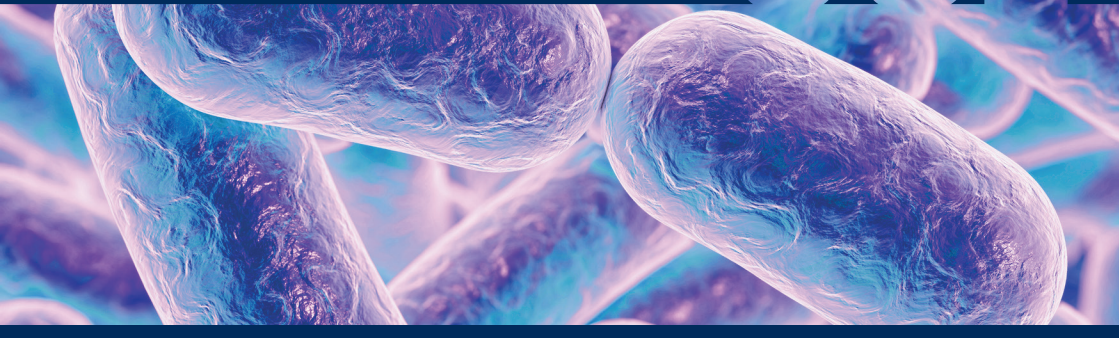
DIVISION OF INFECTION AND IMMUNOLOGY

UCL



HUMAN IMMUNE RESPONSE VARIATION IN TUBERCULOSIS

Participant Information

INVITATION

We would like to invite you to take part in a research study. Before you decide whether or not to participate 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. Talk to others about the study if you wish and ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

NHS

WHAT IS THE RESEARCH ABOUT?

Only a small proportion of people who become infected with the bacteria that causes tuberculosis (TB) ever develop disease. We think this is because the immune system is more effective against TB in some people, but because we don't know how to identify people who are most likely to develop TB disease, we offer everyone preventative treatment with 3-6 months of antibiotics.

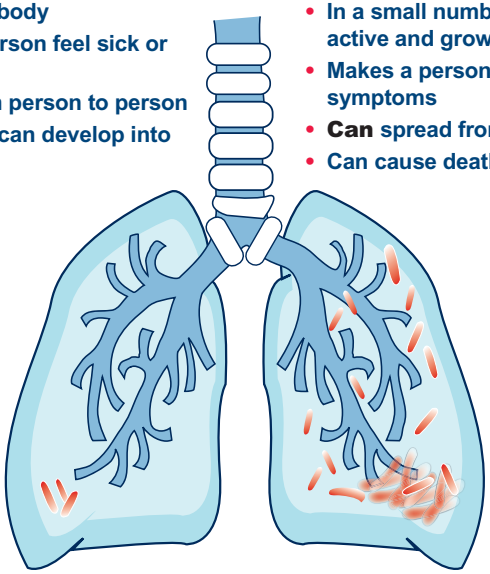
We are doing a study to test how and why immune responses to TB differ between people, and to evaluate a new test that may be able to identify TB disease before people develop the illness.

Latent TB

- TB persists in the body
- Doesn't make a person feel sick or have symptoms
- **Can't** spread from person to person
- In some people, it can develop into TB disease

TB Disease

- In a small number of people, TB is active and grows in the body.
- Makes a person feel sick and have symptoms
- **Can** spread from person to person
- Can cause death if not treated



DO I HAVE TO TAKE PART?

No. It is entirely up to you whether or not you want to take part and you do not have to decide today. You can take your time and ask as many questions as you need to before you make your decision. We will be available to answer your questions and if you wish to participate, we will offer you an appointment to attend the hospital in order for you to give written consent and begin the study.

Even if you have signed the consent form, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect any other healthcare you receive.

WHY HAVE I BEEN ASKED TO TAKE PART?

You have been asked to take part because you have had a blood test which indicates that you have been infected with the TB bacteria at some point in the past.

WHAT WILL HAPPEN TO ME IF I AGREE TO BE INCLUDED IN THIS STUDY?

We will first check that you have no evidence of TB disease by asking about your symptoms, doing a chest x-ray and blood tests. At the same time, we will perform TB skin tests in each arm. We will take a small skin sample from one arm two days later, and the other arm after seven days.

If you have not been exposed to TB recently your participation in the study will end and you will resume routine clinical care. In the absence of any evidence of TB disease, you will be offered preventative TB treatment.

