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PARTICIPANT INFORMATION SHEET – The Fetal Medicine Research Institute
Study title: Amniotic Fluid, placental and fetal stem cells
Researchers: Professor Kypros Nicolaides, Director and Professor of Fetal Medicine
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You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and ask us if there is anything that is not clear.

What is the purpose of the study? We would like to find out whether we can grow stem cells from amniotic fluid, placental tissue and fetal fluid, and whether proteins found in the fluid can be used to indicate long term outcome for problems such as kidney disease.

Stem cells have the remarkable potential to develop into many different cell types in the body. Serving as a repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialised function, such as a muscle cell, a red blood cell, or a brain cell for example. Adults have stem cells that are commonly collected from the bone marrow. Recent studies have found stem cells in the amniotic fluid and the placenta. Stem cells are more abundant in the fetus than the adult. They may be better **able to divide, grow and develop into different cell types.**

We would like to study **amniotic fluid, placental and fetal stem cells** to find out about their characteristics, how they grow and what tissues they can turn into. We will grow them in the laboratory to see if they can repair damaged tissues such as muscle and bone, and analyse the proteins in the amniotic fluid to look for crucial growth factors and chemicals which tell us about the baby's condition. We are keen to check whether genes that are missing in genetic diseases can be introduced into stem cells. We also want to monitor how cells behave in the body and some cells may be introduced into animals to do this. These animal studies have received ethical approval and are in accordance with relevant legislation. In the future it might be possible to use corrected stem cells to treat people with genetic diseases. For example, a stem cell from a patient with thalassaemia, a genetic disease that causes anaemia, could have a gene inserted to correct the anaemia. Introduction of the corrected stem cell into the affected patient might then cure the disease.

We are hoping that our research will show that these stem cells are a potential **treatment of diseases in newborn babies**. Our early data has shown that amniotic fluid stem cells might be useful to treat necrotizing enterocolitis, a serious gut disease that affects up to 1 in 10 premature neonates. These stem cells may also be useful for repairing congenital structural problems in babies such as hernias. For these reasons we would also like to store some cells and tissues for future ethically approved clinical trials in a special cell biobank. To ensure that any cells that are biobanked for potential use as a treatment are free from infection, we would like to collect a sample of your blood (20mls or equivalent to 4 teaspoons) to test for infections such as HIV, hepatitis and toxoplasma. If you would prefer not to biobank the samples, we would still like to study them in our research but we would not use them for future therapy, and you would not be asked to give a blood sample.
We are also studying if there are microorganisms such as bacteria normally present in the womb during pregnancy. Bacteria are present in almost all parts of the body. This is called the **microbiome**, and these bacteria do not usually cause disease. It is unclear if bacteria are normally present in the placenta. We are studying whether bacteria are involved in early miscarriage and we would like to find out more about the microbiome of the placenta and uterus during pregnancy. To do this we will carefully analyse small samples of placenta, amniotic fluid, fetal blood or urine for signs of bacteria and compare them with swabs from the vagina and abdominal skin, where we would expect to find bacteria present. This part of the project is a collaboration with Tommy's National Centre for Miscarriage Research, Imperial College London.

Why have I been invited to participate? We are asking pregnant woman who attend **The Fetal Medicine Research Institute** for any invasive test such as amniocentesis, chorionic villus sampling (CVS, placental biopsy), fetal blood or bladder sampling for prenatal diagnosis whether they would take part in this study.

Do I have to take part? There is no obligation to take part and your decision will not have any affect on your future medical care. It is up to you to decide whether you would like to be involved. We will give you this information sheet to

look at and keep, then ask if you are happy to sign a consent form. You are still free to withdraw at any time without giving a reason even if you decide to take part.

What will happen to me if I take part? The normal procedure when you are having the standard clinical tests is that the samples of amniotic fluid, placenta, fetal blood or urine are sent to the laboratory for testing, then any extra samples are thrown away. We would like to use the spare amniotic fluid, placental, fetal blood or urine cells for research or potential treatments. We are asking for your permission to store and use these tissues or cells for ethically approved research studies and clinical trials. If you agree to biobank your samples we will collect a sample of your blood (20mls or equivalent to 4 teaspoons) from your arm to test for infections.

Just before you have a procedure, we would also like to collect a vaginal swab, and a skin swab from your abdomen. This is performed by gently passing a small cotton bud-type swab into these areas. This will tell us which bacteria are normally present in these areas of the body and allow us to make a comparison with the placenta, amniotic fluid, fetal blood or urine samples.

By gifting the samples to the Principal Investigator, you will give up all rights over the samples. If you agree to the cells being stored in the biobank for future therapeutic use, **you retain the right to withdraw them from the biobank after which they will be destroyed**. After seven years, the cells may become unsuitable for future therapeutic use but they can still continue to be used for research purposes.

We will assign to the samples and the information we collect about you a unique identifying number so that the information becomes anonymous to the researchers. **You do not have to do anything different during your tests or during the rest of your pregnancy if you take part in this study.**

What tests will be done on the amniotic fluid, placental and fetal cells? We will study the chemicals and proteins in the amniotic fluid, how the cells grow and develop, what cell types they become and whether corrective genes can be introduced into them. For some studies the sample may leave the UK for analysis in other countries, but your personal details will not be revealed. If you agree to biobank the cells we will store them for future ethically approved research and clinical studies, and you will retain the right at any time over the next 30 years, to request these cells or tissues are removed from the biobank and then destroyed.

What tests will be done on the vagina and skin swabs? We will study the bacteria that are present in these swabs and compare them with any bacteria that we detect in the amniotic fluid, placenta, fetal blood or urine samples.

What are known risks of the study? There are no additional risks to your health or the health of your baby from taking part in the research because there are no extra procedures. All of the amniotic fluid, placenta, fetal blood or urine samples are being collected as part of your normal clinical tests, and we will just use the extra material which would normally be thrown away. Collection of a small blood sample has momentary discomfort and occasionally results in bruising to your arm. Collection of a swab from the vagina has some momentary discomfort.

What are the possible benefits of taking part? There will be no immediate benefits to your pregnancy, but this research may help us to treat patients with congenital diseases or structural abnormalities better in the future. It may also help us to find out more about why some women have early miscarriage.

What if something goes wrong? As there is no extra intervention being performed other than taking some of your blood or swabs, we do not expect any risks. If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns of this study, the normal National Health Service complaints mechanisms should be available to you.

Will my taking part in this study be kept confidential? All information collected about you during the research will be kept strictly confidential and samples will be anonymised to the individual researchers. Any information about you, which leaves the hospital will have your name, hospital or NHS number and addressed removed so that you cannot be recognised from it. All data will be kept safe and secure in accordance with the Data Protection Act 1998 and will be collected, stored and handled by the researchers listed at UCL.

Who is organising and funding the research? The research is organised by the Tissue Engineering Laboratory and the Nephro-Urology Unit, both at UCL Institute of Child Health and Great Ormond Street Hospital and the UCL Institute for Women's Health. It is funded by Tommy's charity, March of Dimes charity, the Royal Society, UCLH Charities, Kids Kidney Research, Sparks, Wellcome Trust and the European Union.

What will happen to the results of the research study? The results will be analysed, presented in scientific meetings and published in peer-reviewed journals. Your identity will not be revealed in any report or publication. You may obtain a copy of the results from Professor Kypros Nicolaides at the **The Fetal Medicine Research Institute**.

The National Research Ethics Committee has reviewed this study and given its approval.

Thank you for taking part in this study!

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