Embryotools successfully concludes the first trials on an innovative assisted reproduction technique

- The technique, called Maternal Spindle Transfer, is an assisted reproduction therapy—commonly known as a ‘three parent baby’ technique—that leading scientists from around the world are studying to prevent the transmission of mitochondrial diseases.

- Embryotools, headquartered in Barcelona Science Park (PCB), has spent more than three years working on this project, in partnership with the PRBB PCB Animal Facility Alliance and the company Reprogenetics UK, located at Oxford University, a world leader in molecular genetic analysis.

- The results of the study showed not only the efficacy of the new technique in preventing the transmission of mitochondrial diseases, but also in solving infertility problems, since the potential of embryonic development in the in vivo trials significantly increased (10 times more).

- Embryotools will present the results at the next meeting of the American Society for Reproductive Medicine, which is taking place from 28 October to 1 November in San Antonio, Texas (United States). The work has been selected for the “Prize Paper Award” and will compete with 12 finalists.

Barcelona, 27 October 2017. Embryotools—headquartered at Barcelona Science Park (PCB)— has successfully concluded tests on animal models to validate an innovative assisted reproduction technique known as Maternal Spindle Transfer (MST).

This new technique is a mitochondrial replacement therapy which groups of leading scientists from around the world are studying for the prevention of mitochondrial diseases, which are transmitted maternally and currently have no treatment.

Mitochondria are found distributed all over the cytoplasm, the region between the nucleus and the cellular membrane. The technique used by Embryotools consists of extracting the nucleus from the egg of the patient carrying mutations in the mitochondrial DNA and introducing it into the egg of a donor with healthy mitochondria, from whom the original nucleus has previously been extracted. This new reconstituted egg, once inseminated in vitro with sperm cells from the patient’s partner, would result in a healthy child, genetically related to its biological mother and father.

Two... or three parents?

Maternal Spindle Transfer uses gametes from three people—two women and one male—which is why it belongs to the group of therapies commonly known as ‘three parent baby’ techniques, a term which, according to Dr Nuno Costa-Borges, scientific director of Embryotools, does not please the scientific community: “Although gametes are needed from one man and two different women (the patient and the donor), the nuclear or genomic DNA, responsible for the vast majority of phenotypical characteristics of the future baby, would come from the biological mother and father, as
in a normal fertilisation process. The donor would only contribute the mitochondrial DNA, which codifies just 37 genes and represents less than 1% of the human DNA. This mitochondrial DNA from the donor would not be transmitted to the following generations if the resulting baby were male, which is why it is not considered to affect the germinal line”.

Preventing mitochondrial diseases

Mitochondria are cellular organelles that can be found distributed throughout the cytoplasm, and their main function is to produce the required energy that cells need for their various functions. Mutations in the mitochondrial DNA are frequent and are associated with a wide range of diseases that mainly affect the organs and tissues of high metabolic or energetic activity.

This Maternal Spindle Transfer technique replaces the mitochondria of the future mother carrying mutations in her mitochondrial DNA, before the egg is fertilised.

“It is estimated that 1 in 200 people carry some type of mitochondrial mutation, although the incidence in the population of related pathologies is 1 in every 6,500. These diseases present very heterogenous clinical manifestations, the majority of which are serious, such as severe neurodegenerative disorders, muscular and cardiac failures, dementia, apoplexy, blindness, Leigh syndrome, deafness, Leber hereditary optic neuropathy or premature death, among others”, explains Dr Gloria Calderón, director and co-founder of Embryotools.

A promising breakthrough also in infertility cases

Embryotools has been working on this project for over three years in partnership with the PCB-PRBB Animal Facility Alliance—headquartered in Barcelona Science Park—and the company Reprogenetics UK—located at Oxford University—a world leader in molecular genetic analysis.

Although the study’s initial objective was to evaluate the efficacy of the new MST technique to prevent the transmission of mitochondrial diseases, this international team of investigators discovered that it could also be successfully used to solve infertility problems.

“Over the course of the project it was verified that when we applied the technique, the potential of embryonic development, that is to say, the reproductive capacity of a strain of mice with very poor reproductive output, increased enormously (10 times more)”, explains Dr Nuno Costa-Borges. “It is further evidence of the important role of the cytoplasm of the egg, where mitochondria and other cellular organelles and molecular factors are located, which we have seen are decisive in embryonic development”, he adds.