If you have recently been exposed to TB and our tests find no evidence of TB disease, we will not give you preventative TB treatment immediately. Instead, we will monitor you closely by asking you to come to a clinic appointment every 3 months, for up to 2 years. During these clinic visits we will ask about your symptoms, repeat your chest x-ray and blood tests. We will look carefully for any evidence of developing TB disease so that we can start TB treatment for you before any illness. At the end of 2 years, we will also offer you TB treatment.
(See flow chart overleaf)

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If you agree to participate, we will arrange visit 1 at your convenience

Visit 1

- Obtain informed consent
- Complete a symptom questionnaire
- Provide a blood sample
- Administer a TST in each arm
- Chest x-ray if you have not already had one

Visit 2 (48 hours after TST) → **A biopsy of the TST in one arm**

Visit 3 (1 week after TST) → **A biopsy of the TST in the other arm**

Only if you have recently been a contact of someone with pulmonary TB

3 monthly follow up visits for up to 2 years

- Chest x-ray
- Blood samples
- Symptom questionnaire

Only for a small group of participants based on results of the research

One further visit at your convenience → **Blood sample**

WHAT ARE THE BENEFITS OF TAKING PART?

The information we will gain from this research will help us understand how the immune response can fight against TB most effectively. We can then use this knowledge to develop better ways of identifying people who will benefit most from preventative TB treatment, to design new TB vaccines and to develop new TB treatments that improve immune responses.

Although we do not anticipate any direct benefit to you, many people who have been exposed to TB recently, choose not to take up the offer of preventative TB treatment because the likelihood of TB disease for any individual is low. Most TB disease that does occur after recent exposure, develops in the first 2 years. If you have been exposed recently, this study gives an opportunity to take advantage of two years enhanced surveillance for TB disease, instead of taking preventative treatment immediately. After two years the need for preventative treatment is much less. Therefore, participation in this study will offer an opportunity to avoid unnecessary TB treatment.

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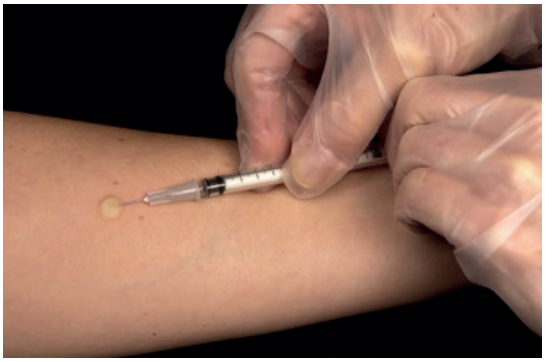
Otherwise, the information obtained from your samples will only be used for health research approved by UK ethics committees. This information will not be made available to you and will not affect your health care in any way. You will have the opportunity to hear about our progress by invitation to scheduled meetings, which will use to update study participants.

WHAT ARE THE DISADVANTAGES TO TAKING PART?

We recognise that your participation involves significant amounts of your time. Each clinic visit is expected to take approximately 30 minutes. All participants will attend the first three visits, for giving consent and undergoing the skin tests. Those who undertake the follow up part of the study will be asked to attend up to seven further clinic appointments at 3 monthly intervals over two years. In order to offset any expenses that you have as result of participating, we will reimburse you £10 for each visit.

The procedures described above have been performed in numerous patients over many years. We have good experience of their safety and we know the vast majority of participants do not have any difficulties.

We recognise that taking blood can cause mild and brief discomfort. In addition, the local anaesthetic that is used at the time of skin biopsies can sting for a few seconds when it is injected, but the skin becomes numb very quickly. Very rarely allergic reactions to the local anaesthetic occur. We will ask you to tell us about any medication you are taking and any previous allergic reactions you have had.



The tuberculin skin test (TST) is widely used to test immune responses to TB

There is a small risk of the biopsy site becoming infected. If this does occur you might need treatment with antibiotics. A small scar might develop at the biopsy site, but often this is barely visible after a few months. There is also a small risk of keloid (firm, raised or fibrous) scarring. Keloid scarring is more common in people with highly pigmented skin, although this risk is low and very unlikely to occur if you have not had this problem before. You may also have a small amount of pain at the

biopsy site after the anaesthetic wears off but this is usually controlled with simple pain relief medicine, like paracetamol or Ibuprofen.

Very rarely, a small wound may appear at the skin test site if the immune response is very strong. This can be treated effectively with anti inflammatory ointments. In the unlikely event that you do experience a strong reaction, we will arrange an appointment for you to be seen for further assessment in an appropriate clinic depending on your personal preferences and circumstances.

