A Metal-Polymer Nanosystem for Combined Chemotherapeutic and Photothermal Cancer Treatment

K. Homan[*], L. Brannon-Peppas[**], S. Emelianov[*].
[*]The Department of Biomedical Engineering, The University of Texas at Austin, Texas, USA.
[**]Appian Labs, LLC, Austin, Texas, USA.

Statement of Purpose: As cancerous cells continue to acquire resistance to single chemotherapy or radiation regimens, combined treatment strategies become increasingly vital. Colloidal nanosystems designed for injection in the bloodstream can now provide a platform for multiple therapeutic means within a single carrier. Indeed, one such nanosystem consisting of a new metal-polymer composite is shown in Fig. 1. This metal-polymer composite is capable of carrying multiple chemotherapeutic drugs and/or imaging contrast agents in its core.[1,2] Furthermore, the silver outer cage[3] allows for the possibility of photothermal therapy once these composites extravasate and latch onto upregulated receptors on the surface of cancerous cell membranes *in vivo*.

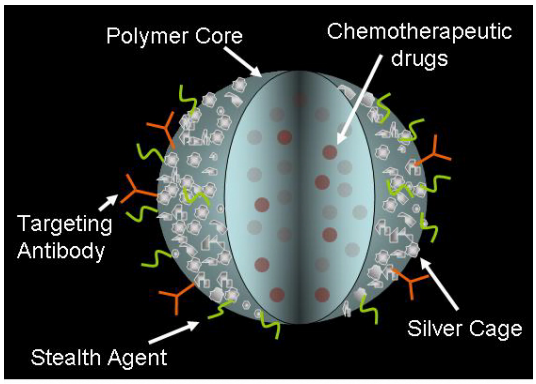

Figure 1. Metal-Polymer Composite Nanosystem

Methods: Oil-in-water emulsion methods[1] were used to encapsulate the chemotherapeutic drug, doxorubicin, in a matrix of poly(lactic-co-glycolic acid) (PLGA). A porous silver layer was then photoreduced onto the PLGA surface in the presence of 254nm light. The nanosystem was subsequently mixed in cell growth media and incubated with the breast cancer cell line MDA-MB-231 for 24 hours. Cytotoxicity studies and darkfield microscopy techniques were used to investigate the interactions of these cancer cells with the metal-polymer composites *in vitro*.

Results: The metal-polymer composite was constructed as shown in the scanning electron micrograph (SEM) in Fig. 2. The polymeric core averaged 210nm in diameter and the thickness of the porous silver layer varied between 20-60 nm. Cytotoxicity studies showed that the nanosystem containing the drug doxorubicin was significantly more toxic to cells than the same nanosystem without inclusion of drug. In fact, these empty silver-PLGA nanosystems showed no cytotoxic increase over controls, indicating that silver may not be toxic to cancer cells in concentrations up to 3.0 mg/ml.

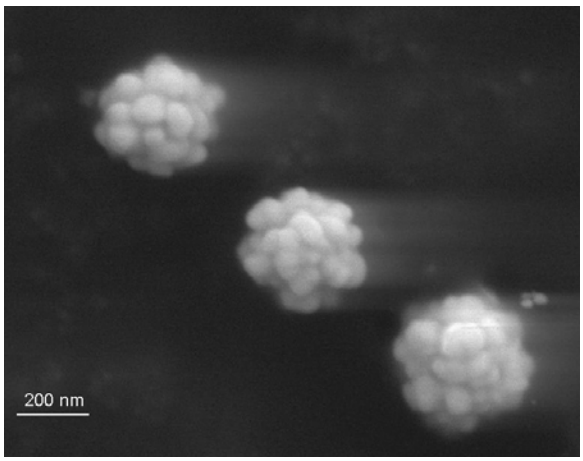

Figure 2. Silver coated PLGA composites

Conclusions: A metal-polymer composite nanosystem can be constructed with encapsulated drugs or other small imaging molecules. This nanosystem offers several potential advantages (1) large payloads of one or more drugs can be delivered directly to cancerous sites (2) the metal outer shell increases the light absorption properties of the system, allowing for photothermal therapy, as well as multimodal image-guided therapy approaches. Future studies will focus on chemical conjugation of the targeting antibody followed by injection in mice with xenograft tumor growth to evaluate the nanosystem accumulation and toxicity *in vivo*.

References:

1. Betancourt B., Brown B., Brannon-Peppas L. *Nanomedicine*. 2007;2:219-32.
2. Doiron A., Homan K., Emelianov S., Brannon-Peppas, L. *Pharm. Res*. 2008; in press.
3. Homan K., Gomez S., Gensler H., Shah J., Emelianov S., Brannon-Peppas L., *Proc. SPIE 2009*.