Participant Information and Consent Form

Full Project Title: Comparisons of human embryonic development in culture medium with and without antioxidant supplementation

Principal Researcher: Professor David Gardner

Site: Melbourne IVF

You are being invited to take part in a clinical research trial. Before you decide on your participation, it is important that you understand why the trial is conducted and what is expected from you, as well as the benefits, risks and inconveniences that may be related to participating in this trial. Take your time reading the information and do not hesitate to ask your doctor or the Principal Investigator if you have any questions.

1. Introduction

Culturing human embryos outside the body during routine IVF has motivated extensive research into development of media to ensure the most optimal culture conditions. This research has resulted in many different culture media types that have been used in the past. However, it is known that the in-vivo environment is much more diverse than our media and includes numerous substances. One such group of substances found native in our bodies are antioxidants. The function of antioxidants is to protect cells and tissues from oxidative damage often created by reactive oxygen species (ROS).

The antioxidants acetyl-L-carnitine (ALC), N-acetyl-L-cysteine (NAC) and α-lipoic acid (ALA) are shown to be involved in protecting cells from oxidative damage. Recently, a study performed in the mouse model and in humans showed a clear benefit of using the combination of the three antioxidants on embryo development as well as implantation potential and foetal growth. Consequently, we want to investigate in a larger group, if the combination of these three antioxidants may favour embryo development in human IVF.

We therefore want to study, in a time-lapse monitoring system, the possible advantage of using a medium containing three known antioxidants compared with the standard medium currently being used in our laboratories at MIVF.

2. What is the purpose of this research?

Scientists at Melbourne IVF are undertaking this research in order to improve the quality and potential of the embryos and consequently improve the success of IVF.

3. What will happen to my embryos?

A traditional IVF procedure will be performed including ovarian stimulation and oocyte pick-up using the standard methods at the clinic. The resulting embryo is then randomly allocated to the standard culture media or the standard culture media supplemented with the antioxidants. Time-lapse imaging will allow embryos to be closely monitored and embryo development and quality (stage and grade) will be scored daily and recorded. Embryos will be cultured up to 5 – 6 days. Embryo transfer will occur according to treatment protocol discussed with your doctor.

4. What does participation in this research involve?

Participation in this research involves patients agreeing to scientists culturing their embryos in either standard culture media or culture media supplemented with antioxidants.

5. What are the possible benefits?

A recent study performed in the mouse model showed a clear benefit of using the combination of the three antioxidants on mouse embryo development as well as implantation potential and foetal growth; we anticipate the same results in the human model.

6. What are the possible risks?

It is possible that there will be no difference or poor embryo development in the supplemented culture media compared with the standard culture media. Given embryos of participants will be cultured using a time-lapse incubator (Embryoscope), Investigators will be able to closely and regularly monitor embryo development and any potential adverse events.

However, the results of a recent study conducted at two IVF centres in Japan, where 115 patients were recruited, generating a total of 1350 embryos were cultured in the presence or absence of antioxidants, showed an improved fertilisation rate, good quality embryos on day 3 and good quality blastocysts and improved ongoing clinical pregnancy rates. Encouragingly, there were no adverse effects observed in embryos cultured in the antioxidant supplemented media. Hence we do not anticipate any risks in applying this methodology.

7. What if new information arises during this research project?

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and your doctor will discuss whether this new information affects you.

8. Can I have other treatments during this research project?

Participation in this research does not prevent you from undergoing any other treatments, or accessing any other medical attention which you may require.

9. Do I have to take part in this research project?

Participation in any research is voluntary. If you do not wish to take part you don't have to. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Melbourne IVF.

10. What if I withdraw from this research project?

If you decide to withdraw from the study prior to oocyte pick-up experimentation will not occur. If you decide to withdraw at any time after this point, only data collected up to the date of withdrawal from the study will be used in the analysis and no further data pertaining to you will be collected beyond the date of withdrawal. Embryos however will continue to be cultured in the media in which they were initially placed.

11. Could this research project be stopped unexpectedly?

Given the promising results published to date and the importance of improving our protocols and furthering our medical knowledge to improve the outcome for our patients, it is unlikely that this study will be stopped unexpectedly.
Also, with the recent introduction of a new type of imaging system for embryo observation, called time-lapse, surveillance of embryo development will be continuous. Time-lapse monitoring will therefore allow us to closely monitor the embryo development and any potential adverse events.

12. How will I be informed of the results of this research project?

At the completion of the study you will be notified which group you were allocated to.
Results of this study may be published in medical journals and on the Melbourne IVF website. Publication will be in such a manner as to ensure that no participant can be identified.

13. What else do I need to know?

- **What will happen to information about me?**

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project.
Information about you may be obtained from your health records held at Melbourne IVF for the purposes of this research.
Your health records and any information obtained during the study are subject to inspection for the purpose of verifying the procedures and the data by the relevant authorities and authorised representatives of the Ethics Committee approving this study by law.

In any publication and/or presentation, information will be provided in such a way that you cannot be identified. No identifiable data will leave Melbourne IVF.

- **Is this research approved?**

The ethical aspects of this research project have been approved by The Melbourne IVF Human Research Ethics Committee.
This project will be carried out according to the *National Statement on Ethical Conduct in Human Research* (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

14. Who can I contact?

The person you may need to contact will depend on the nature of your query. Therefore, please note the following:

- **For further information:**

If you would like any further information concerning this research you can contact:

  - Professor David Gardner, Principal Investigator, at david.gardner@mivf.com.au or
  - Your IVF doctor

- **For complaints:**

If you wish to discuss the study with someone not directly involved, in particular in relation to policies, your rights as a participant, or should you wish to make a confidential complaint, you may contact the HREC Secretariat on 9473 4444 or via the following link, http://mivf.com.au/fertility-specialists/ivf-ethics-committee

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

Consent Form
Version: 3 Dated: 22nd June 2018
Site: Melbourne IVF

Trial Title: Comparisons of human embryonic development in culture medium with and without antioxidant supplementation

I have read, or I have had read to me in a language that I understand, this document and I understand the purposes, procedures and risks of this research project as described within it.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to MIVF concerning my treatment that is needed for this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described.

I understand that I will be given a signed copy of this document to keep.

Participant's name (printed):

……	……
(woman)	(partner)
Signature:……..	Signature:……..
Date:	Date:

Declaration by researcher*: I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Researcher's name (printed) ……

Signature Date

** A senior member of the research team must provide the explanation and provision of information concerning the research project.*
Note: All parties signing the consent section must date their own signature.

Withdrawal of Consent Form

Version: 3 Dated: 22nd June 2018

Site: Melbourne IVF

Trial Title: Comparisons of human embryonic development in culture medium with and without antioxidant supplementation

I hereby wish to WITHDRAW my consent to participate in the research proposal described above and understand that such withdrawal WILL NOT jeopardise any treatment or my relationship with Melbourne IVF.

Participant's names (printed):

……	……
(woman)	(partner)
Signature:……..	Signature:……..
Date:	Date: