legacy blood

UNIVERSITY OF CAMBRIDGE

NHS
Cambridge University Hospitals
NHS Foundation Trust

Longitudinal **E**valuation of the **G**rowth and **A**cquisition of **C**lones over **Y**ears in the **blood**

Participant Information Sheet

You are invited to take part in a research study called **LEGACY**. Before you decide whether to take part, it is important that you understand why this study is being done and what it would involve for you. Please take the time to read this information sheet carefully. If anything is not clear, or you would like more information, please speak to a member of the study team (contact details at end).

What is the purpose of the study?

As we age we acquire DNA changes (mutations) in our blood cells, a phenomenon called 'clonal haematopoiesis'. In the vast majority of people these mutations do not cause any problems, but in a small number of people, if these mutations grow to high enough levels in the blood, they can increase the risk of developing a blood cancer (e.g. leukaemia) and/or cardiovascular disease (e.g. heart attack). Unfortunately, we are currently unable to reliably predict which mutations are associated with the highest risk of these conditions, or what specific factors drive or impede the growth of mutations in the blood over time. In order to understand this, we need to address the following questions:

- What happens to the growth and survival of blood cells harbouring acquired mutations over time?
- What effect do health and lifestyle factors have on the growth and survival of these blood cells?
- How do changes in the immune system correlate with changes in health and lifestyle, and how does this affect the growth and survival of these blood cells?
- How does the growth of mutations in the blood cells compare to the growth of mutations in other cell types in the same person, e.g. in the cells lining the mouth ('buccal cells')?

The **LEGACY** study will aim to answer these questions by studying blood samples and mouth ('buccal') swab samples collected at regular intervals over a period of ~18 months (total of 12 study visits), from the same individuals, together with concurrent information on their health and lifestyle, collected through questionnaires, NHS medical and health-related records and wearable devices (Fitbit). By then continuing to follow the health of participants long-term (through medical and other health-related records), we hope to assess whether particular changes detectable in the blood might be predictive of future illness.

Having to attend for regular blood tests limits the number of participants that can be recruited to longitudinal studies such as **LEGACY**, and so an additional aim of the study is to assess whether self-collected fingerprick blood samples and saliva samples can provide results that are of comparable accuracy to traditionally collected blood samples. If they can, then this will be invaluable for planning future studies with larger numbers of participants as it may allow participants to post self-collected samples from home, which will minimize the time and cost associated with frequent face-to-face study visits.

Who can take part in this study?

Anyone aged 40 to 80 years old can volunteer to participate in the **LEGACY** study.

Unfortunately you will not be eligible to join the **LEGACY** study if:

- you are known to be iron deficient or are currently receiving treatment for iron deficiency.
- you are currently receiving treatment for cancer.
- you have (or suspect you might have) hepatitis B, hepatitis C or HIV infection.

- you do not have capacity to give informed consent for yourself.
- you do not have a phone compatible with a Fitbit® activity tracker. Your phone needs to be running either Apple iOS 12.2 (or higher) or Android OS 7.0 (or higher) and should not be a Huawei P8 Lite, Huawei P9 Lite or Xiaomi Mi 6 as these phones may have compatibility issues.
    - The iOS version on an iPhone can be found in 'Settings' > 'General' > 'About' > 'Version'.
    - The Android version on an Android phone can be found in 'Settings' > 'About phone' > 'Android Version' or 'Settings' > 'System' > 'Advanced' > 'System update' > 'Android Version'.

If any of these criteria become relevant during your participation in the **LEGACY** study, whether or not it is appropriate for you to continue will be discussed on an individual basis.

What will happen if I take part?

Taking part in this study will involve attending the Cambridge Biomedical Campus for a 'study visit' once every ~6 weeks for a total of 12 visits (over a period of ~18 months).

At each visit you will see a member of the research team and will be asked to:

1. **Provide a blood sample**, which will be taken from a vein in your arm by a healthcare professional. 30 to 35 ml (just over 2 tablespoons) of blood will be collected from your arm at each visit.
2. **Provide a fingerprick blood sample**. You will be randomly assigned to one of two groups, which will determine the method by which you will be asked to self-collect your fingerprick blood sample during your study visits. You will be asked to self-collect your sample using the same method at each visit.

   Group A: Fingerprick blood sample collection in to blood tubes.
    - You will be provided with a device containing a small non-visible needle, for you to prick your fingertip. You will be asked to drip ~0.5 ml of blood drops into 2 small blood collection tubes.

