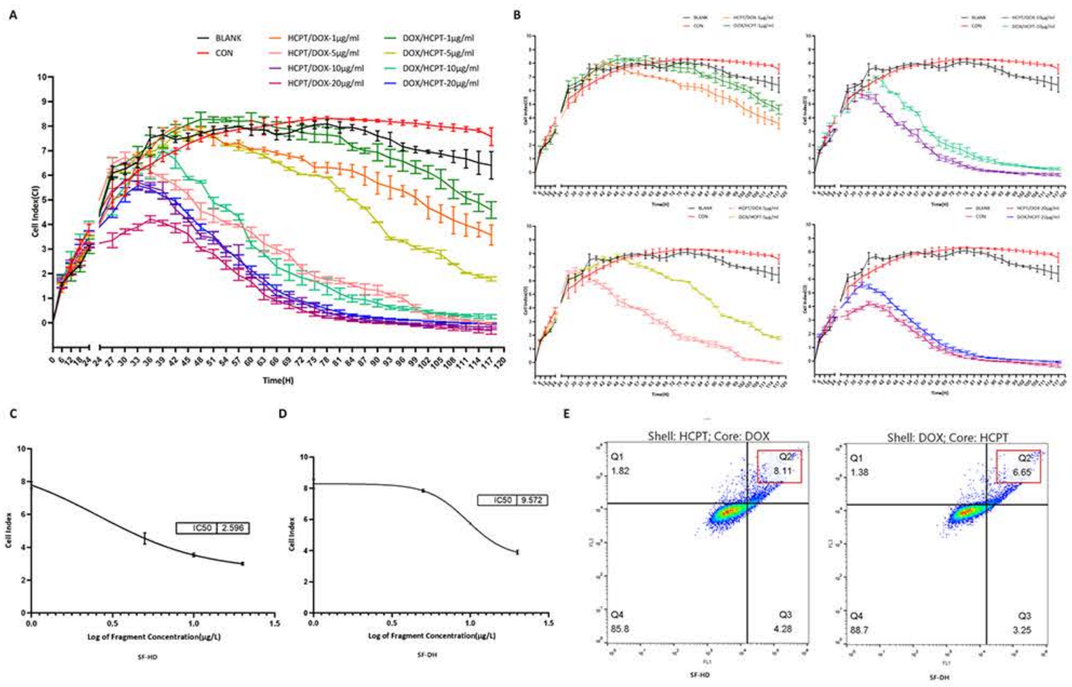

Fig2. A&B. The different programmed co-axial electrospun injectable nanofibers had different therapeutic effects for lung cancer. The better efficacy of human lung cancer cells appeared in SF-HCPT/DOX. C. The IC50 of SF-HCPT/DOX and SF-DOX/HCPT for A549. D. Apoptosis assay of SF-HCPT/DOX and SF-DOX/HCPT for A549.

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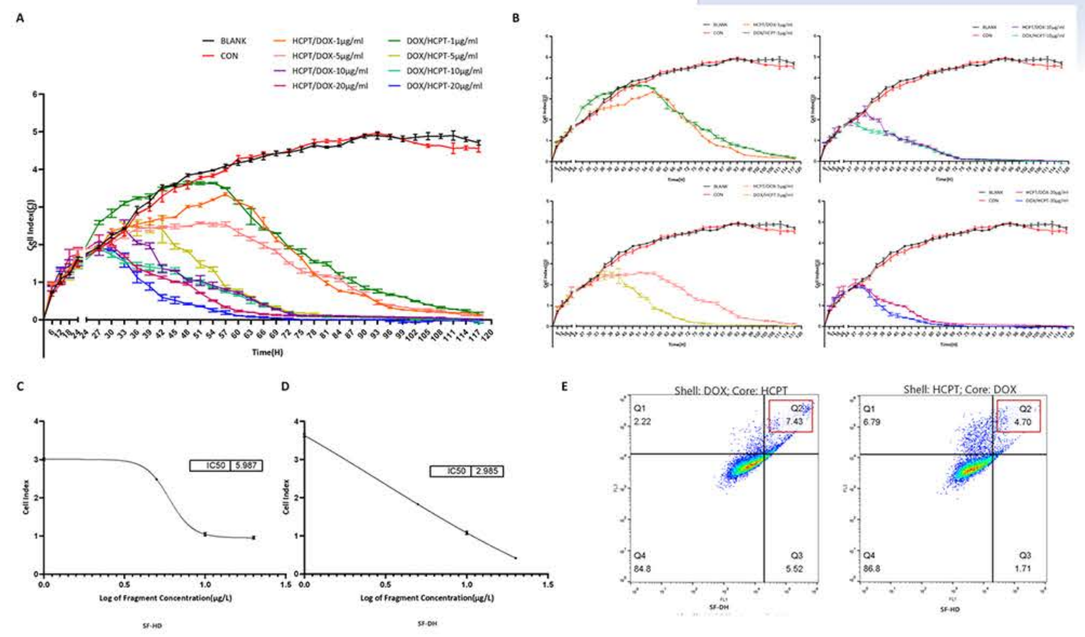

