Stem Cells Rescue Patients from Mitochondrial Disease

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Neuronal progenitor cells differentiated from somatic

nuclear cell transfer-embryonic stem cells. [Center for

Embryonic Cell & Gene Therapy]

Mitochondrial DNA diseases are a set of mutations that that cause a wide range of fatal or severely debilitating diseases affecting roughly 1:2500 individuals born in the U.S. each year. Mutations that can cause disorders ranging from deafness, eye maladies, and dementia to life-threatening gastrointestinal disorders and heart disease.

Now, researchers from the Center for Embryonic Cell and [Gene Therapy](http://www.genengnews.com/search?q=Gene+Therapy) at Oregon Health & Science University and the Oregon National Primate Research Center have revealed what they believe is the first critical step to developing novel therapies for patients with mitochondrial disease.

"To families with a loved one born with a mitochondrial disease waiting for a cure, today we can say that a cure is on the horizon. Over the past several years, we have been working to generate [stem cells](http://www.genengnews.com/search?q=Stem+Cells) for use in combating disease,” explained senior author Shoukhrat Mitalipov, Ph.D., associate professor at the Oregon Stem Cell Center. “This critical first step toward treating these diseases using gene therapy will put us on the path to curing them and unlike unmatched tissue or organ donations, combined gene and cell therapy will allow us to create the patients' own healthy tissue that will not be rejected by their bodies."

The findings from this study were published online today in Nature through an article entitled “Metabolic rescue in pluripotent cells from patients with mtDNA disease.”

Mitochondria, often called the cell's powerhouse, are small organelles where cellular respiration occurs and the bulk of the cell’s usable energy is created. Uniquely, this organelle contains a circular “plasmid-like” genome, just under 17 kilobases in length. While most of the genes that code for proteins utilized by the mitochondria are contained within the nucleus, there are several key genes that reside within mitochondrial DNA that are critical to normal organellar function.

Mutations within the tiny circular genome are the underlying cause of many heritable diseases and in this study the Oregon scientists used mitochondrial replacement therapy to create an embryonic stem cell with healthy mitochondria from a patient's skin cell containing mitochondrial DNA mutations.

Specifically, the investigators collected skin cells from research subjects with mitochondrial DNA mutations and removed the nucleus from the skin cells. The nucleus is then paired injected into a donor egg cell containing healthy mitochondria. The egg cell is allowed to grow and divide creating a pool of non-mutant mitochondrial stem cells.

"Regenerative technologies offer the prospect of transformative solutions to correct tissue defects in disease. Current care for [mitochondrial diseases](http://www.genengnews.com/search?q=Mitochondrial+Diseases) is limited to addressing patient symptoms, but falls short from providing a definitive cure," said Andre Terzic, M.D., Ph.D., director in the Center for Regenerative Medicine at Mayo Clinic. "Resetting or replacing disease-corrupted mitochondria to produce healthy patient-derived stem cells paves the way towards targeting the root cause of the problem. The present study exemplifies how the synergy of multidisciplinary teams advances the field."

The researchers are looking forward to using this technique, which combines somatic cell nuclear transfer and the creation of pluripotent stem cells, in order to repair diseased tissue. Nuclear transfer is more precise than classic gene therapy techniques, since it uses donated healthy mitochondria rather than inserting synthetic genes into patients delivered by viruses, which often miss the intended target tissue and produce undesirable side-effects.

"Induced pluripotent stem cell and somatic cell nuclear transfer are two complementary cell reprogramming strategies that hold great potential for patient-specific cell replacement therapies," said Jun Wu, Ph.D., senior postdoctoral researcher at the Salk Institute for Biological Studies and co-author on the current study. "Both technologies have been successfully harnessed in our study for eliminating mutant mitochondrial DNAs, offering an important step forward toward therapeutic interventions for patients with mitochondrial diseases."