

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 the 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 culture system that has been developed for mouse embryos¹ that permits correct development of the mouse cells that form the embryo proper, and of the flanking cells that eventually develop into associated placental tissue, through the implantation stages; events which are normally hidden from view. This will allow us to observe the developmental process at these stages in human embryos for the first time. Development of the mouse embryo through these stages requires that the embryonic cells become arranged like the petals of a flower in the centre of which the amniotic cavity will form. This rosette then develops into the foundation for the entire body. We wish to determine whether similar events take place in the initial development of human embryos and how morphogenesis (the shapes of cells over time) then differs so that the foundations of the body acquire the characteristic shape appropriate for each species.

The approach to undertaking this will first determine whether the culture medium developed for the culture of mouse embryos through the implantation stages will permit the development of human embryos over the similar period. Development of the embryos will be recorded by highly specialized time-lapse microscopy according to established protocol. Culture conditions may be varied to permit the development to give structures resembling the human embryo at the designated time.

To assess whether correct development has taken place in culture we will also use chemical technology to reveal markers of specialized cells (epiblast, visceral endoderm; extra-embryonic tissues) to establish their presence, and also markers for specific genes that we know appear in specialized cells at precise times of development.

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

¹ Self-Organizing Properties of Mouse Pluripotent Cells Initiate Morphogenesis upon Implantation. Cell (2014), <http://dx.doi.org/10.1016/j.cell.2014.01.023>

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scientifically and the information gained published in the appropriate medical and scientific journals.

Where will this work be performed?

These studies will be done in collaboration with researchers at the University of Cambridge, under a research licence issued by the Human Fertilisation and Embryology Authority (HFEA).

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.

Important Regulatory Aspects

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.

The funding for this research is in part from Grant funding to the Gurdon Institute collaborators, and funding from the CARE Fertility Group and its Rachel Foundation. No financial benefits will accrue from this research, but we hope to increase knowledge and understanding of the development of the embryo around this crucial time.

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.

Glossary

Amniotic cavity	The area between the embryos and the membrane which is filled with amniotic fluid.
Early Miscarriage	The loss of a pregnancy in the first 12 weeks.
Embryo	The name given to the zygote once it divides into two cells, and continues cell division
Implantation stages	The very early stages of pregnancy when the embryo attaches to the lining of the uterus.
In Vitro	In the controlled environment of the lab
Placental Tissue	The tissue that connects the developing baby to the lining of the uterus.
Time-lapse	Multiple images taken over a period of time are played back in a shorter timeframe.