PGD can permit the birth of healthy children to women carrying mitochondrial DNA disease

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Pre-implantation genetic diagnosis (PGD) can give women at risk of passing on a mitochondrial DNA disorder to their offspring a good chance of being able to give birth to an unaffected child, a researcher told the annual conference of the European Society of Human Genetics today (Monday). Dr. Debby Hellebrekers, from Maastricht University Medical Centre, Maastricht, The Netherlands, said that the scientists' findings could have a considerable effect on preventing the transmission of mitochondrial diseases.

Mitochondria are cellular organelles involved in the conversion of the energy of food molecules into ATP, the molecule that powers most cellular functions. Disruptions of this energy-producing process, due to a defect in the mitochondrial DNA (mtDNA) or nuclear genes, can cause mitochondrial disorders which represent the most common group of inborn errors of metabolism. The manifestation of mtDNA disorders can be quite varied, but the diseases are almost always serious and, if they do not lead to death, they can result in life-long serious disability for children born with them. Symptoms of mtDNA disorders include loss of muscle co-ordination, visual and hearing problems, poor growth, mental retardation, heart, liver and kidney disease, neurological problems, respiratory disorders and dementia.

Prenatal diagnosis is in general not possible for mtDNA diseases, because the clinical signs cannot be reliably predicted from the mutation

load (the relative amount of mutated mtDNA molecules) in chorionic villus sampling, so the team of scientists from The Netherlands, Australia, and the UK decided to look at whether PGD would be a better alternative. "If we could find a minimal level of mtDNA mutation load below which the chance for an embryo of being affected was acceptably low", said Dr. Hellebrekers, "we could offer PGD to women who otherwise had little chance of giving birth to a healthy child."

The researchers studied data on 159 different disease-causing mtDNA mutations derived from 327 unrelated patients or families. They combined data on muscle mutant levels – which correlate best with prenatal tissues - of affected individuals and relatives on their mothers' side who were not affected., and were able to predict that a 95% or greater chance of being unaffected was linked to a mtDNA mutant level of 18% or less.

Mitochondria have their own DNA, which is strictly inherited from the mother. Normal and mutant DNA co-exist in most disease-causing mtDNA mutations, and there is a threshold of mutant mtDNA which must be exceeded before clinical symptoms occur. The mtDNA mutation level inherited by the offspring of a female mutation carrier can vary greatly, and even in twin births, it is possible for one baby to receive considerably more of the mutant mtDNA molecules than the other.

"Being able to find the minimal level of mutant mtDNA below which the chances of passing on a disorder is low was therefore very important", said Dr. Hellebrekers. Currently, there are no effective treatments for mtDNA disorders. Although we cannot guarantee that a mutant mtDNA level of 18% or lower will result in the birth of an unaffected child, we think that the chances of having a healthy child are high enough to make using PGD in this instance morally acceptable.

"Our research enables us to give genetic counselling to women at risk with respect to their reproductive choices and to provide them, for the first time, with the opportunity to give birth to a healthy baby. The prevalence of mtDNA disorders is 1 in 5,000, which means that the families of about 146,000 patients in Europe can now have the option of having a healthy child. This is a choice that they do not currently have", she concluded.

Provided by European Society of Human Genetics

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