Participant information sheet V.1 15th January 2025

SHORT TITLE

Developing Tools for Prenatal Therapy using Fetal Fluid and Tissues
(IRAS number: 329244)

PART 1

We would like to invite you to take part in our research study.

Joining the study is entirely optional, however we would like you to understand the purpose of the research and what it would involve for you, before you decide. One of our team will go through this information sheet with you, to give you the opportunity to ask any questions you may have and to help you decide whether or not you would like to participate- we anticipate this will take approximately 15 minutes. Please feel free to talk to others about the study if you wish.

The first part of the Participant Information Sheet tells you the purpose of the study and what your participation will involve. The second part will give you more detailed information about the conduct of the study. Please ask if anything is unclear.

What is the purpose of the study?

This study aims to advance our understanding of how blood cells are formed, hematopoiesis, during fetal development and the interaction between immune cells and stem cells, which regulate tissue structure and function. (b)Stem cells are cells within the body that can divide and renew themselves for long periods and can also turn into other cell types. By collecting and analyzing fetal tissues, including the liver, lungs, spleen, kidney, bowel, placenta, amniotic fluid, and blood from the umbilical cord, we hope to uncover insights into the generation and maintenance of hematopoietic stem and progenitor cells (HSPCs). These cells have the highest blood regenerative potential, meaning they can self-renew and replenish blood cells during human life, making them crucial for improving transplantation therapies for blood cancers and understanding the origins of infant and childhood blood cancers. Additionally, our research seeks to enhance treatments for hereditary anemias, such as sickle cell disease.

A novel aspect of our study focuses on the interactions between immune cells and stem cells, which play a pivotal role in maintaining the balance and health of tissues (tissue homeostasis). These interactions are crucial for the development of effective immune responses and the regeneration of tissues. Understanding these complex relationships will provide new insights in to how the immune system influences stem cell function and tissue repair, opening avenues for innovative therapeutic strategies targeting a range of diseases.

Why have I been invited?
You have been invited to take part in the study because you are undergoing a termination of pregnancy procedure between 12-24 weeks of pregnancy at King's College Hospital and meet the study criteria. Patients from hospitals (King's College Hospital, Denmark Hill) will be invited to take part. We are aiming to recruit approximately 300 patients.

Do I have to take part?
Your participation is optional and you are able to withdraw your consent at any time. Withdrawal of consent can be verbal or written and you do not need to provide a reason. This would not affect the standard of care you receive. If you decide to withdraw from the study, you may also request that any data and biological samples you have provided be destroyed and not used in the research. If your samples or data have not yet been de-identified or used in analysis, we will honour this request and securely destroy them. However, if your data has already been de-identified and/or analysed, we may not be able to remove it.

What will happen to me if I take part?
If you decide to participate, we will collect fetal tissues, such as bone marrow, liver, and lung, during the termination of pregnancy procedure. These tissues will be used to study how the cells work, including how they interact with immune cells, through various laboratory tests. (h) Some of the cells in the provided samples will be 'fixed' using a solution that preserves them by stopping all activity within the cell. This helps researchers study the cells safely and accurately. Fixed cells are no longer alive and cannot be used to identify you.

In some cases, we may also need to take cells from your blood,. To ensure safety and ethical use of these cells for potential future treatments, we will ask for a small blood sample (d) (up to 30ml, about 6 teaspoons) to check for infections like HIV, hepatitis, and toxoplasmosis. (c) This part of the study is optional, and you can still participate in the research without donating your blood for future storage. If you prefer, we can take these samples while you are under general anaesthesia during your procedure. (j) Should a blood borne virus, such as HIV or hepatitis be discovered in your blood, we will request consent to refer you to the appropriate medical team and inform your GP.

In certain cases, genetic testing may be carried out on some samples. Should a condition of clinical significance be detected, we would ask for your consent to refer you to the trusts genetic counselling services and to inform your GP.

At the termination clinic, you will be asked to complete a sensitive disposal form, to detail how you would like the remaining pregnancy tissue to be handled. Should you wish to arrange private funeral arrangements, the mortuary details will be made available for you, with a window of 30 days if you wish to change your mind.

What are the alternatives for treatment?
There are no extra procedures involved beyond standard clinical practice.

What are the possible benefits of taking part?
While there may not be immediate benefits to you, your contribution will significantly aid advancement in medical research and potential development of new treatments for genetic diseases and blood disorders, including blood cancers, and structural abnormalities.

