

## 3-Parent babies

In vitro fertilization with a third party involving Mitochondrial Donation

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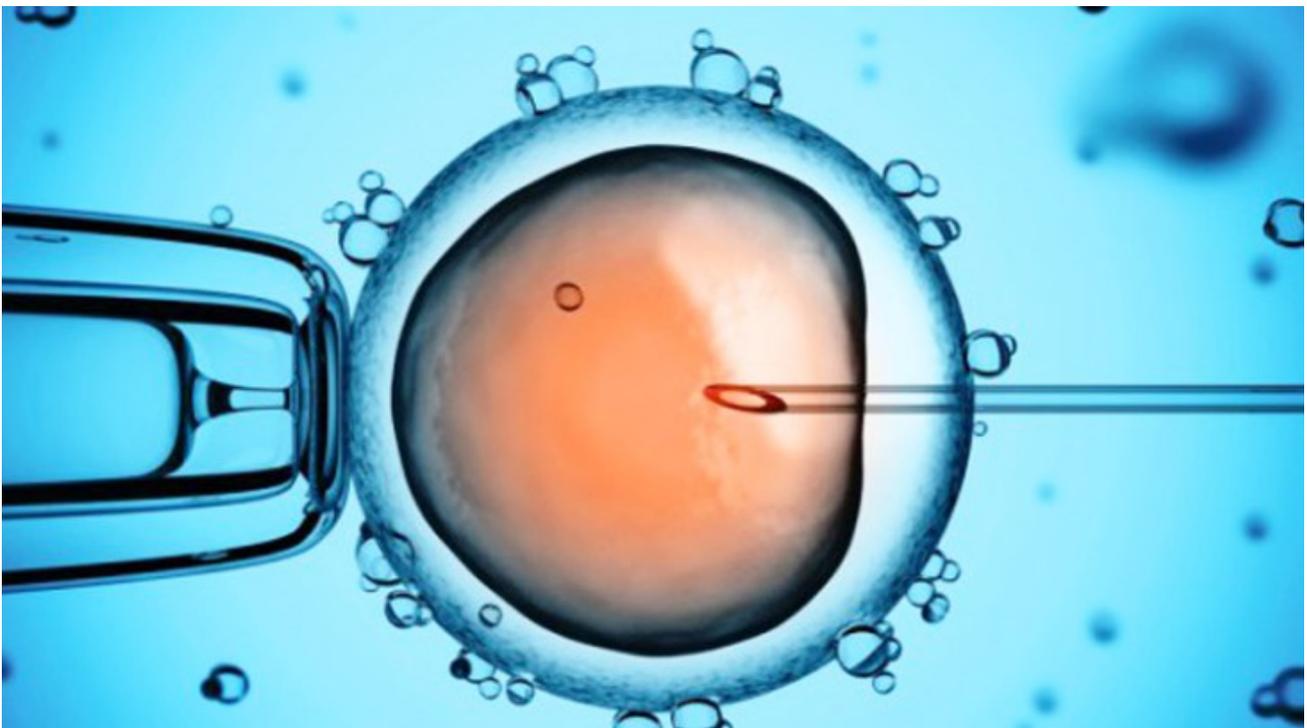


Image 1

GYMNASIUM KIRSCHGARTEN, BIOLOGY TERM PAPER

Class 4e bZ

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## 1. Preface

1 out of 4,000 people in the world is a carrier of the so called mitochondrial disease. Many of them do not even know that they are infected. The symptoms can vary from person to person. And only the female can pass on the disease to their children. Mitochondrial Donation is a new technique to give women with the disease the chance to have genetically related children with healthy mitochondria. This is our topic.

We chose the topic of “3-Parent babies” because we spoke about it in school. It is a rather new topic and here in Switzerland not many people know about it. We are really interested in the ethical aspects or if it ever will be legal in Switzerland. We are fascinated of the technical procedures with the DNA because of its very small size. But especially interesting is the fact that it is new and what the chances will be in future.

The following quotations show that there are people against and people for Mitochondrial Donation:

“This is very good news for patients with mitochondrial DNA disease and an important step in the prevention of transmission of serious mitochondrial disease.”

- **Prof Doug Turnbull**, Professor of Neurology, Newcastle University

“Even if these babies are born they will have to be monitored all their lives, and their children will have to be as well.”

- **Dr Trevor Stammers**, Programme Director in Bioethics and Medical Law at St. Mary's University, Twickenham

But what are the disadvantages and advantages really? This and the following questions will be answered in this paper.

How does this new technique work? How do the doctors exchange the mitochondria? What will be the consequences in the future and is it ethically acceptable?

