Cisplatin-Loaded Biodegradable Nanofiber Meshes for Treating Malignant Pleural Mesothelioma

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Statement of Purpose:

Local drug delivery is a promising strategy for treating cancer, as it may be able to minimize side effects traditionally seen with systemic chemotherapy, while also reducing the risk of local recurrence caused by residual tumor cells left behind after cytoreductive surgery. In soft tissue cancers like the lung and thorax—and especially in malignant pleural mesothelioma—local recurrence is common, with rates reaching upwards of 80%, and 5-year survival rates less than 40%[1-3]. In addition, the recurrent disease may be diffuse and unsuitable for additional surgical removal. Therefore, the purpose of this study is to develop a biodegradable cisplatin delivery device (i.e., a nanofiber mesh) that can be sutured to the disease site to locally deliver chemotherapy, which may supplement cytoreductive surgery and potentially improve treatment outcomes.

Methods:

Solutions containing polycaprolactone, poly(glycerol monostearate-*co*-caprolactone), and cisplatin (3% per total polymer mass) were electrospun and collected onto an aluminum foil-wrapped, rotating and translating metallic drum collector. The resulting meshes were characterized by contact angle goniometry, scanning electron microscopy, and by tensile testing. The release kinetics of cisplatin from the meshes was studied by platinum detection using graphite furnace atomic absorption spectroscopy (GF-AAS) with Zeeman background correction. Finally, the meshes were tested for prolonged tumor cell killing ability against a human malignant pleural mesothelioma (MSTO-211H) cell line in an *in vitro* cell assay.

Results:

To prolong the release of cisplatin and prevent a burst effect, commonly observed in drug delivery systems, we constructed the mesh from polycaprolactone and a superhydrophobic copolymer dopant[4]. The resulting mesh consists of a three-dimensional network of ~500 nm fibers (Figure 1). The air-filled pores of the mesh create a barrier to water infiltration, and allow cisplatin to be slowly released over 21 days in the presence of 10% serum. In addition, these cisplatin-eluting meshes are effective against a human mesothelioma cell line *in vitro* for 20 days (Figure 2). In contrast, nanofiber meshes without the superhydrophobic dopant release their cisplatin payload in just 5 days, due to the fast rate of water infiltration.

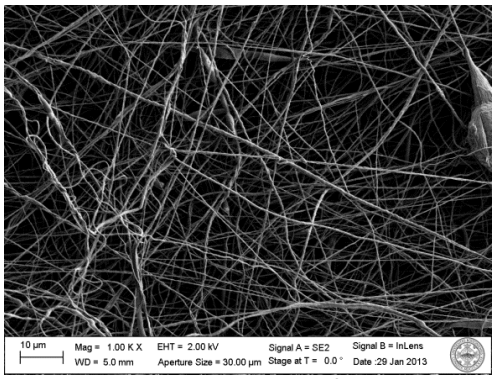

Figure 1. Scanning electron micrograph of a superhydrophobic cisplatin-loaded biodegradable nanofiber mesh.

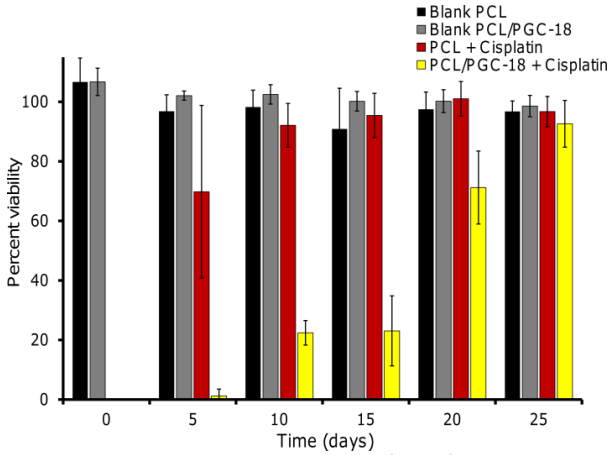

Figure 2. Tumor cell toxicity assay of nanofiber meshes

Conclusions:

Previous work involving drug-eluting superhydrophobic 3-D nano- and microfiber meshes had focused on the delivery of the hydrophobic drug 7-ethyl-10-hydroxycamptothecin[4]. Here we have successfully applied this strategy to the hydrophilic chemotherapy agent cisplatin, which is actively used in the management of malignant pleural mesothelioma. The sustained release of cisplatin *in vitro*—and in the presence of serum—provides evidence of a universal strategy for local drug delivery after cytoreductive surgery, and may improve treatment outcomes for patients suffering from mesothelioma.

References:

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