What are the possible disadvantages and risks of taking part?
There are no additional risks to you as the identification and collection of tissues will be done after the procedure is complete, and your blood taken during the cannulation process in theatre, which is required for your general anaesthetic or whilst you are asleep if you prefer. Given there are no extra procedures involved beyond standard clinical practice, risks are minimal. However, should you have any concerns or complaints, you are encouraged to contact the research team (Dr Panicos Shangaris, panicos.shangaris@kcl.ac.uk) or log your complaint through the NHS complaints procedure ("Patient Advice and Liaison Service")

Who is organising and funding this study?
The doctor in charge of this study is: Panicos Shangaris. The study is funded by the Medical Research Council (MRC) and the Fetal Medicine Foundation, and is being sponsored by King's College London/King's College Hospital NHS Trust.

How have patients and the public been involved in this study?
Service users, the Sickle Cell Society and opinions from stakeholders involved with Sickle Cell patients helped develop the research topic and what research questions should be asked, and one of them is a co-applicant who will continue to be involved in the study.

Who has reviewed this study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the Surrey Research Ethics Committee. The Health Research Authority has also approved it and each local hospital will also give confirmation that the study can proceed.

Expenses and Payments
There are no funds available to pay those participating in this study.

This completes Part 1 of the Information Sheet.

If the Information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making your final decision.

PART 2

What if new information becomes available?

Sometimes, we get new information about the treatment being studied. If this happens, your study doctor will tell you and discuss whether you should continue in the study. If you decide not to continue, your study doctor will arrange for your care to continue outside of the study. If you decide to continue in the study, he/she may ask you to sign an agreement outlining the discussion. This new information may specifically affect you and your health. If this happens, your study doctor might consider that you should withdraw from the study. He/she will explain the reasons for withdrawing from the study and arrange for your care to continue. If the study is stopped for any other reason, we will tell you and arrange for your continuing care.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time; and if you would like to do so; please speak to your study nurse or doctor. This will not affect the care you receive, and you do not have to provide reason. Wherever possible, any stored blood or fetal samples that are yours will be destroyed if you wish.

What if there is a problem?

If you are concerned about any aspect of this study, you should ask to speak to your study doctor, who will do their best to answer your questions (Dr Panicos Shangaris, panicos.shangaris@kcl.ac.uk). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office.

Details of your local office can be obtained by asking your study doctor or GP, telephoning your local hospital or looking on the NHS website. https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available.

In the event that something does go wrong and you are harmed during the research due to someone's negligence, then you may have grounds for a legal action for compensation against KCH, NHS Trust, but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal NHS complaints

mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Will my taking part be kept confidential?

All information collected will be kept strictly confidential. Samples and data will be de-identified, and any personal information will be removed before analysis. Your data will be stored securely in compliance with the Data Protection Act 1998.

If you consent to take part in the research, any of the information collected about you may be inspected by the sponsor (including representatives of the sponsor). These inspections are solely for the purposes of the research and analysing the results. Your records may also be looked at by the regulatory authorities or ethics committees to check that the study is being carried out correctly.

The organisations listed above will keep information about you confidential and secure. Your name will not be used in any reports about the study and all data is stored in accordance with the principle of the Data Protection Act 2018. However, your hospital doctor may tell your GP about your participation if you agree to enter the study.

Involvement of the General Practitioner/Family Doctor (GP)

With your consent, your GP will be informed of your involvement in the trial. Any other medical practitioners who treat you, e.g. should you be admitted to the hospital for any reason, will also be informed.

What will happen to any samples that I give?

The samples you provide will be de-identified, ensuring your personal information is kept confidential. They will be collected by a member of the research team and sent for processing or storage to one of the research laboratories listed below:

- Immunoregulation Laboratory, Dr. Panicos Shangaris, panicos.shangaris@kcl.ac.uk
- Immunoregulation Laboratory, Dr. Niwa Ali, niwa.ali@kcl.ac.uk
- UCL and UCL Institute for Child Health, Dr. Stavros Loukogeorgakis, Prof David, Dr Nikolic
- Cambridge University, Dr. Eliza Laurenti
- Institute of Hepatology, Dr. Luca Urbani
- Brunel University, Dr Cristiano Scotta
- Imagine Institute, Dr Annarita Miccio

The samples will either be used immediately for ongoing experiments or stored in liquid nitrogen for future research. We may use the samples to study fetal stem cells and immune interactions and for

potential therapeutic applications. The samples may be stored long-term for future use, and they will not be destroyed at the end of this study unless you request otherwise. We maintain strict confidentiality by using de-identification, and any data linked to the samples will comply with all data protection laws. If samples are shared with other researchers or institutions, within or outside the UK, the appropriate ethical approval obtained and all data will be de-identified.