## 2. Introduction

### 2.1 Mitochondrial diseases

Our chosen topic "3-Parent babies" is about an in vitro fertilization (IVF) procedure for women who have to deal with mitochondrial diseases.

The mitochondria are the so-called powerhouses of our bodies. They are cell organelles and their most important function is to generate energy through cellular respiration, which is needed for metabolism. The mitochondrial DNA, also known as mDNA, is the DNA inside the mitochondrion and only maternally inheritable. If more than 60 % of the mitochondria are dysfunctional the individual suffers from the disease. The dysfunctional mitochondria will not produce enough energy for the cell. As there exist different forms of the disease it can cause damage in brain, liver, kidney and other organs, as well as cognitive disabilities such as loss of muscle coordination, vision or/and hearing and learning disabilities. Until now there is no cure for people with this disease. Therefore, all women who have mitochondrial diseases are not able to have children without passing on their genetic condition.

### 2.2 Mitochondrial Donation

The Mitochondrial Donation is a new and special form of in vitro fertilization, where the baby has the DNA of its father and its mother who suffers from mitochondrial disease, as well as the DNA of a second woman who donates her healthy mDNA. Summarized, the baby is "created" from three people, which leads to the common name of the procedure: "3-Parent baby". The treatment is used to give women with mitochondrial diseases the chance to give birth to a genetically related child. The donor has no legitimate claim for the baby.

It is a very new procedure and in October 2015 the United Kingdom has legalized it as the first and only country in the world. Many other countries are sceptical towards it, because it is ethically questionable and due to religious aspects. In Switzerland this topic is quite unknown and only discussed among experts.

Around 1997 there was a similar in vitro fertilization introduced which was about cytoplasmic transfer. A third person donated her healthy cytoplasm and 17 babies were created that way in the United States. Alana Saarinen and Emma Ott are two of those children, now living a healthy life. One of them has been tested and only the mDNA of the donor was found. On the other hand there are still children carrying the mDNA of the donor and the mother therefore still passes on the disease to the next generation.

After the acceptance of the treatment with Mitochondrial Donation in the UK in March 2015 and the legalization of it in October the recent news are that the first "3-Parent babies" should be born in 2016.

In February 2016 an expert panel from the United States advised the United Kingdom to only create boys with the help of Mitochondrial Donation for the moment. Their explanation for this advice was to prevent the disease from being passed on to the next generations in case the mitochondrial transfer did not work out properly.

“Because men don't pass down mitochondrial DNA to their children, this would stop modified mitochondrial DNA from being passed down through generations. This restriction differs substantially from last year's UK approval because lawmakers there included no restrictions on the sex of embryos.”

- **Arielle Duhaim-Ross**, science reporter at The Verge, USA, explains the panels statement

Alternative options and treatments are adoption or in vitro fertilization with a donor egg. In both cases the mother and in case of adoption the father as well are not blood-related to the child. On the other hand prenatal diagnosis would give the possibility to abort, if the unborn child is diagnosed with the mitochondrial disease.

### 3. Description of engineering technique

Before the procedure with the Mitochondrial Donation can start you have to remove the needed eggs out of the mother's and the donor's womb. This happens under ultrasound and with a thin needle. Through this thin needle the eggs are aspirated with follicular fluid. In the lab the follicular fluid is separated from the eggs and after that there are two different techniques.