   Group B: Fingerprick blood sample collection on to a 'blood spot collection card'
    - You will be provided with a device containing a small non-visible needle, for you to prick your fingertip, and will be asked to drip ~9 blood drops on to special pieces of paper designed to collect/ store blood drops.
3. **Provide a saliva sample**. You will be provided with a small tube to spit in to and no more than 2 ml (<1/2 tsp) of saliva will be required at each study visit. You should ideally not eat, drink, kiss or smoke in the 30 minutes prior to providing your saliva sample.
4. **Answer a short written questionnaire**.
    - The questionnaire at your first study visit will ask questions about your personal and family medical history (specifically about cancer, cardiovascular, blood disorders and inflammatory conditions), medications, diet and lifestyle (e.g. smoking and alcohol).
    - Questionnaires at subsequent study visits will ask about any changes in your health, medications and lifestyle since your last study visit.
    - At your final study visit you will be given a study feedback questionnaire to ask about your experience of participating in the **LEGACY** study.

At every other visit you will also be asked to:

5. **Provide a buccal (mouth) swab sample**. After you have provided the saliva sample you will be provided with a swab to roll against the inside of your cheek on each side of your mouth, in order to collect a small sample of cells from the lining of your mouth.

At the first study visit you will also be asked to sign a consent form and will be **provided with an activity tracking device (Fitbit).** We would like you to wear the Fitbit for as many hours per day as possible, including at night. You will be asked to set up a Fitbit account and to authorize **LEGACY** research staff to access de-identified data collected from your Fitbit (see 'What data will be collected from the Fitbit and how?').

What if I already have a Fitbit?

If you already have your own Fitbit this does not prohibit you from receiving a Fitbit from us. If you would prefer to continue using your own Fitbit, however, you will be asked to authorize research staff to access the data collected from your own Fitbit (see 'What data will be collected from the Fitbit and how?').

What data will be collected from the Fitbit and how?

You will be asked to create a Fitbit account, which will collect and store data from the Fitbit. In order for **LEGACY** research staff to access your Fitbit data you will be asked to authorize a third party, Fitabase, owned and operated by Small Steps Labs LLC, via an online form. Fitabase is a research platform that collects data from internet connected consumer activity devices and will connect to your Fitbit account, so that research staff can access your data. Upon authorization, Fitabase may collect the following data from your Fitbit account:

- Personal details added to your Fitbit account, such as height, weight, gender and age.
- Information sent wirelessly from the Fitbit that is stored in your Fitbit user account.
- Information added manually to the Fitbit service and stored in the Fitbit user account.
- Day-, hour- and minute-level data collected from the Fitbit including:
    - Daily steps total
    - Distance moved
    - Intensity of movement metrics
    - Estimated energy expenditure
    - Sleep length, quality, and movement
    - Heart rate and heart rate variability
    - Manually entered and automatically detected physical activities, e.g. walking, running.

This data will be downloaded by the **LEGACY** research team and will be stored in a secure database. A de-identified study ID number will be used within the Fitabase platform and your Fitbit username and password will not be accessed, viewed or stored by Fitabase, Small Steps Labs LLC, or any **LEGACY** study personnel. After ~18 months, or if you leave the study before then, your Fitabase profile will be deleted and Fitabase will no longer be authorized to access your Fitbit account. This means that the **LEGACY** research team will not be able to access any new data collected by the Fitbit after this time. You are welcome to keep the Fitbit, even if you leave the study early.

What will happen to the blood, saliva and buccal swab samples and information I give?

The blood samples taken from a vein in your arm will be taken to the Cambridge Blood and Stem Cell Biobank for processing on the same day as your study visit. The fingerprick blood samples and saliva samples will be sent in the post to either the Cambridge Blood and Stem Cell Biobank or the Blundell Lab (Hutchison/MRC Research Centre), in order to mimic the conditions and time-delay that might be associated with self-collection and postage of samples from home. The buccal (mouth) swab samples will be sent in the post to the Martincorena lab at the Wellcome Sanger Institute. Your blood samples will be processed in order to allow long-term storage of whole blood, as well as its constituent parts, including DNA, white blood cells, serum and plasma. Your saliva samples and buccal swab samples will also be processed to allow long-term storage (including of DNA). All your samples will be processed and stored in accordance will all applicable legal and regulatory requirements.

Tests that will be undertaken on your blood, buccal and saliva samples as part of this study include both genetic tests (e.g. DNA sequencing) and non-genetic tests (e.g. blood count analysis, inflammatory mediator (cytokines) analysis). These tests may be carried out by the **LEGACY** study team, Blundell lab, Martincorena lab, academic collaborators or industrial/ commercial partners in this country or abroad. These collaborators and partners may also be given access to your data, but this will be anonymised and so it will not be possible to trace the information back to you, nor will it be combined with other information in a way that could identify you.