Fig3. A&B. The different programmed co-axial electrospun injectable nanofibers had different therapeutic effects for adenoid cystic carcinoma. The better efficacy of human adenoid cystic carcinoma cells appeared in SF-DOX/HCPT . C. The IC50 of SF-HCPT/DOX and SF-DOX/HCPT for ACC2. D. Apoptosis assay of SF-HCPT/DOX and SF-DOX/HCPT for ACC2.

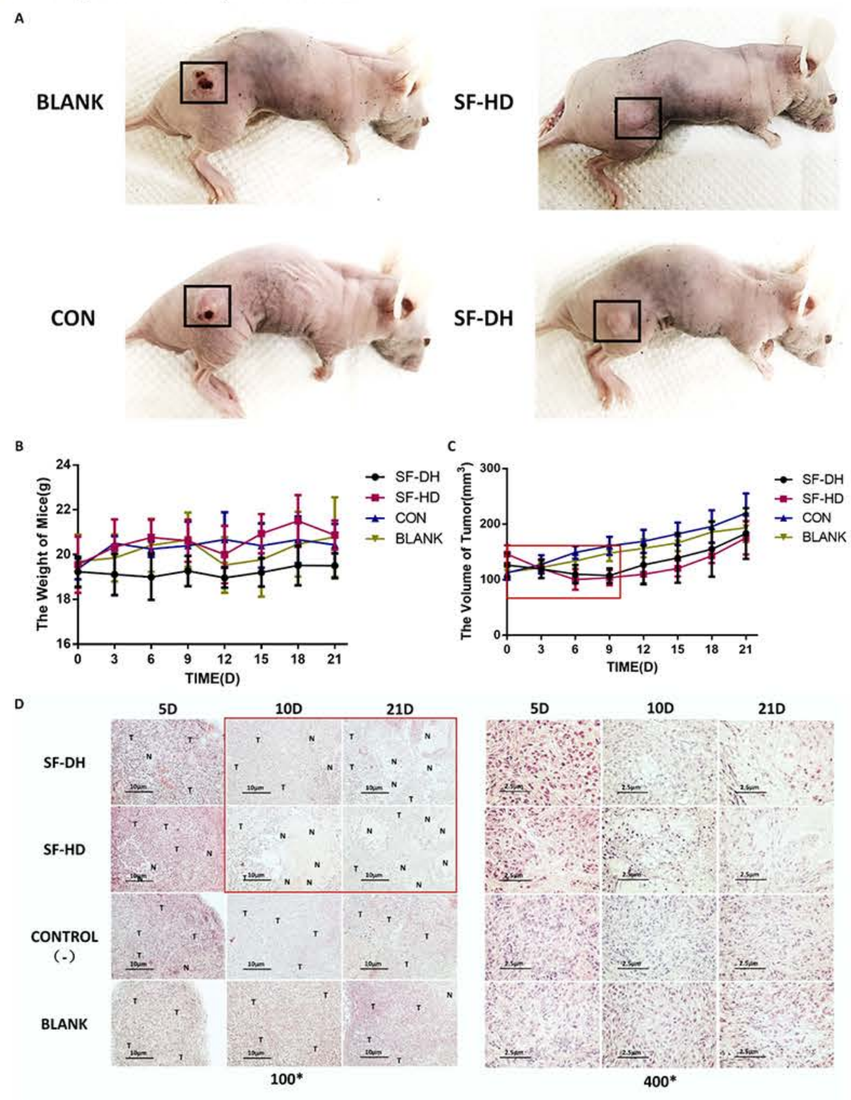

Fig4. A&B&C. The weight and volume of tumor from ransplanted tumor models of lung cancer in mice. D. The different programmed co-axial electrospun injectable nanofibers had different therapeutic effects for