#### a) Embryo repair / Pronuclear Transfer (PNT)

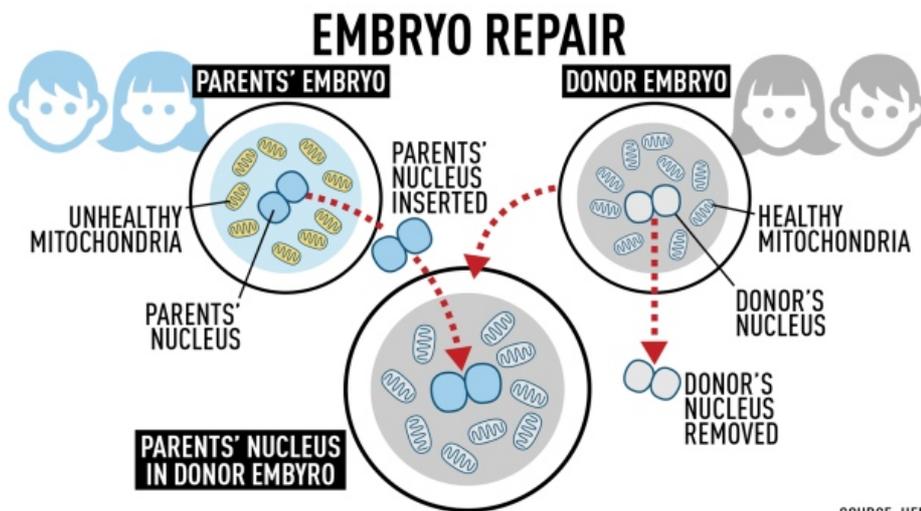


Image 2

In this procedure the eggs of the mother and the donor are fertilized with the sperm, thus two embryos are created. The next step is to separate the mDNA and the nDNA, the nuclear DNA, in both embryos. The nDNA of the parents is inserted into the healthy embryo of the donor with its mDNA, as you can see on the last step of the image above. Afterwards the "repaired" embryo is put into the womb of the mother.

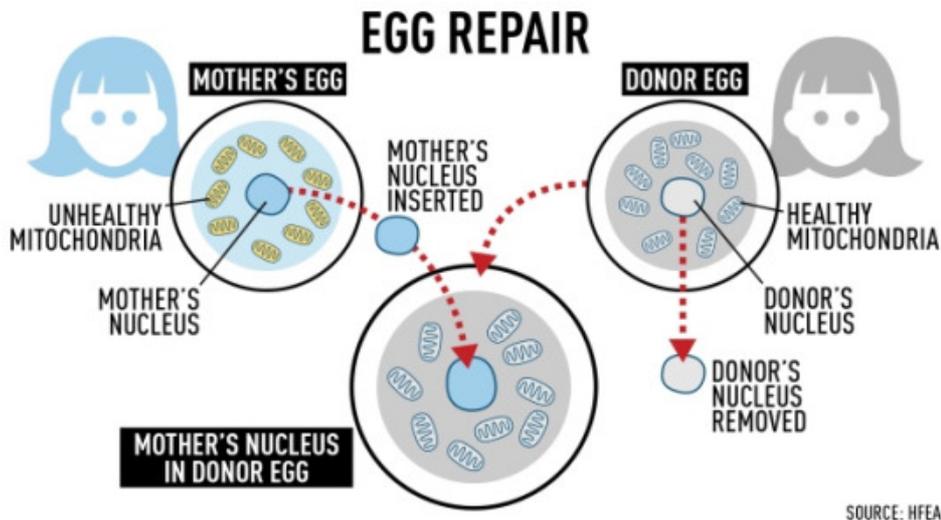
**b) Egg repair / Maternal Spindle Transfer (MST)**

Image 3

In this procedure the first step is to take the nDNA of the mother and the donor out of their eggs. Then the nDNA of the mother is inserted into the healthy mitochondria containing egg of the donor, as you can see on the last step of the image above. After that the “repaired” egg can be fertilized with the sperm of the father and finally implanted into the womb of the mother.

Both techniques are very similar: in one the fertilization happens before the mitochondria are transferred and in the other after the transfer.

## 4. Documentation

### 4.1 Interview partner

Our interview partner was Prof Dr med Christian De Geyter. He is the head physician in the section of gynaecologic endocrinology at the University Hospital of Basel. He is one of the leaders of a project in Basel that will be explained in the following interview. Right now he is searching for sponsors for the project. The interview took place on the 26<sup>th</sup> of April in the University Hospital and was conducted in German.

We asked if he could give us the opportunity to make photos of a labour or the instruments but unfortunately this was not possible.

### 4.2 Interview

**1. Wieso heisst es "3-Parent babies"?**

Da es das genetische Material des Vaters, der Mutter und das genetische Material einer Spenderin enthält. Jedoch ist das Verhältnis der DNAs nicht gleich. Das Kind erhält lediglich 0.1% DNA der Spenderin.

**2. Kamen sie beruflich schon in Kontakt mit dem Thema "3-Parent babies"?  
Wenn ja, auf welchen Wegen?**

Ja, öfters wird in Gremien darüber diskutiert. Und ja, eine Patientin gab es, jedoch war sie nicht behandelbar und sowieso ist es in der Schweiz illegal.

**3. Was sind Ihre Ansichten zum Thema?**

England übernahm mit der Legalisierung die Vorreiterrolle. Jedoch gibt es andere Lösungen. Momentan ist ein Projekt in Basel in der Vorbereitung, welches versucht durch die wenigen gesunden Mitochondrien der Mutter ein Kind zu zeugen, welches auch gesunde Mitochondrien hat. Für dieses Projekt werden momentan Sponsoren gesucht, da das Projekt über fünf Jahre Forschungszeit ca. fünf Millionen Franken kosten wird.

