Progress Report, Regenerative Medicine Minnesota Grant, 7/18/2016

Original Proposal Title: Quantifying the DNA Damage Response in Clinical Grade Pluripotent Stem Cells; An Efficient, Highly Sensitive Means of Establishing a Quality Control Standard in Large Scale Pluripotent Stem Cell Production

Amount Requested: $99,360.00

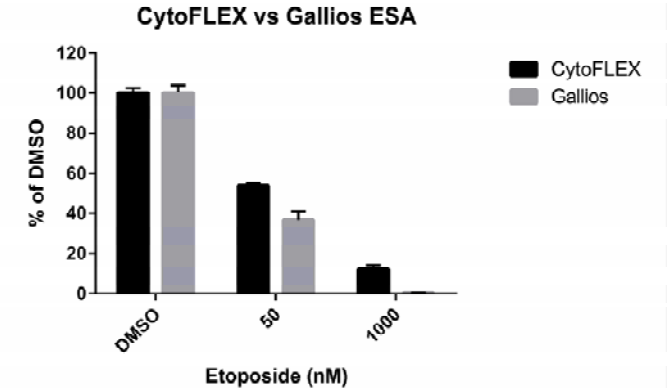
Proposal Description:

Human induced pluripotent stem cells (hiPSC's) hold tremendous potential as a regenerative therapy. However, approval of hiPSC's for clinical use faces significant obstacles, including the ability to quality control the bioengineered cells. We have developed an efficient, cost effective pluripotency assay based upon the sensitivity hiPSC's exhibit to DNA damage. Fully reprogrammed hiPSC's exhibiting an ideal pluripotent ground state will immediately begin to die when treated with etoposide, and the rate of death can be quantified to determine optimal vs. suboptimal cell lines. Initial experiments on over 126 randomly selected hiPSC clones were performed on non-validated equipment to establish the value of this assay. To expand towards clinically oriented applications of hiPSC technology, our etoposide sensitivity assay (ESA) must be completed on a dedicated flow cytometer validated for patient specific applications.

- The original ESA developed in our laboratory has been submitted for publication, as wells as a patentable technology.

The flow cytometer described in this proposal is a necessary tool for the commercial and biobusiness translation of our ESA technology.

- We have established that ESA results obtained on our older FLOW cytometer are similar to those generated using the cytometer purchased (CytoFLEX) using funds obtained from this Regenerative Medicine Minnesota Grant. See figure below;



We believe our ESA will provide the critical platform for establishing quality control standards essential for future production of clinical grade hiPSC's within the Minnesota regenerative medicine community, and ultimately translate hiPSC technology into a clinical reality.

- Toward this goal, we have initiated the patent disclosure process as described above, and additionally, are employing the CytoFLEX in two new studies with Dr. Timothy Nelson's laboratory at Mayo Clinic. One of these studies involves developing a potency assay for an ongoing clinical trial designed around administering autologous cord blood cells to patients afflicted with hypotrophic left heart syndrome (HLHS), while the other aims to produce a diagnostic tool capable of screening for drug sensitivity/toxicity using hiPSC's derived from patients diagnosed with various cardiomyopathies including HLHS. Both studies will depend on ESA results generated by the CytoFLEX cytometer, and will begin by August of 2016. A copy of the submitted manuscript and patent disclosure are attached to this report.