

Regenerative Medicine Minnesota

Progress Report

Due: May 30, 2016

Grant Title: Advanced Reproduction Laboratory to Drive Innovations in Regenerative Medicine.

Grant Number: MRM 2015 BB 003

Requester: Daniel F. Carlson, PhD

Project Timeline: May 1, 2015 – April 30, 2016

Brief description of project: The goal of the project was to purchase capital equipment necessary to kickstart the Advance Reproduction Technology (ART) laboratory at Recombinetics. We specialize in genome engineering of pigs as models of human disease and novel approaches for exogenic production of human cells and tissues in gene-edited pigs. Both of these lines of business required ART to produce prototype animals and conduct the appropriate R&D efforts towards exogenic production of human cells/tissues. The ART laboratory will serve as a nucleus for innovation in both areas with our strong Minnesota collaborations.

Where did this project take place? Recombinetics' Laboratory space is located at 1246 University Avenue West, St. Paul, MN 55104. The ART laboratory renovation took place over the last 6 months and the equipment purchased with grant funds are installed in the laboratory.

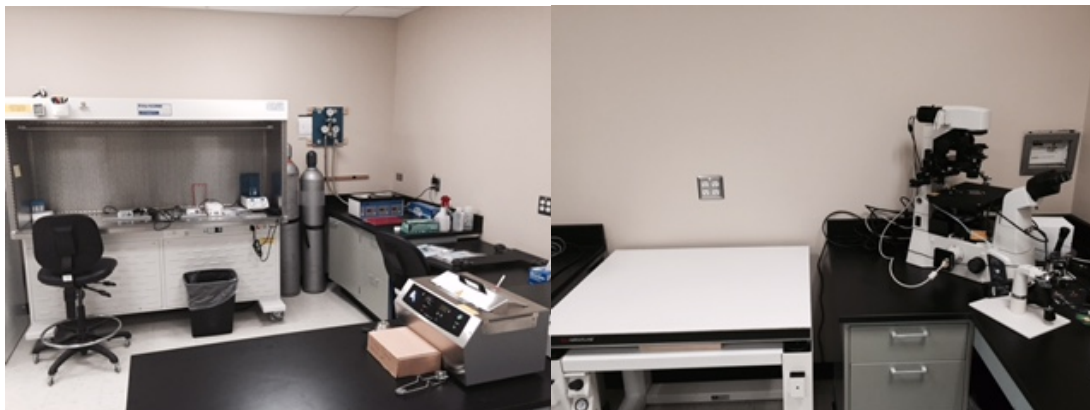
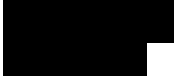
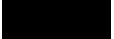
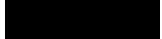
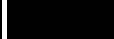
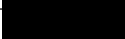
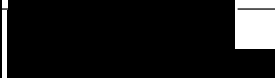
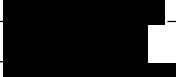


Figure 1: The ART lab at Recombinetics. The lab is in the final stages of completion waiting only on compressed air lines for the air anti-vibration tables, and the second inverted scope to arrive in June. Upper left, Astec Drawer type incubator, lower left, workstation 2 and laminar flow hood outfitted with Recombinetics funds, upper right, stereoscopes with thermal plates, lower right, workstation 1 with Nikon TiS inverted microscope. The scope will be moved onto the white air table after the compressed air lines are installed.

People impacted by project and where they are from:

Innovation happens when researchers are able to put their heads together, iteratively refine procedures and repeat experiments in a timely basis. Under our current paradigm, this innovation process is crippled by lack of interactions between scientists and the ART group, inhibitory costs, and limited access to ART services. Establishing the ART lab in Minnesota will restore the innovation process and stretch the research dollars of Recombinetics and our local collaborators. Finally, the ART lab will create jobs in Minnesota, not only for ART lab operations, but also to translate and commercialize the novel findings enabled by it. Currently the ART lab is only partially operational as the final pieces of equipment are installed and staff are trained. During this transition, we continue to collaborate with several Minnesota researchers through and external ART provider.

What was the outcome of the project? (Did the project work the way you expected it to? What were the successes? What were the failures? How did it impact regenerative medicine in Minnesota?)

We are very happy with the equipment purchased with the Regenerative Medicine Minnesota. Through competitive quotes and product research, we believe the tool within the laboratory are state-of-the-art, and will be operational for many years to come. We identified the Astec drawer type incubator as an upgrade over the originally proposed water jacketed CO2 incubator. In contrast to the conventional incubator, the Astec incubator has incredibly fast recovery gas and temp recovery times (< 1 minute) that will improve the development of engineered embryos. In addition, each of the 4 drawers acts as a separate incubator allowing different temperatures and atmosphere conditions.

Some challenges of the project were infrastructure related. High building vibration forced us to abandon our passive microscope tables in favor of active tables powered by compressed air. This accounts for > 3 months delay and additional expense incurred by Recombinetics.

Once operational in June, the ART lab will be the nucleus of swine innovation in Minnesota for both production of models and R&D efforts related to exogenic organ production.

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

- **Publications and/or manuscripts submitted for publication**
 - None as of yet related to our ART lab
- **Disclosures/patents**
 - None as of yet related to our ART lab
- **Other grant applications and/or awards**
 1. Mayo Clinic Translational Polycystic Kidney Disease Pilot and Feasibility award.
 - Title of Proposal: Evaluation of an ad hoc method for production of swine models of ARPKD
 - Amount Requested/# years: \$80,000 / 2 Years
 - PI: Daniel Carlson
 - 7/1/2016-6/30/2018
 - This is the first grant to 100% rely on the Recombinetics ART laboratory.

Responsible Spending:

Please let us know how you spent the money. Any unspent funds must be returned.

TABLE of RMM Grant Expenditures.

Item Description	Number	Total
Nikon TiS Inverted Microscope w/ DIC Optics • Narishigi Micromanipulation System • Heated stage • Fluorescence package • Nikon Fi1c Camera System	1	\$68,553

Nikon SMZ745 Stereomicroscopes w/ Thermo Plate	2	\$11,691.05
AD-3100GC Astec Drawer type incubator (4 drawers) with independent temperature, CO2 and O2 control. IR CO2 sensor and Galvanic O2 sensor. Alarm (BMS) system included and analogue boards for data logging standard.	1	\$29,900
Total:		\$110,144.05
<i>RMM Biotechnology/Biobusiness Development Grant</i>		<i>(\$100,000)</i>
Recombinetics' portion not including other capital expenditures on a second inverted scope, air tables, laminar flow hoods and small lab equipment.		\$10,144.05