According to Jesús González, veterinarian supervisor in animal welfare and head of Services and Projects of the PCB-PRBB Animal Facility Alliance, “We have developed a very extensive study to verify and demonstrate the safety of the technique. The mice generated show to be perfectly normal and fertile. Furthermore, their offspring was duly assessed through various generations, without any alteration in behaviour or health being observed”.

Currently, many cases of sterility are attributed to problems in embryonic development caused by the poor quality of the eggs, which are usually resolved through conventional egg donation.

“By replacing the cytoplasm of a poor quality egg with the cytoplasm of a higher quality egg using the MST technique, we could resolve many of those cases of infertility without needing to resort to full egg donation, since this technique would only use the cytoplasm of the donor’s egg. This is a very important aspect for both the patient and donors”, explains Dr Costa-Borges.

The technique developed by Embryotools opens up a promising area of research in the field of assisted reproduction to also help women with fertility disorders, who wish to have children who are genetically related to them.
“Spain is the frontrunner in assisted reproduction treatments and, each year, patients from all over the world come to our country to be treated with donor eggs. Egg donation works very well, is totally anonymous, and allows us to treat many patients, but it has a limitation in that the patient’s genetic characteristics are not transferred to the future baby”, explains Dr Calderón.

The project (Ref. RD 15-1-0011) was co-funded by the European Regional Development Fund, within the framework of the FEDER Operative Programme of Catalunya 2014-2020 and following the call by the Generalitat de Catalunya “Nuclis de Recerca Industrial i Desenvolupament Experimental d’ACCIÓ”.

Embryotools will present the results at the next meeting of the American Society for Reproductive Medicine, 2017 ASRM Scientific Congress & Expo, which is taking place from 28 October to 1 November in San Antonio, Texas (United States). The work has been selected for the “Prize Paper Award” and will compete with 12 finalists.

An experimental technique and controversial birth

On 16 December 2016, the Human Fertilisation and Embryology Authority (HFEA) approved the use of donation or mitochondrial replacement techniques for specific cases in which the heredity of the disease may cause death or serious pathologies.

Although the United Kingdom was the first country to give the green light to the clinical use of these techniques, the first baby in the world conceived through the Maternal Spindle Transfer technique was born in Mexico in 2016. The event caused enormous controversy because the procedure was carried out by the team at the New Hope Fertility clinic in New York in an isolated and experimental manner, without approval from the United States authorities. “The embryos were created in New York and sent to Mexico, where the transfer to the patient was performed taking advantage of the lack of legislation for this type of technique in this country”, explains Dr Calderón.

In Spain, the Assisted Reproduction Law does not prohibit a specific technique, but it establishes the authorised practices in an annex and also requires special permission for other techniques not provided for.

“Maternal Spindle Transfer has enormous potential. However, even though a baby has already been born through this technique, it is still an experimental procedure. Investigations need to be continued with care and without rushing in order to complete all the necessary steps that demonstrate that it is a safe technique”, warns Dr Calderón.

About Embryotools

With over 30 years of experience in clinical embryology and human and animal assisted reproduction, Embryotools is a leading centre in this field. It was founded by two scientists: Gloria Calderón and Nuno Costa-Borges, both embryologists, motivated by innovation and excellence, and they are passionate about continuous improvement of assisted reproduction techniques. In 1984, Dr Calderón formed part of the team that achieved the first pregnancy by in vitro fertilisation in Spain, and in 2009 Dr Costa-Borges successfully achieved the first cloned animals in Spain.

Today, Embryotools offers the most complete and advanced Quality Control Services to test all types of materials, culture mediums or products used in IVF laboratories; a Training Centre for sharing their experience and knowledge with professionals looking for theoretic and technical excellence; independent Scientific and Clinical Advice and Consultancy Services, aimed at reproduction centres looking to optimise results by implementing better practices and protocols, as well as at manufacturers who intend to develop and optimise new products for in vitro fertilisation, and the Animal Reproduction Centre, where the most innovative techniques are applied to improve the reproductive outputs of elite animals.

More information: Azucena Berea • Head of Press • Barcelona Scientific Park • Tel. +34 93 403 46 62 • aberea@pcb.ub.cat