In those who agree to defer preventative TB treatment and participate in the follow up part of the study, there is a small risk of developing TB disease in the intervals between clinic visits. On the basis of the available evidence, we have estimated this risk to be less than 1%. In the event that you develop any symptoms of concern between clinic visits, our team will be contactable by telephone and email to see you within one week.

Our research team is made up of nurses and doctors with experience of tuberculosis and trained to carry out all of the steps in this study. You will be able to contact us using the details at the foot of this information booklet if you experience any problems.

Notes:

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WHAT WILL HAPPEN TO THE SAMPLES I GIVE?

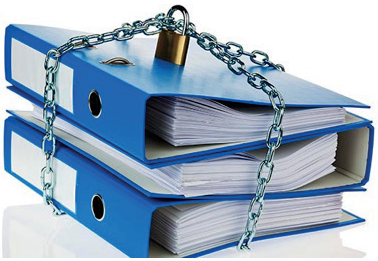
The samples collected in this study will be used to measure immune responses relevant to TB, and how differences in immune responses are related to differences in the genetic (DNA) code.

The blood, tissue and DNA samples collected for this research study will be anonymised by labelling them with a unique identification number before being transferred to research laboratories involved in this study. It may become necessary to transfer samples to other research laboratories inside or outside the United Kingdom for additional analyses related to this study. If this is needed, the samples will be transferred under legally binding restrictions about their use.

In addition, some samples will be stored indefinitely in secure research facilities at UCL in accordance with Human Tissue Authority (HTA) guidelines, for use in future studies related to this one. Research ethics approval will be sought for any additional analysis of these samples.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

All information which is collected about you during the course of the research will be kept strictly confidential. All our research staff will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site. The Chief Investigator of the study will be responsible for ensuring security of your personal information. At the end of the study, all personal information with which you can be identified will be destroyed.



CAN I KNOW THE RESULTS OBTAINED FROM MY STUDY SAMPLES?

Any results that provide evidence of TB disease and may require TB treatment will be explained to you by the study team.

Otherwise, the information obtained from your samples will only be used for health research approved by UK ethics committees. This information will not be made available to you and will not affect your health care in any way. You will have the opportunity to hear about our progress by invitation to scheduled meetings, which will use to update study participants.

WHAT WILL HAPPEN IF I DON'T WANT TO CARRY ON WITH THE STUDY?

You may withdraw from the study at any time. This will not affect your routine health care in any way. If you withdraw from the study we will keep any data or samples that have already been collected for analysis, unless you ask us to destroy these.

WHO IS RESPONSIBLE FOR THIS STUDY

Chief Investigator: **Dr Mahdad Noursadeghi**
Senior Lecturer in Infection & Immunity, University College London
and Honorary Consultant in Infectious Diseases & General Medicine -
Cruciform Building, Gower Street, London WC1E 6BT.

Tel: +44 203 108 2128 / Fax: +44 7053406942

WHAT IF THERE IS A PROBLEM?

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 you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this. In the unlikely event that you are harmed by taking part in this study, compensation may be available.

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If you suspect that the harm is the result of the Sponsor's (XXXXX) or the hospital's negligence, then you may be able to claim compensation. After discussing your concerns with the study team, please make the claim in writing to Dr Mahdad Noursadeghi who is the Chief Investigator for the research and is based at University College London. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

This research is funded by the Wellcome Trust & the study is sponsored by University College London.

WHO HAS REVIEWED THIS STUDY?

This study has been reviewed and approved by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity.

General Data Protection Regulation for health and care research

UCL is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. UCL will keep identifiable information about you for 25 years after the study.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Our Data Protection Officer is Lee Shailer and you can contact them at data-protection@ucl.ac.uk

UCL will collect information about you for this research study from the NHS site you were recruited from. This information will include your name, Hospital number, contact details, blood and x-ray results, current medications and other health diagnosis, which is regarded as a special category of information. We will use this information to check if you are eligible for the study, to monitor your disease progression, contact you for follow up study visits and oversee the quality of the study.

Individuals from UCL and regulatory organisations may look at your research records to check the accuracy of the research study. The only people in UCL who will have access to information that identifies you will be people who need to contact you to discuss the study and arrange study visits or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name and contact details.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be 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.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only 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.

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THANK YOU

Patients and doctors rely increasingly on the results of clinical studies to make sure they are making the right decisions about treatment.

Thank you for taking the trouble to read this information, we hope that it will have been helpful in enabling you to decide whether or not you would like to participate in this study.

CONTACT DETAILS

If you have any questions or would like further information, please contact:

Research Nurse: **Naomi Cocks**

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Hospital of Tropical Diseases
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149 Tottenham Court Road
London
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