**4. Wie funktioniert das ganze Verfahren?**

Im ersten Schritt werden der Mutter mit einer mitochondrialen Erkrankung und der Eizellenspenderin die Eizellen entnommen und die nDNA vom Rest getrennt. Im Weiteren wird die nDNA der Mutter mit der Eizelle und den enthaltenen gesunden Mitochondrien der Spenderin zusammengefügt. In einem letzten Schritt wird diese Eizelle mit dem Sperma der Vaters befruchtet.

**5. Wie viel kostet ein Versuch? Und wie lange dauert es?**

Eine Behandlung dauert etwa gleich lang, wie eine „normale“ künstliche Befruchtung, also ca. 6 Wochen. Die Kosten betragen rund 12'000 CHF.

**6. Ist die Behandlung sinnvoll?**

Ob es sinnvoll ist, ist fraglich. Jedoch sind andere Optionen wie z.B. Adoptionen durch bürokratische Verfahren im Gegensatz zu vor zwanzig Jahren

verkompliziert worden. Und auch Adoptionen können ethisch verwerflich sein, da Kinder verkauft werden.

**7. Was sind die Folgen und Auswirkungen für Patienten mit Fehlfunktionen von Mitochondrien (Mitochondriopathie)?**

Diese können variieren. Meist zeigt es sich in Form von Organversagen oder Schädigungen an den Nerven. Jedoch gibt es auch Fälle, in denen keine Symptome auftreten und die Erkrankung nicht diagnostiziert wird.

**8. Wie stark beschäftigt sich die Schweiz mit dem Thema momentan?**

Dieses Thema beschäftigt so gut wie niemanden in der Schweiz. Nur in spezifischen Fachkreisen wird teilweise diskutiert, aber die ethische Einstellung der Schweizer Bevölkerung ist noch nicht bereit für derartige Eingriffe in die Natur. Aus diesem Grund wird auch nach alternativen Lösungen geforscht.

**9. Denken Sie, dass die Methode der mitochondrialen Spende in absehbarer Zeit in der Schweiz legalisiert wird? Wieso?**

Nein, vermutlich wird auch in den nächsten 20 Jahren dieses Verfahren in der Schweiz nicht legalisiert werden. Die Schweiz profitiert oft von den Erfahrungen der anderen Länder, so auch bei diesem Thema. Wenn das Projekt in Basel durch einen Geldgeber ermöglicht wird, könnte es aber in den nächsten zehn Jahren eine Methode geben, ohne Involvierung einer Drittperson.

**10. Was sind die Folgen für "3-Parents babies" und die Gesellschaft?**

Die Folgen für die Kinder sind noch nicht absehbar und die Gesellschaft ist noch nicht bereit für dieses Thema wegen den religiösen und ethischen Einstellungen.

**11. Was ist der Standpunkt der Gesellschaft in verschiedenen Ländern?**

Grossbritannien ist ein sehr progressives Land, die Schweiz das Gegenteil. Generell ist die Weltbevölkerung aber noch nicht bereit für dieses Thema.

**12. Ist England gegenüber anderen Ländern im gesellschaftlichen/medizinischen Bereich voraus?**

Ja, da England sehr progressiv ist und offener gegenüber neuen Verfahren.

**13. Gibt es noch andere Behandlungsmöglichkeiten?**

Momentan noch nicht. Jedoch würde das Projekt in Basel in diese Richtung arbeiten.

**14. Ist eine Behandlungsmethode gegen Mitochondriopathie in Entwicklung?**

Ja, das Projekt in Basel hat sich genau dies zum Ziel gesetzt.

**15. Ist das Verfahren ethisch vertretbar?**

Inwiefern das Verfahren ethisch vertretbar ist, ist Ansichtssache, da die 0.1% Abweichung des genetischen Materials durch den Mitochondrientausch kaum Auswirkungen hat auf das Kind.

### 4.3 Summary of the interview

The following is a summary of the interview because we did it in German.

The topic is called “3-Parent babies” because the children who are born throughout this method have the DNA of three people: the father’s, the mother’s and the donor’s. Prof. Dr. med. Christian De Geyter once had a patient with a mitochondrial disease but she was not treatable.

