Smart Hyperthermia Nanofibers with 'On-Off' Drug Release

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Statement of Purpose: During the past few years increased attention has been given to stimuli-responsive or smart polymeric nanofibers owing to their ability to act as an 'on-off' switch. Dynamically and reversibly tunable structures of smart nanofibers have the potential to be utilized for 'on-off' delivery of drugs[1] or cells[2]. Since smart polymers respond to small changes in external stimuli with large discontinuous changes in their physical properties, the incorporation of a further functionality such as self-heating properties into smart nanofibers opens novel opportunities in biomedical fields such as hyperthermic therapy and beyond. Here we report on hyperthermia nanofibers with both heat-generating and drug releasing abilities for improved hyperthermic chemotherapy. The hyperthermia nanofibers are composed of magnetic nanoparticles (MNPs) and temperature-responsive polymers, which serve as a source of heat and a trigger of drug release, respectively. We demonstrate that the heat-generating MNPs can induce collapse of the nanofiber networks followed by release of anticancer drug[3].

Methods: First, P(NIPAAm-co-HMAAm) (HMAAm: 20 mol%) was copolymerized by free-radical polymerization. The hyperthermia nanofibers were successfully developed by electrospinning P(NIPAAm-co-HMAAm) blended with MNPs (20-30 wt%) and DOX (0.15 wt%). The nanofibers were subsequently crosslinked by self-condensation of the methylol group of HMAAm upon heating at 130 ^{o}C for 12 h. The self-heating properties of the MNP-incorporated nanofibers in AMF were also investigated. A cytotoxicity study was evaluated using human melanoma cell line COLO 679 cells.

Results: The nanofibers were randomly distributed to form the continuous fibrous structure with an average diameter of 350 nm. Incorporation of MNPs did not alter the structure. TEM images showed that the MNPs were uniformly dispersed in the fiber. The self-heating properties of the MNP-incorporated nanofibers in an AMF were also evaluated. Figure 1a shows the infrared thermal images of nanofiber in an AMF. Moreover, 'on-off' self-heating property was monitored in response to alternating 'on' and 'off' switching of AMF (Figure 1b). Figure 1c shows the changes in the swelling ratio of the MNP-nanofiber and the resulting drug release from the fibers in response to alternating 'on' and 'off' switches of AMF. The swelling ratio was found to change reversibly and recovered within each cycle. Correspondingly, the 'on-off' release of DOX from the nanofiber was observed in response to temperature changes. To test both hyperthermia and DOX effects of the DOX/MNP-nanofiber in vitro, the cytotoxicity to COLO 679 cells were evaluated by MTT assay for 1, 3, 4 and 5 days. Cell viability decreased to 70% by AMF application in the presence of the DOX/MNP-nanofiber. These results indicate that the double effect of DOX treatment and hyperthermia effectively induced apoptosis while the effect of a single hyperthermia on apoptosis was not significant for a short time AMF treatment.

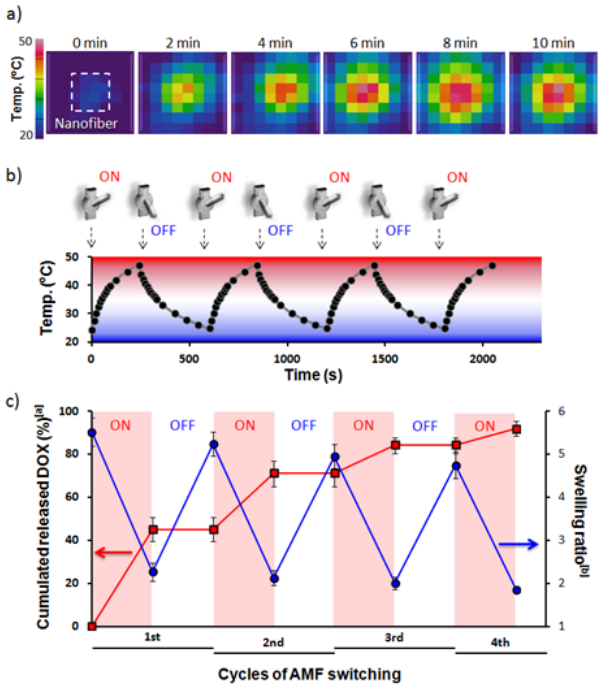

Figure 1. a) Time-dependent Infrared thermal images of the DOX/MNP-nanofiber in an AMF. b) Heating/cooling profile of the DOX/MNP-nanofiber in response to AMF. c) Reversible changes in the swelling ratio of the DOX/MNP-nanofibers and the resulting DOX release profiles from the fibers in response to AMF.

Conclusions: This study extends the further functionalization of the nanofibers for the immobilization of peptides or antibodies, which are highly promising for separation, purification, preservation, and the delivery of the target molecules and cells.

References: [1] Kim YJ et al., Angew Chem Intl Ed. 2012; 51: 10537-10541. [2] Kim YJ et al., Sci Tech Adv Mater. 2012; 13: 064203. [3] Kim YJ et al., Adv Func Mater. in press.