Patient Information
Investigating Human Blastocyst Embryos in Vitro R0193

Background

Only about 30-40% of human embryos transferred to the womb develop into full term babies. A high proportion of natural abortions occur as a result of developmental failure as the embryo implants into womb. To avoid such failures in the IVF clinic, it would be helpful to know what an embryo has to achieve while it is developing in vitro to the point at which it would normally be placed in the mother. Further, we have very little knowledge about the structure of the embryo as it implants in the womb, and how the cells move and interact during this vital period. The more we can learn about embryo development during this period of a few days will help us understand the normal developmental patterns of early embryonic growth, and also how we may learn about the problems associated with early miscarriage.

How will the work be carried out?

We shall grow human embryos in a new culture system that permits correct development up to day 13 of development[1]. This will allow us to analyse the developmental processes that remodel the human embryo during the early stages of post-implantation development. This period is associated with high rates of pregnancy loss. Our goal is to understand the basic mechanisms of development to shed light on the reasons underlying miscarriage.

To achieve this goal, we will analyse the transformations of both the embryonic tissue that will form the future foetus, and the extra-embryonic tissues, which will form the future placenta and the yolk sac. Culture conditions may be varied by adding specific compounds to understand their effect in terms of embryo development. Development of the embryos may also be recorded by highly specialized time-lapse microscopy according to established protocol.

To assess whether correct development has taken place in culture we will utilize different technologies. We will use chemical technology to reveal markers of specific embryonic or extra-embryonic cells to establish their presence, and also markers for specific genes that we know appear at precise times of development. We will also analyse embryos by applying single cell sequencing technologies, which allow us to obtain a detailed map of all the genes expressed in every single cell of the embryo.

We shall also establish stable stem cell lines from embryos. This will be carried out from the embryonic epiblast and the two extraembryonic lineages that will form the future placenta and yolk sac. Our objective will be to generate cellular models to study placenta and yolk sac formation as well as a model to study embryonic epiblast development in vitro. To derive stem cells, an embryo is separated into its individual cells or groups of cells. The embryo itself is no longer intact and does not retain the ability to develop further as an embryo. The separated cells can be cultured in the laboratory indefinitely. Any stem cells lines derived in this research project will be deposited in the UK Stem Cell Bank. They may be made available to other research groups nationally and internationally to minimize the number of embryos used for research. It will not be possible for you to control any future use of the embryonic cells, or any derived stem cells/stem cell derived product. The stem cells, or any discoveries made using them, could potentially be patented and used for commercial purposes. In this case you will not have any financial benefits.

How will this help me?

The research we do will not help you specifically, and we are unable to provide any information on any particular embryo. The collective information will be studied scientifically, and the information gained published in the appropriate medical and scientific journals. You will not receive any financial benefits arising from patents or commercial use of any embryo/stem cell derived lines or products.

Where will this work be performed?

These studies will be done in collaboration with researchers at the University of Cambridge, in the Department of Physiology, Development and Neuroscience (PDN), under a research licence issued by the Human Fertilisation and Embryology Authority (HFEA) and overseen by the University of Cambridge Human Biology Research Committee (HBREC).

The scientists involved in the research may have access to identifiable information, which cannot be erased before providing the researchers with the straws containing the frozen embryos. The identifying information will however be discarded with the straws after the embryos are thawed and will not be used by the researchers.

Will my taking part in this study be kept confidential?

Yes. The proposed research includes careful procedures to protect your identity. The research is done under a license from the Human Fertilisation and Embryology Authority (HFEA) and with approval of Local Research Ethics Committees and the Human Biology Research Ethics Committee. These organisations impose strict requirements about maintaining your confidentiality. The embryos will be coded and your identity and participation in the research will be kept strictly anonymous. This code will allow researchers to access clinical data on your embryos (i.e. parameters of embryo quality), as this information is potentially relevant for the research studies. The information identifying your embryos will be visible to a member of the research team when he or she verifies that consent for the research has been obtained, but your identity will not be recorded by them. If stem cells are generated in the research, a sample of these will be deposited with the UK Stem Cell Bank. In this case only, it will be necessary for your treatment clinic to provide a copy of your consent form in confidence to the Secretary of the UK Stem Cell Steering Committee. Your identity will not be disclosed to the staff of the UK Stem Cell Bank or to anyone else.

Who is paying for this research?

The research is funded by the Wellcome Trust. The researchers and the University of Cambridge may receive financial benefits arising from patents based on the research of the embryos or embryo derived stem cell lines. For more information on the Department of PDN or the Zernicka-Goetz laboratory, please visit:
https://www.pdn.cam.ac.uk/ and https://www.mzglab.com/human-research/

Important Regulatory Aspects

Counselling is available to you should you wish to discuss your decision to donate your embryos to scientific research. Please contact the Centre should you wish to access this service. If you have consented to the use of your embryos in the research project you can still withdraw your consent to research at any time up to when the embryos are used in the research project. If you choose to do this, it will have no effect on you or your treatment if that is still on-going. If you wish to withdraw your consent, please

email alison.campbell@carefertility.com, or contact the unit at which you were treated and ask to communicate with the Laboratory Manager.

Your decision on whether or not to donate to the research project will have no influence on your on-going fertility treatment, as only embryos considered unsuitable for use in treatment, or excess to treatment requirements, will be used in the research project. As explained in the Consent Form, this does mean you will not be able to gain any information relating to your particular embryo.

At the end of the research all embryos will be allowed to perish.

Please note that we encourage you to ask any questions that are on your mind at the time of signing the Consent Form or anytime thereafter. If you have any later questions, you should contact the Laboratory Manager at the CARE clinic at which you had your treatment.

1. Shahbazi, M.N., *et al.* Self-organization of the human embryo in the absence of maternal tissues. *Nat Cell Biol* **18**, 700-708 (2016).