

Regenerative Medicine Minnesota
Progress Report
Due: August 31, 2016

Grant title: Advanced Product Incubator Capital Equipment Proposal

Grant number: MRM 2015 BB 006

Requester: Melinda Rice

Project Timeline: May 1, 2015 – July 31, 2015

Brief description of this project

The Advanced Product Incubator platform is GMP facility designed to accelerate the discovery, translation and application of novel products with the express focus on regenerative cell-free biologics-based platforms. The Advanced Product Incubator is a first-of-its-kind platform to fulfill an unmet need in regenerative medicine, developing cell-free, molecular regenerative therapeutics. The mission of this incubator is to be highly collaborative within the Mayo Clinic and fully collaborative with the other 3 platforms within the Center for Regenerative Medicine (Regenerative Medicine Biotrust, Human Cellular Therapy Laboratories, and Biomaterial Unit) to help advance clinical trials in the regenerative space.

This distinctive platform will allow Mayo Clinic to expand its reach across disciplines in the rapidly evolving regenerative therapeutic space. The Advanced Product Incubator will support clinical translation of innovative discoveries within Mayo Clinic, in tandem with attracting regenerative industry aligning with Mayo Clinic Ventures, Global Business Solutions, and Destination Medical Center initiatives. Launch of the Advanced Product Incubator will be inaugurated by a series of pathfinder projects spanning medical/surgical specialties. These include product development in cardiovascular, orthopedics, and plastic & reconstructive surgery.

Where did this project take place?

The newly designed state-of-the-art GMP facility on the third floor of the Minnesota Biobusiness Center located at 101 3rd Street SW, Rochester, MN houses the equipment. The GMP facility is approximately 3,000 square feet of space with two separate clean rooms allowing for dual, simultaneous product production. State-of-the-art technology within this space will foster the production of medical and surgical products specifically for regenerative therapies. This facility is strategically located near the Cardiac Regeneration Program which resides at 300 Second Avenue SW, Rochester, MN. Both of these facilities will work collaboratively to expedite the translation of basic science discovery toward application of novel products.

People impacted by project and where they are from:

The mission of the Advanced Product Incubator at Mayo Clinic is to develop cell-free, off-the-shelf products to achieve low-cost regenerative products for patients with currently irreversible chronic disease. Individuals impact by the project include patients on current and future clinical trials, as well as employees in the Advanced Product Incubator as it provides the necessary toolkit for fulfilling the Advanced Product Incubators mandate of accelerating novel regenerative products to patients.

What was the outcome of the project?

With the support from Regenerative Medicine Minnesota, the Advanced Product Incubator was able to acquire a Sepax 2 RM Cell Separation System. In addition, this support allowed for the expansion of needed equipment, with matching dollars from Mayo Clinic, to acquire a custom-configured autoclave system that supports a broad spectrum of product development activities, including but not limited to:

- **Wound healing:** Novel matrix-based wound healing products to enhance dermal progenitor cell growth by over 10-fold, and in pre-clinical studies, has shown to increase the rate of healing from 4 weeks down to 1 week
- **Acute myocardial infarction:** A major burden on society, acute myocardial infarction continues to impose a significant impact on health care worldwide. Recently, the Cardiac Regeneration Program at Mayo Clinic has identified a unique set of proteins that are deregulated in patients who suffer the greatest degree of injury. These proteins can be microencapsulated for delivery into the myocardium after infarction; however, the size of microencapsulation (10 μ m needed) cannot be controlled. To this end, the Sepax System will have the capability to isolate in GMP fashion the encapsulated size of interest to create a high precision in the delivery of these regenerative proteins.
- **Chronic myocardial infarction:** A direct consequence of heart attacks, this disease affects significant number of Minnesotans. The Cardiac Regeneration Program at Mayo Clinic has developed a cellular product, termed Cardiopoietic Stem Cell which is now in Phase III testing within Europe and has received approval in the United States for Phase III evaluation (start of trial in Late spring 2015). In order to wash Cardiopoietic Stem Cells following cryopreservation, the Sepax 2 RM system is needed to ensure sterility and high cellular quality.

Did the project work the way you expected it to?

The addition of a Sepax 2 RM system has fostered Mayo Clinic enterprises leveraging through transfer of a related wound healing clinical trial from outstate into Minnesota. The reach of the new Sepax unit has un-expectedly opened opportunity to support existing clinical trials from outstates that were unable to complete patient recruitment or continue trials due to other logistical issues. The fully automated, no operator intervention device creates consistent results utilizable by multiple enterprise and state locations. The single use components add patient safety not found in other instruments. Addition of GMP compliance meets strict FDA regulatory requirements in a rapidly changing field. The resulting increase in consistent Minnesota driven patient trials has expanded regenerative exposures and focalized a regenerative leadership role in our state.

What were the successes? What were the failures?

One successful measure from a Regenerative grant standpoint is the leveraging of greater dollars from Mayo Clinic through matching funds. The procurement of the Sepax machine allowed the API to garner further dollars in support the autoclave, further expanding the reach of the grant.

Successful procurement of the Sepax unit has generated a maelstrom of new ideas and possibilities driving IP, development and clinical trial opportunities by clinicians, physicians, clinical scientists and principal investigators. While the machine was originally designated to Regenerative projects as outlined above, success has been attributed to increasing interest in the Regenerative space in general by those not directly associated with the field. Examples include benefactors whom upon view of the instrument, garnered interest in Regenerative Medicine through focused discussions about the machines ability. The unit brings visibility to a field which exists without visibility, barring successful treatments, due to the abstract nature of regenerative medicine. The unit is designed to drive science forward; however, it continually becomes a focal point when explaining regenerative ideas to non-science speaking parties interested in supporting the regenerative space. In the same stroke, the unit's diverse functions have driven idea initiation and interest by collaborators within the Regenerative Medicine space but not associated with the primary projects listed above.

How did it impact regenerative medicine in Minnesota?

The unit has:

1. Generated institutional interest, understanding and contribution willingness by providing a visually didactic platform to explain and forward abstract regenerative ideas. Resultant support dollars have greatly impacted the API and its capacity to support trials.
2. Positioned the API to support outstate trials in Minnesota not previously accessible.
3. Generated a myriad of new ideas and regenerative concepts by investigators previously unaware of the Sepax unit's ability.
4. Provided safety and continuity by generating reliable and consistent products in a GMP environment with single-use disposable consumables used in an operator free manner for continuity.

Please list any of the following that have resulted from your Regenerative Medicine Minnesota grant funding:

- Publications and/or manuscripts submitted for publication
Plast Reconstr Surg. 2016 May;137(5):1498-506.
Eur J Heart Fail. 2016 Feb;18(2):160-8.
J Arthroplasty. 2016 Apr;31(4):893-8.
- Disclosures/patents
- Other grant applications and/or awards Mayo Clinic contributed to the Regenerative Medicine grant by funding greater than \$34,306 dollars to further support infrastructure not covered by the grant. These dollars are value added and only available because of the RMM grant.

Responsible Spending:

The money was spent to build out needed capital infrastructure in support of product development and clinical trial manufacturing. After acquiring the Sepax machine and with approval from RMM, the funding was also used to acquire a cGMP-grade autoclave system. The autoclave is currently in manufacturing awaiting a factory acceptance test late November. The unit is due to ship December 12th where it will receive a site acceptance test upon arrival. This unit stands as the only cGMP compliant unit available in the Mayo Clinic System.