National Academy of Medicine Supports Replacing Faulty Mitochondrial DNA

By Lila Abassi — February 10, 2016

If it seems that the Americans are always a step behind our British counterparts with respect to stem cell research, it’s because they are.

Last year, the United Kingdom’s House of Commons [2] voted overwhelmingly in favor of fertility treatments using mitochondrial DNA (mtDNA) replacement therapy (MRT), to enable women with heritable diseases caused by faulty mitochondria to have children without disease.

Now, the National Academy of Medicine [3] recently approved conservatively a similar measure by stating that it is ethically permissible to allow MRT studies in women with mitochondrial diseases to determine efficacy and safety, and research into this therapy should proceed under limited conditions. The NAM (formerly known as the Institute of Medicine until last July) is a non-profit, advisory organization which operates outside the sphere of the U.S. government.

Why the hesitation here in the U.S.?

As I recently wrote [4], a great fear of many people with respect to genetically engineering offspring is creating designer babies. Similar [5] to editing the nuclear DNA in embryos which would create changes in the genome that can be inherited by subsequent generations the same would be true for MRT. Mitochondria have their own DNA that is separate from the nucleus but can still be transmitted through generations which qualifies it as germline (cells that pass on their genetic material to subsequent generations) gene therapy.
The US has been fairly conservative about a lot of embryo research and embryo manipulation, said Marcelle Cedars [6], MD, from the University of California, San Francisco. The fear that people will utilize this technique to create smart or athletically superior kids, she feels, is a slippery slope argument and not justifiable the reality is that genetic engineering is not used for this purpose.

The mutation rates [7] in mtDNA are high and prone to damage by oxygen radicals (more than 200 mtDNA mutations have been reported). Additionally, mitochondria are almost solely passed on through maternal inheritance. Sperm, in contrast to the egg it fertilizes, brings along with it a relatively small number of mitochondria, which are either destroyed or diluted with subsequent cell divisions.

Inherited diseases that result from mutations [5] in mtDNA affect between one in 5,000 and one in 10,000 children. They present with severe and diverse clinical symptoms: most often, vital organs are affected that heavily rely on energy production such as the brain, heart, kidney, liver, pancreas and muscle. The type and severity of the illnesses depend on the specific type of mutation and the ratio of mutated mtDNA to healthy mtDNA (aka heteroplasmy).

Depending on which cells are affected, symptoms [8] may include:

- loss of motor control
- muscle weakness and pain
- gastrointestinal disorders and swallowing difficulties
- poor growth
- cardiac disease
- liver disease
- diabetes

Up to 200 diseases are linked to mitochondrial dysfunction. Some of those affected die shortly after birth.

MRT [5] is a promising avenue of treatment that allows for the efficient replacement of mutant mtDNA with normal donor mitochondria in either the pre-fertilization egg, or newly fertilized egg at the one-celled stage (zygote). The procedure also allows for the prospective mother to be genetically related to her offspring. The procedure has been tried and tested clinically using animal models with an established record of safety and efficacy and under these circumstances, ethically acceptable for families to use.

The child born of this method would technically be considered to have a genetic connection to not just the mother and father but the donor as well. However, the total genetic contribution of mtDNA from the donor constitutes only 0.1 percent of the total DNA and has no impact on their hair color, eye color or anything else about the child except fixing an inability to metabolize properly.

It's with considerable anticipation that I monitor the progress of this endeavor. This brings science one step closer to helping cure other genetic diseases and it provides the opportunity to give birth to healthy children in a population of women who did not have that choice before.