What do Muhammad Ali and Michael J. Fox have in common? They are both extraordinary individuals who developed an all-too-common disease and developed it at a particularly tragic early age.

Approximately one to two percent of the population over the age of sixty receives a diagnosis of Parkinson’s disease, although scientists believe that may be a very conservative estimate. At least one million Americans are currently known to be living with the condition, which begins with a slight tremor of the hands and progresses until the patient cannot walk without assistance.

These symptoms are associated with the death of cells in a part of the brain called the substantia nigra, which produces the neurotransmitter dopamine. The cause of the cell death that begins the symptoms of Parkinson’s is unknown, although a combination of genetic and environmental factors is suspected.
New Possibilities

Harvard Stem Cell Institute (HSCI) researchers are making rapid progress in our understanding of Parkinson’s disease.

A Patient Disease Model

HSCI Principal Faculty member and Director of the Neuroregeneration Research Institute at McLean Hospital Ole Isacson, MD, with funding from HSCI, the Harvard Miller Consortium for the Development of Nervous System Therapies, and the National Institutes of Health, has generated brain cells that produce dopamine, collected from the skin cells of patients with Parkinson’s.

Isacson orchestrated the transformation by biologically reprogramming the mature skin cells into induced pluripotent stem cells, and then encouraging the stem cells to become dopaminergic neurons. Neurons were also made from skin cells collected from individuals with genetic mutations associated with high risk for Parkinson’s disease.

The creation of this *in vitro* disease model provides a powerful platform for studying Parkinson’s outside of the body. In the journal *Science Translational Medicine*, Isacson and his team reported that many of the mutations implicated in Parkinson’s affect the function of the mitochondria, the cellular organelle responsible for energy production. In collaboration with HSCI Director of Translational Medicine Lee Rubin, PhD, Isacson’s lab started to identify compounds that could eliminate disease symptoms in cell lines derived from people carrying Parkinson’s mutations.

Repairing the Brain

HSCI scientists are also exploring how to replace the neurons destroyed in Parkinson’s disease and other nervous system disorders. The lab of HSCI Principal Faculty member Paola Arlotta, PhD, is developing new approaches to restore nervous system function by turning one type of already differentiated motor neuron into another. Her work, which is primarily used to study Amyotrophic Lateral Sclerosis (commonly referred to as ALS or Lou Gehrig’s disease), has broad implications for Parkinson’s. Arlotta wants to know how these reprogrammed cells function within the brain and use this understanding to recreate brain cell connections destroyed by ALS and Parkinson’s.

Another facet of Parkinson’s disease is being pursued by HSCI Affiliate Faculty member U. Shivraj Sohur, MD, PhD. He and his colleagues focus on the molecular changes that cause the growth of nerve cells in both development and adulthood. These studies are the first steps to repairing brain regions affected by diseases like Parkinson’s.

HSCI investigators are taking a range of complementary approaches that will aid our understanding of what causes Parkinson’s disease, how it progresses, and how damaged neurons can be replaced. The collaborations made possible by the HSCI network will accelerate the translation of basic Parkinson’s research into clinical treatments for the disease.