Regenerative Medicine Minnesota Final Report for MRM 2015 BB 001

Grant Title: *Manufacturing Cell Therapies using Induced Pluripotent Stem Cells in Minnesota*

Grant Number: MRM 2015 BB 001 **Requester:** James R Dutton, Ph.D, UMN Stem Cell Institute

Project Timeline: May 1, 2015 – April 30, 2016 **Direct Costs: $75,188**

Brief Description of the project: *This RMM Biobusiness grant was designed to develop local infrastructure to enable pluripotent stem cell-derived therapeutic products to be manufactured at UMN.* Regenerative medicine therapies using cell products made from human pluripotent stem cells are beginning to be tested in clinical trials around the world. Examples include embryonic stem cell (ESC)-derived oligodendrocyte progenitor cells and pancreatic progenitors in the US, and ESC or induced pluripotent stem cell (iPSC)-derived retinal pigmented epithelium in the US, Europe and Japan. Therapeutic products made using pluripotent stem cells have the potential to treat diseases and injury conditions for which there are currently no effective treatments and this ability to change the practice of medicine means that pluripotent stem cell-derived therapies have the potential to generate businesses that will match or exceed the value of the current medical device industry. However, for Minnesota to benefit from the growth of this type of regenerative medicine it will require expertise and infrastructure to develop, validate and deliver cellular products generated using pluripotent stem cells. Fortunately, the State and University of Minnesota has had the foresight to invest in two areas critical for this initiative. The first is the UMN Stem Cell Institute which has developed scientific expertise in manipulating pluripotent stem cells to generate clinically relevant cell types as potential therapeutic products. Secondly, the UMN possesses a clinical cell manufacturing facility, Molecular and Cellular Therapeutics (MCT) on the St Paul campus. The MCT facility provides the building and cell manufacturing expertise where many cell products already in clinical use at UMN are prepared, but MCT staff had no experience with human pluripotent stem cells.

In this grant we requested funds to support personnel at both the SCI and MCT to allow mutually beneficial exchanges of expertise to help train the manufacturing staff to culture and manipulate human induced pluripotent stem cells and to educate the SCI researchers in cell manufacturing techniques and compliance. The ultimate aim was to establish the ability to generate human iPSCs at the MCT under conditions compliant with current good manufacturing practices (cGMP). These cells would then be able to be used subsequently to generate clinically useful cell products. We also requested support for a clinical and translational support services (CTRS) team who manage institutional and federal compliance for research projects involving human subjects and who we utilize to manage all clinical contact with patients, tissue donors etc.

Where did this project take place? The project took place on the UMN East bank and St Paul campuses. The Stem Cell Institute is located in the UMN Biodiscovery district by the TCF stadium and our CTRS team is based in the 717 Delaware building close to Moos tower. MCT is located next to the Raptor center on the St Paul Campus.

People impacted by project and where they are from: The people impacted by this funding all work or study in Minnesota. The PI Dr James Dutton has his research group at the Stem Cell Institute and with this funding partially supported two research members of staff, both previous MS graduates of the Stem Cell Biology Masters degree program at UMN. The Chief User is Dr David McKenna, the Scientific Director at MCT, who utilized the funds to support training his technical staff and transfer the technology for cGMP-compliant iPSC manufacturing to the MCT facility. The CTRS team are based at UMN and manage regulatory compliance and clinical patient contact. With their expertise we were able to set up and run a donor screening protocol to identify healthy donors with a preferred haplotype who would be willing to be re-contacted as potential tissue donors to generate iPSCs. We contacted a number of individuals who responded to our on campus advertisements and they were consented and provided a buccal swab for genotyping. The genotyping was carried out at Fairview and the DNA is stored at UMN. We did identify a potential donor from the UMN with the preferred haplotype and the

DNA and contact details from all the responders has started to establish a database of healthy donors at UMN for future projects.

What was the outcome of the project? The project was completely successful in accomplishing our main aim of beginning to develop the necessary infrastructure and support for pluripotent stem cell-derived product manufacturing at UMN. A primary aim was to generate the ability to derive, culture and bank iPSCs at MCT under conditions that can be scrutinized by the FDA. Cells derived from these iPSCs would be delivered to patients. The liaison between the SCI and MCT has been especially successful and as a result of the technology transfer funded by this grant we are currently deriving the first cGMP-compliant, clinical grade iPSCs at UMN (May 2016). This is a critical step in developing the manufacturing expertise and capacity to make pluripotent stem cell products for therapies. We are now developing the infrastructure to transfer the techniques for differentiating the iPSCs into the specific cells required for each disease or injury condition. We have this expertise at the SCI and the infrastructure and expertise being developed with support from the RMM Biobusiness grant will help speed up this next transition. With the establishment of our CTRS team we have also gained the ability to screen and contact potential tissue donors. The experience gained by the CTRS staff regarding potential stem cell therapies and the lines of communication established between SCI, MCT, CTRS and others will be invaluable as we begin to apply for and implement local and Federal permission to generate and utilize stem cell products for the clinic at UMN.

This project has had a major impact in moving this aspect of Regenerative Medicine closer to reality in Minnesota. We now have a pool of identified potential tissue donors and have established the ability to generate clinical grade iPSCs at UMN. This is the first step in making an iPSC-derived clinical therapeutic product in the state. With the infrastructure we have begun to establish as a result of this grant we are now well placed to continue with our success. The next stage will be establishing the support for differentiating the iPSCs into a clinical cell product. We have identified a number of potential products in our therapy pipeline and are working to move the technology to manufacture these cells to MCT. The infrastructure and expertise provided by this grant will provide a critical foundation for these endeavors.

Continued support from the state, RMM, the University and philanthropic donors will be critical in determining the speed of future progress.

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

The aim of this grant was to develop specific expertise and infrastructure at UMN to move the translation of the promise of pluripotent stem cell-derived therapies towards a clinical reality for patients in Minnesota. Our success using this funding to transfer a critical stem cell technology to the UMN cell manufacturing facility now means that we are poised to generate and validate the first iPSC-derived stem cell product in Minnesota. In addition, as we are now deriving and banking cGMP-compliant iPSCs at MCT we are able to emphasize this real translational effort in our current grants and research applications, providing a clear advantage over groups and institutions that do not have this capability.

Responsible Spending:

The funding was disbursed essentially as designated in the budget submitted with the grant proposal. Funds were utilized to partially support salary of the PI and research staff at the Stem Cell Institute and to provide resources for training staff at MCT. Funds were used to purchase research reagents and consumables at both SCI and MCT to support the iPSC technology transfer and the preparation of validation assays. Finally, funds were used to support the work of the CTRS team preparing and running the donor screening IRB protocol and for haplotype testing of the the donors.

A final comprehensive financial report will be provided to Regenerative Medicine Minnesota from the UMN department of the PI (contact dmarney@umn.edu)