Your data and information cannot be used to contact you or to affect your care and will not be used to make decisions about future services available to you, such as insurance. We will store your samples and information indefinitely, unless you withdraw from the study and request that your samples and data are destroyed (see 'What happens if I don't want to carry on with the study?').

What happens after I have completed all 12 study visits?

Once you have completed all 12 study visits (after ~18 months), your face-to-face involvement in the study will be complete and your Fitbit data will stop being collected by the **LEGACY** research team. By taking part in the study, however, you would be agreeing to allow **LEGACY** research staff to continue to **follow your health for up to 15 years starting from the time of your enrolment in the study, through direct access to your medical and other health-related records,** including those held and maintained by your GP, NHS Digital, Health and Social Care Information Centre, Office of National Statistics, Public Health England, and other central UK NHS bodies. Accessing this information may involve the **LEGACY** research team sending your name, date of birth, NHS number and postcode to these bodies to receive this information.

You may be contacted by **LEGACY** research staff and asked to provide further blood and/or buccal and/or saliva samples, or answer more questions, after you have completed the 12 face-to-face study visits. This may involve you being invited to self-collect and post fingerprick and/or buccal and/or saliva samples from home. These additional samples and questionnaires are entirely optional and you can refuse without giving any reason.

Why do you need my written consent?

Your participation in this study is entirely voluntary and no explanation is required if you choose not to take part. By signing the consent form, you would be confirming your willingness to take part.

What are the advantages of taking part?

The aim of the study is to observe what happens in the blood over time and how this relates to health and lifestyle, and to determine whether self-collected saliva samples and fingerprick blood samples are a feasible alternative means of monitoring this. The study findings will not directly benefit the study participants, but it is hoped that the results will benefit future generations by contributing to research on the early detection of diseases.

You will be provided with a Fitbit as part of this study (unless you prefer us to collect data from a Fitbit you already own) and you will not be required to return the Fitbit to us, even if you leave the study early.

What are the possible disadvantages of taking part?

Taking part in this study should not cause you any harm. You may feel some discomfort when you have blood taken, although the person taking your blood will be specially trained to reduce this risk. You may also feel some discomfort when you take your own fingerprick blood sample. It is possible that you might be slightly uncomfortable with some of the questions in the questionnaires. You can skip questions if you do not want to answer them.

In signing the consent form, participants transfer all intellectual property rights in their samples and data to the **LEGACY** study. The research results may feed into a discovery of commercial value, but you will not benefit financially in any way if commercialisation of any research findings are successful.

Will I be given any results from the tests on my samples?

None of your results (including genetic results) will be given to you or your doctors. The only exception to this is if the results of non-genetic tests suggest the possibility of a significant and previously unknown health condition that requires further investigation, in which case both you and/or your GP will be contacted. You should not, however, regard non-contact from us as reassurance about your health and you should still see your GP about any health concerns you might have. The reason no other results will be given is because many of the tests we are performing are for “research use only” (i.e. not clinically accredited tests) and such feedback outside of the normal clinical setting is of uncertain value, and might even be harmful, particularly without prior counseling.

What will happen to the results of the study?

When the results of the study are available they may be published in journals and used for presentations and conferences. The results will be completely anonymous and you will not be identifiable from any data presented. You will be offered the option of being sent an email newsletter of any publications that arise from this study. Anonymised genetic information may also be published and held indefinitely on international databases with controlled access for researchers worldwide.

Will my participation be kept confidential?

Great care will be taken to ensure the confidentiality of your samples and data. You will be allocated a unique participant ID number on enrollment to the **LEGACY** study and will be identified by this number on all **LEGACY**-related study documentation throughout the study and when data analysis processes are applied. Any information that could identify you will be removed from study data and samples as soon as possible after collection.

Your study and clinical data (identified by your unique participant ID number) will be kept in a password-protected secure database, in accordance will all applicable legal and regulatory requirements, and will be accessible only to authorized members of the **LEGACY** research team. Any personal identifiable data will be encrypted and kept in a password-protected database separately from your study data and clinical data. Only specific authorised **LEGACY** research team members holding appropriate clinical contracts, honorary contracts or University of Cambridge research passports will have access to personal identifiable data and non-anonymised medical/health-related records. Accessing your non-anonymised medical/health-related records may involve these authorised **LEGACY** research team members sending your name, date of birth, NHS number and postcode to NHS-related bodies or other health-related bodies in order to retrieve your information, but only the minimal necessary amount of personal identifiable information will be used. Handling of all paper-based and electronic personal identifiable information will follow local NHS policies.

If you consent to your samples and data being used in future research projects, these will be available only to researchers who have relevant scientific and ethics approval for their planned research and any details that might identify you will be removed in order that your samples and data cannot be traced back to you.