The procedure of Mitochondrial Donation goes as follows: The eggs of the mother and the donor are taken out and the nDNA is separated from the rest. Then the nDNA of the mother is introduced in the donor’s egg containing the healthy mitochondria. This egg is then fertilized. (This refers to the egg repair method; remark of the authors)

There are different opinions whether Mitochondrial Donation is meaningful or not. The costs do not differ from those of a normal in vitro fertilization, which are around 12,000 CHF. The procedure’s duration is about six weeks. In Switzerland the topic is not really discussed yet. Only scientists and doctors talk about it in special committees. The reason for this is that the society is not yet ready for such a change in fertilization methods and gene manipulation. That is why Dr. De Geyter thinks the technique will not be legalized in the next 20 years in Switzerland. This is due to its conservative attitude compared to England, which is a very open-minded and progressive country according to De Geyter. Therefore a group of specialists, including himself, is working on a method in which the few healthy mitochondria of the mother are being used to conceive a healthy child. The difficulty right now is the huge amount of money needed for the research, which is around five million Swiss francs. Therefore the specialists are looking for sponsors.

The opinions about ethical aspects of the topic are very subjective. Nevertheless Dr. De Geyter says that there is hardly any consequence for the child due to the very small difference of the DNA.

## 5. Discussion

The scientists are not in agreement about whether the advantages outweigh the disadvantages or not.

Last year the United Kingdom legalized the procedure for tests on humans. Before the legalization it was only tested in the lab and on animals. But the development of a human embryo and an animal embryo is different. So only because it works on animals does not say that it will work for humans. The first children who have been fertilized with the help of the Mitochondrial Donation are born this year in the United Kingdom. But no one knows what the consequences for the children of the next generation will be. Whether it will be possible to cure the mitochondrial disease or to find another method to fertilize an egg with healthy mitochondria is also not clear.

The whole topic has many Pros and Cons as mentioned above. The most important and often mentioned Cons are the ethical aspects. Is the technique ethically correct? The critics say it is too far across the ethical boundaries. It could be the start of the human gene modification that leads to “designer-babies”. And this is a big intervention in nature.

The Human Genetic Alert, an independent public interest watchdog group, the Roman Catholic Church of England and Wales think that it is ethically not acceptable and that the decision to legalize it in the United Kingdom is too hastily. The methods had only been tested in labs and on animals before it was legalized. Right now it is not easy to get the chance of a Mitochondrial Donation because it is only in a test phase. After the first applications everything will clarify the medical situation of the women as well as social consequences for both parents and children. But after gaining all this information it is still not clear to researchers whether it is really safe for humans. Critics say that serious problems can potentially arise and affect the personal traits as well as the metabolism in unforeseen ways. It could have a lot of influence on how the genes work like switching genes on and off or even change them permanently. Even a “carry-over” would be possible. This means that if the mDNA is not purely separated from the nDNA it could transport a part of the sick mDNA and pass on the mitochondrial disease to the child. The supporters of the technique say that the chance of a carry-over is so small that it is no risk for the mother or the child. And every medical technique is bound to some risks.

The ethical part of the discussion is mostly based on the question: Is this the start for designer babies or not? An advantage of the procedure is that you can exchange an unhealthy part of the DNA with a healthy donor DNA but the critics are afraid of the consequences. Designer babies are one possible consequence. The parents could select how their children should look and be like. This would lead to a completely new way of in vitro fertilization. In ethical ways this is a huge intervention in nature. For devout religious people this is not acceptable because it changes God’s will. There is an unwritten law among experts which states that it is not allowed to change the DNA of humans.

## 6. Summary

Mitochondrial Donation is a new method of in vitro fertilization for women suffering from mitochondrial diseases. The concept of the procedure is to create a baby with the help of a third party who donates its healthy mitochondria. The UK is the only country that legalized it. Some other countries such as the United States are discussing it critically. Most other countries are not ready for the idea of creating a child from three people. That is because of the ethical and religious aspects the procedure brings up. On the one side it helps people that suffer from a disease like this to have a blood-related child, but on the other hand it is a manipulation of nature and the baby can be seen as a “designer-baby”.

As from our side, we are fascinated with the medical techniques our time has come to. The fact that it might be possible to create a child without the genetic dysfunction its mother has is incredible and shocking at the same time. We believe that this controversial procedure is worth discussing but should not be rushed over because the ethical aspects are important to look at. If we start of preventing the next generation from diseases, we might later on even be able to prevent an allergy for example, which would lead more to interfering in nature.

We thank Prof. Dr. med. Christian De Geyter who answered all our questions. He provided us a good insight into the topic of “3-Parent babies” and Mitochondrial Donation.

## 7. Sources

Most of our knowledge we got from the interview with Prof. Dr. Med. Christian De Geyter, which we conducted on the 26.4.2016.

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Last check of all sources: 2.5.2016

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