In the unlikely event that future use of your samples reveals health-related findings that could be important to you, we will discuss how best to communicate this information. Finally, we have plans in place to ensure that any remaining samples will be destroyed responsibly if they are no longer required for research.

This ensures that your participation remains ethical, secure, and meaningful for advancing scientific knowledge.

Will any tests be done?

All samples will undergo genetic testing, including whole genome sequencing,
to explore genetic factors that influence fetal development and to identify potential genetic disorders. This testing will be carried out with the highest level of confidentiality, and the genetic data will be de-identified. The results will be used strictly for the purposes of this research study and will not be linked back to you personally. All genetic information will be handled in accordance with data protection laws, ensuring your privacy and security throughout the study.

What will happen to the results of the research study?

The findings will be analysed, presented at scientific meetings, and published in peer-reviewed journals. Your identity will not be disclosed in any reports or publications. You may request a copy of the study results from Dr Panicos Shangaris at King's College London.

How we will use your data

We will need to use information from you for this research project.

This information will include:

- Background demographics
- Age
- Any genetic conditions which have affected the fetus, such as sickle cell disease.

This information will be used for research purposes or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

King's College London is responsible for looking after your information. We will share your information related to this research project with the following types of organisations:

- UCL and UCL Institute for Child Health
- Cambridge University
- Institute of Hepatology
- Brunel University
- Imagine Institute
- Research collaborators
- Funders
- Regulators
- Specialist laboratories

We will keep all information about you safe and secure by:

- Storing identifiable information in an NHS computer/ server secured in rooms with additional security, such as key cards and mechanical locks
- Storing hard copies of data in the termination of pregnancy clinic at King's College Hospital NHS Foundation Trust, in a secured, locked drawer within a locked room
- Limiting access to identifiable data to leading researchers in the study - external researchers will not have access to this data
- De-identifying samples and personal information prior to analysis
- Storing data securely in compliance with the Data Protection Act 2018
- Only accessing sections of your medical notes, where prior consent has been given
- Ensuring your data is only shared when necessary, with the correct protection in place

International transfers

We may share or provide access to data about you outside the UK for research related purposes to:

- Research collaborators for expert opinion
- Update funders
- Satisfy regulators where required
- Specialist laboratories for perform testing not available within our organisation

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Brunel University, Dr Cristiano Scotta
- Imagine Institute, Dr Annarita Miccio
- Specialist laboratories

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- Some of the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/uk-gdpr-guidance-and-resources/international-transfers/
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when this is legally required. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach

How will we use information about you after the study ends?

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for the minimum period required by the Good Clinical Practice and UK policy Frameworks, of 25 years. The study data will then be fully de-identified and securely archived or destroyed.

What are your choices about how your information is used?

- You can stop being part of the study at any time, but we will keep information about you that we already have.
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.
- If you agree to take part in this study, you will have the option to allow your data saved during this study to be used for future research. The data will be de-identified. If you wish to withdraw from the study, the data can be deleted from our database at your request.

Where can you find out more about how your information is used?

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK:

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available entitled 'How we use your data' which you can request from the study team
- by asking one of the research team
- by contacting our DPO at [KCL: info-compliance@kcl.ac.uk or KCH: kch-tr.dpo@nhs.net]

By visiting our webpage https://www.kcl.ac.uk/research/research-environment/rgei/research-ethics/use-of-personal-data-in-research

Thank you

Thank you for considering taking part and taking the time to read this information sheet.
If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.

Further information and contact details

Dr. Panicos Shangaris, panicos.shangaris@kcl.ac.uk, 07725578001
For more information or if you have any questions, please get in touch with Dr. Panicos Shangaris at the details provided above.

Local Contacts:

Study team contact: Research Nurses Precious Villaverde/ Shimmarie Riley - 07890251949
or email at **kch-tr.womenshealthresearch@nhs.net**