Regenerative Medicine Minnesota Progress Report

Grant Title: Controllable and automated system for synthesizing GMP magnetic nanoparticles for regenerative medicine applications

Grant Number: RMM-2017-BB-02

Requester: Dan Dragomir-Daescu, PhD

Project Timeline: 6/1/2017 – 5/30/2018

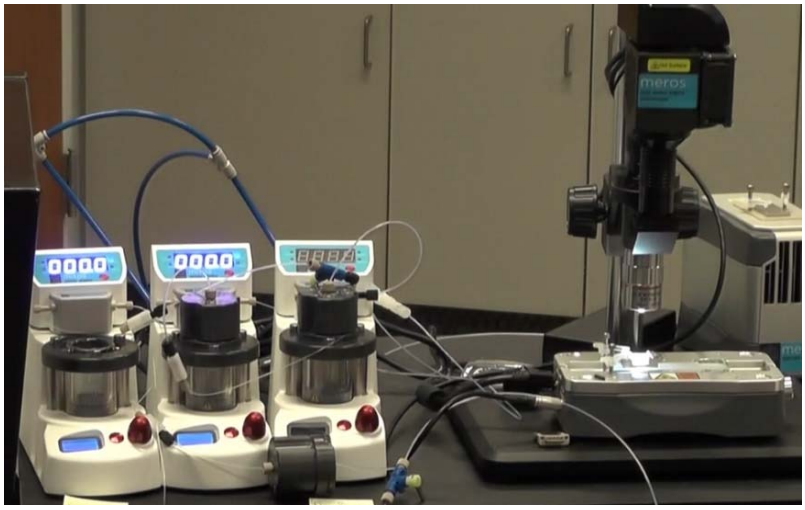
Brief description of project:

The goal of this equipment grant was to purchase, implement, and develop standard operating procedures for research laboratory equipment that can be used to synthesize Good Manufacturing Practice (GMP) magnetic nanoparticles at Mayo Clinic in Rochester, MN. The Atlas and Dolomite systems (Figs. 1 and 2) are automated and software-controllable GMP-compliant systems that can synthesize nanoparticles. The Atlas batch chemistry system (Fig. 1) synthesizes nanoscale magnetite cores for the magnetic nanoparticles, and the Dolomite flow chemistry system (Fig. 2) coats these magnetic cores in PLGA, which is necessary for biocompatibility. These nanoparticles can be utilized in a variety of regenerative medicine applications including targeting cells to cardiac valves and acellular xenogeneic scaffolds. The ability to magnetically direct stem cells, growth factors, and other therapeutic agents to target sites within the body will enable these and other regenerative medicine applications, as well as applications within other areas of medicine including targeted delivery of oncolytic agents to tumors. Creating high-quality nanoparticles using GMP will be critical for translating this promising regenerative medicine strategy into clinical practice, as GMP is an FDA requirement. With these new systems, nanoparticle production yield will increase to the order of grams per day (1000x improvement over our current process). This increased capacity will allow us to expand our regenerative medicine research efforts, as well as providing a shared resource for other investigators at Mayo Clinic. Additionally, these new systems allow for scale-up in the future, which will be critical for delivering these promising therapeutic strategies to patients in Minnesota and worldwide.

Figure 1. Photograph of Atlas batch chemistry system during training and programming of magnetite core protocol into Atlas software.

Upon receiving this grant, we customized and then purchased batch and flow chemistry systems that maximize our nanoparticle synthesis capabilities, and also have the flexibility to produce components for other regenerative medicine applications. We received the equipment in April 2018, and assembled and trained on the systems in May 2018. We videotaped the training sessions, for use in training other Mayo Clinic research collaborators to use the systems. Our existing protocol for producing magnetite cores was programmed into the Atlas system software for semi-automated production. In addition, we worked with a Dolomite system expert to develop a protocol for that system to coat the magnetite cores with PLGA. We are awaiting delivery of an emulsion stabilizing oil necessary for PLGA coating, and then we can begin nanoparticle synthesis. We are currently working on a marketing plan to share the capabilities of these new systems with other Mayo Clinic researchers, to encourage collaborations that utilize this equipment.

(a)



(b)

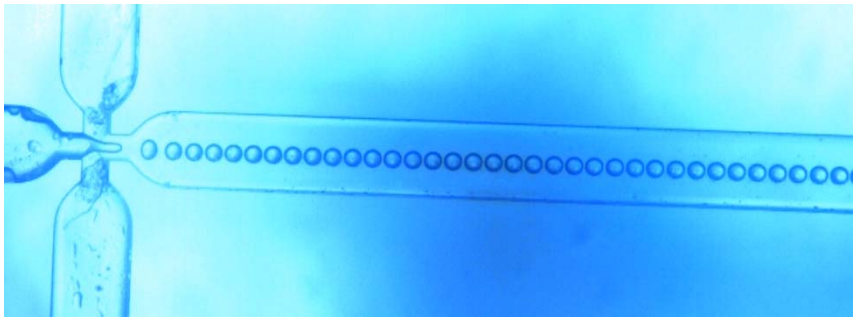


Figure 2. The top image (a) shows the Dolomite flow chemistry system pumps and microscope. The bottom image (b) shows a screenshot captured from a video of uniform-sized droplets created in a micro-mixer chip during training. The outlet channel diameter is 100 mm.

Please list any of the following (manuscripts/disclosures/grant applications) that have resulted from your Regenerative Medicine Minnesota grant funding:

We are in the process of writing three grant applications that utilize magnetic nanoparticles, which will be synthesized using the equipment purchased with this grant.

Grant Spending Summary:

Award amount: $98,446

Atlas batch chemistry system: $36,483

Dolomite flow chemistry system: $49,548

Cart for systems: $385

Dr. Dragomir-Daescu salary/benefits: $5,011

International shipping: $3,837

Indirect costs: $3,182

Total spent: $98,446