IRB Protocol Development for iPSC Derivation from Patient Blood Samples for the Study of Mitochondrial Optic Neuropathies and Other Neurodegenerative Diseases

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Background/Objective: Abnormal mitochondria have been the primary suspect for Mitochondrial Optic Neuropathies (MONs), such as Leber's hereditary optic neuropathy (LHON), dominant optic atrophy (DOA), and a subset of primary open angle glaucoma (POAG). Mitochondrial abnormalities are not confined to conditions of the eye, but have also been implicated in other neurodegenerative diseases, namely, Parkinson's, Alzheimer's, Huntington's, and ALS. These neurodegenerative diseases affect over 100 million Americans annually, but our knowledge of molecular defects is limited due to the unavailability of patients' neurons. To overcome this challenge, we seek to derive affected neurons for the above diseases using patient derived induced pluripotent stem cells (iPSCs). In this project, we developed a detailed IRB protocol and other documents required to obtain IRB approval for derivation of iPSCs from patient blood samples.

Methods: The protocol developed here is to receive IRB approval to derive iPSCs from patient blood samples (10mL) with the above diseases. iPSC derivation will be performed by isolating CD49f+ Long-Term Hematopoietic Stem Cells (LT-HSCs) from blood and reprogramming LT-HSCs by Sendai Virus Transduction kit (thermo). iPSCs will be characterized for the gene mutations and subsequently differentiated to the disease specific neurons for molecular level analysis. As such, this project required completion of the appropriate IRB documents following a thorough study of relevant literature.

Results: The following documents were prepared for IRB approval: Authorization for the Release of Health Information for Research, Assent to Participate in Research, Informed Consent Statement for Research, Medical and Family History Form, and Protocol for blood draw.

Conclusion & Potential Impact: This effort will permit access to patient blood samples for the derivation of iPSCs and will help us understand neurodegenerative diseases and Mitochondrial Quality Control mechanisms in human neurons for the first time for the development of future mitochondrial-targeted therapy.