

Smart Hyperthermia Nanofiber Meshes With 'On-Off' Drug Release For Cancer Therapy

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Statement of Purpose: Squamous cell carcinoma is an epithelial malignant tumor found in mucous membranes lined by stratified squamous epithelium and in the skin. At present, the main therapeutic methods are surgery, radiation therapy and chemotherapy, according to the stages of the cancer. In recent years, thermotherapy (or hyperthermia), which takes advantage of the fact that cancer cells are more sensitive to heat than normal cells, has attracted great attention. Since thermotherapy is also effective for enhancing drug efficacy and relieving pain, high expectations are placed on its combined use with chemotherapy and other types of therapy. In this research, we developed a mesh material which can be applied directly to the affected part, and which is capable of simultaneously performing thermotherapy and chemotherapy for treating epithelial malignant tumors.

Methods: First, N-isopropylacrylamide was copolymerized with hydroxylate co-monomer by free-radical polymerization. The hyperthermia nanofibers were successfully developed by electrospinning the temperature-responsive polymer blended with magnetic nanoparticles (MNPs) and anticancer drug. The nanofibers were subsequently crosslinked by self-condensation of the functional co-monomers upon heating at 130 °C for 12 h. The self-heating properties of the MNP-incorporated nanofibers in alternating magnetic field (AMF) were also investigated.

Results: The nanofiber is composed of a chemically-crosslinkable temperature-responsive polymer with an anticancer drug and MNPs, which serve as a trigger of drug release and a source of heat, respectively. By tailoring the nanoarchitectures of polymer networks in the fiber, the nanofiber mesh shows switchable changes in the swelling ratio in response to alternating 'on-off' switches of AMF because the self-generated heat from the incorporated MNPs induces the deswelling of polymer networks in the nanofiber. Correspondingly, the 'on-off' release of drug from the nanofibers is observed in response to AMF. Both in vitro and in vivo studies show that the majority of tumor cells died in only 5–10 min application of AMF by the double effects of heat and drug. Taken together these advantages on both the nanoscopic and macroscopic scale of nanofibers demonstrate that the dynamically and reversibly tunable structures have the potential to be utilized as a manipulative hyperthermia material as well as a switchable drug release platform by simply switching an AMF 'on' and 'off'.

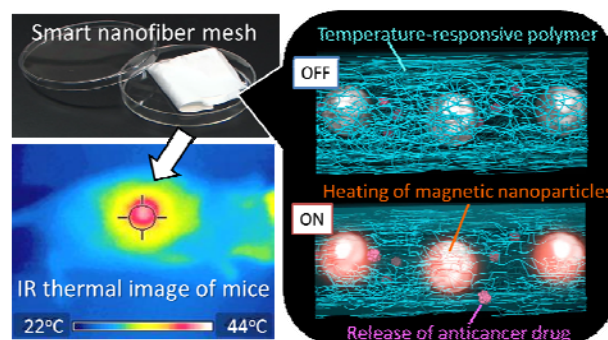


Figure 1. Infrared (IR) thermal image of mice after the transplantation of smart anticancer nanofiber mesh which is composed of a chemically-crosslinkable temperature-responsive polymer with an anticancer drug and magnetic nanoparticles.

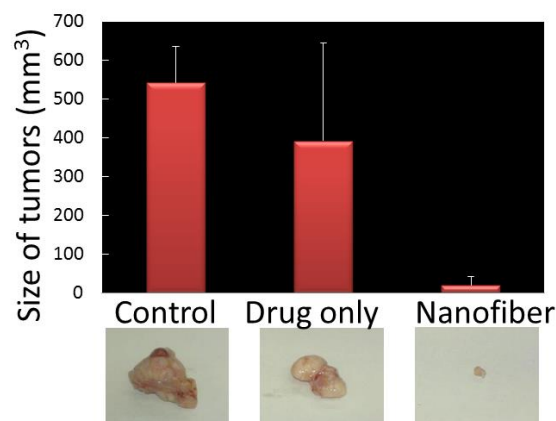


Figure 1. In vivo studies show that sizes of tumor were successfully reduced by implantation of the smart nanofiber via double effects of heat and drug.

Conclusions: We believe that the development of a manipulative material is very likely to lead not only to improving the survival rate of cancer patients but also to providing minimally invasive treatment methods in combination with endoscopic surgery.

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.* 2014; 23: 5753-5761.