Will my samples and data be used in other projects?

Your samples and data will only be allowed to be used in other research projects if you have explicitly confirmed you are happy with this on the consent form and if the project has been ethically approved. These other projects may be carried out by collaborators in universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/). Your information will not identify you and will not be combined with other information in a way that could identify you. The information will be used for the purpose of health and care research and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

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

Participation is entirely voluntary. After giving signed consent, you can withdraw at any time by contacting the study team (contact details at the end of this information sheet). You will be given a choice of level of withdrawal from the study:

- "No further samples or data", but allowing continued use of already collected samples and data.
- "No further use", requiring destruction of all of your samples and data.

"No further use"

If you opt to withdraw with "no further use", the questionnaires, Fitbit data, information and samples already collected from you will be destroyed so no new data can be generated from your samples. If data has already

been generated from your samples, we will prevent its use in further analysis, if possible, but removal of data that has already been incorporated into integrated datasets will not be possible. Your identifiable information (e.g. name and contact number) will be retained in archive so that a record remains available of your participation in the study and to have a full documentation of your withdrawal. If you have consented to your samples being used in other research studies and your samples and/ or data have already been shared with other researchers then it will not be possible to destroy or withdraw these samples or data.

If you have been provided with a Fitbit you will not be required to return this when you leave the study. When you leave the study, your Fitabase profile will be deleted and Fitabase will no longer be authorized to access your Fitbit data. This means that the **LEGACY** research team will not be able to access any new data collected by the Fitbit after you leave the study.

Can I claim travel expenses?

We are happy to reimburse the following travel expenses, up to a maximum of £15 per LEGACY study visit:

- Public transport (e.g. bus or train)
    - Please buy standard tickets (i.e. not first-class)
- Private transport (e.g. car or motorcycle)
    - A mileage allowance of 45p per mile for car or 24p per mile for motorbike will be reimbursed.
- Car parking
    - Car parks are available on the Cambridge biomedical campus and we are happy to cover the cost of the car parking ticket associated with your LEGACY study visit.

To claim reimbursement for your travel expenses, please keep your travel receipts and ask for a travel expenses claims form when you attend for your study visit.

Who is organising the study?

The **LEGACY** study is led by Dr Caroline Watson and Dr Jamie Blundell and is run with the help of ACED Clinic Cambridge. Dr Caroline Watson is a haematology doctor and Visiting Researcher in the Blundell Lab at the Hutchison/MRC Research Centre (Cambridge Biomedical Campus). Dr Jamie Blundell is a Group Leader in the CRUK Cambridge Centre Early Detection programme, at the Hutchison/MRC Research Centre (Cambridge Biomedical Campus).

Who is reviewing the study?

The study will be reviewed by the Health Research Authority (HRA) and NHS/HSC Research Ethics Committee.

Who is sponsoring the study?

Cambridge University Hospitals NHS Foundation Trust (CUHNFT) and the University of Cambridge are joint sponsors for this study based in the United Kingdom. CUHNFT and the University of Cambridge will be using information from you and your medical records in order to undertake this study and will act as joint data controllers. This means that both organisations are responsible for looking after your information and using it properly. The University of Cambridge will keep identifiable information about you until 15 years after your enrollment in the study. CUHNFT will keep identifiable information about you until 15 years after your enrollment in the study.

How will we use information about you?

We will need to use information from you and your medical records for this research project. This information will include:

- your name
- date of birth
- contact details
- your GP details
- your NHS number
- notes and reports about your health, treatment and care, including your medical conditions and results of investigations, such as x-rays and laboratory tests.

People will use this information to do the research or to check your records to make sure that the research is being done properly.

We need to manage your records in specific ways for the research to be reliable. This means that you we won't be able to let you see or change the data we hold about you. If you withdraw from the study, we will keep the information about you that we have already obtained, unless you request that your samples and information are destroyed (see 'What will happen if I don't want to carry on with the study?'). To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information using the following links:
For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/patient-privacy/patient-privacy-notice/, or email the Data Protection Officer at: gdpr.enquiries@addenbrookes.nhs.uk

For University of Cambridge, please visit: https://www.medschl.cam.ac.uk/research/information-governance/, or email the Information Governance team at: researchgovernance@medschl.cam.ac.uk

What if there is a problem or something goes wrong?

The risks of participants suffering harm as a result of taking part are minimal, but insurance (provided by the University of Cambridge or the NHS indemnity scheme) will provide compensation for any negligent harm caused by participation.

Contacts for further information

ACED Clinic Cambridge Research Nurse – Tel 01123 763353

www.legacy-study.org

Thank you for taking the time to read this information and for considering taking part in this study.