lung cancer. The better efficacy of human lung cancer cells appeared in SF-HCPT/DOX. (T: Tissue, N： necrosis). E. Heart, kidney, liver, and lung shown no obviously toxicity.

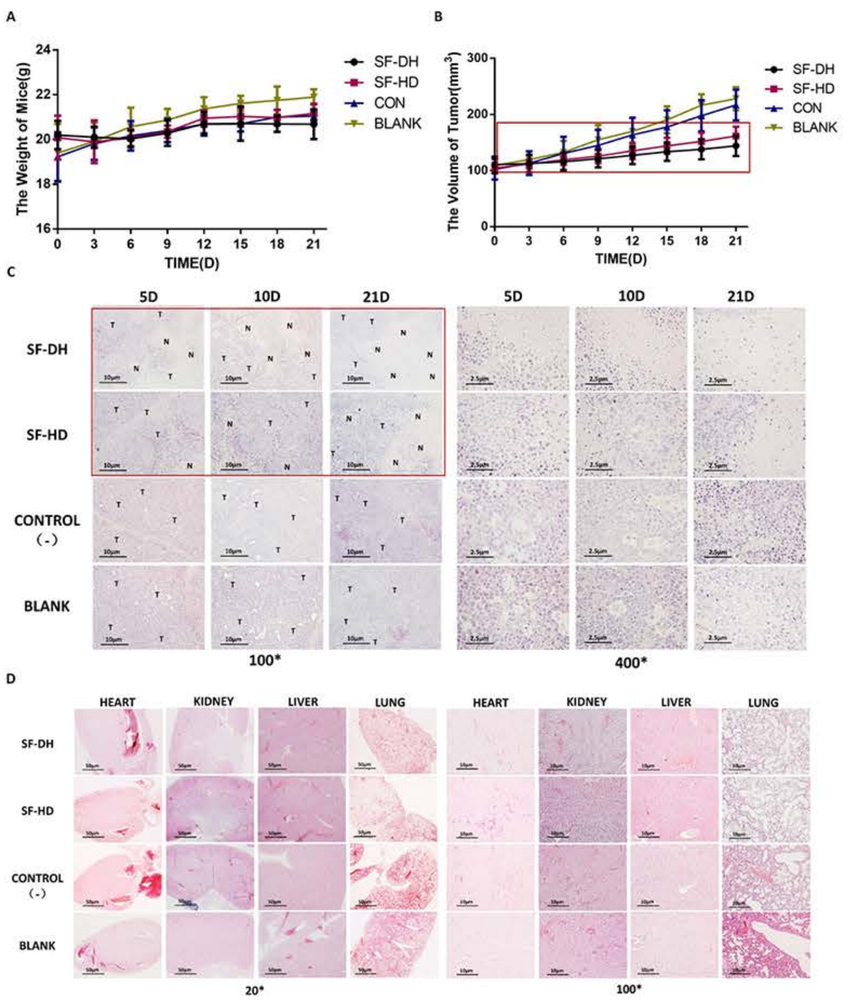

Fig5. A&B. The weight and volume of tumor from ransplanted tumor models of lung cancer in mice. C. The different programmed co-axial electrospun injectable nanofibers had different therapeutic effects for lung cancer. The better efficacy of human lung cancer cells appeared in DOX/ SF-HCPT. (T: Tissue, N： necrosis). D. Heart, kidney, liver, and lung shown no obviously toxicity.