Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

European Research Council
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Swiss Tropical and Public Health Institute (Swiss TPH)
Basel, Switzerland
National Center for Tuberculosis and Lung Diseases (NCTBLD)
Tbilisi, Georgia

Consent to be a Research Participant (Patient with Tuberculosis (TB))

Title of the study:	"Linking Within-host and Between-Host Evolution in Multidrug-resistant Mycobacterium tuberculosis" (ECOEVODRTB)
Funding Source(s):	ERC-2019-AdG
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Principal Investigator:	Prof. Sébastien Gagneux
Co-Investigators:	Levan Jugheli, MD, PhD Nestani Tukvadze, MD Sergo Vashakidze, MD, PhD
Study site:	National Center for Tuberculosis and Lung Diseases (NCTLD), Tbilisi, Georgia

We are asking you to volunteer for a medical research study because you have been diagnosed with tuberculosis (TB). This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study at any time. The decision to join or not to join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, you will be provided all necessary standard of care to treat you for TB. Please ask questions if this is not clear. Take your time to think about it and talk it over with family and friends. By signing this study, you will not give up any legal rights.

You will be given a signed copy of the full Informed Consent Form.

Background

What is the purpose of the study?

Mycobacterium tuberculosis (Mtb) can cause infection and sickness – Tuberculosis, in any part of the body, especially in the lungs where it can form cavernous lesions. The treatment of this disease is complex. Additionally, some TB bacteria are resistant to the standard medications used to treat TB infection and are called drug resistant TB. Drug resistant TB is more difficult to treat and requires a long course of medical treatment with alternative medications called second line medications. Recently, new TB drugs have been approved for the treatment of drug resistant TB, however, here is a real danger that resistance to these new drugs will arise rapidly. Generally, little is known on how *Mtb* develops resistance inside TB patients undergoing treatment. Such knowledge could help reduce the development of resistance to these and future new TB drugs. The goal of this study arm is to explore why Mtb is spread so well and to study development of drug resistance within individual patients who undergo surgical intervention as a part of anti-TB treatment.

Specifically, we are asking you to participate in this study, as your treatment plan includes undergoing surgical intervention on your lungs. If you accept to participate, we will use the part of your lung tissue removed during planned surgery (no extra tissue will be removed). This will not be any added procedure to your clinical management and will not interfere with your prescribed routine treatment

Who is eligible for the study?

- ✓ All culture positive pulmonary TB patients undergoing lung surgery, except children and adolescents below 18 years of age and prisoners.

How is the study being done?

We will recruit all TB patients undergoing lung surgery. We will only take advantage of the availability of resected lung tissue samples that were generated because of routine TB treatment processes and would be discarded otherwise.

We will first conduct a brief 20-minute interview with you while you are in the hospital awaiting your TB related surgery. You will be asked about your medical and TB treatment history with specific questionnaire and we will fill additional forms (CRFs) with clinical and laboratory information. After the surgery, resected lung tissue will be used to isolate the *Mtb* bacteria by culture and/or direct molecular test of bacterial DNA. An additional sputum sample will be collected right before the surgery for comparing two research tests - i) direct sequencing (molecular test A) of *Mtb* bacteria (without previous culturing step), and ii) sequencing (molecular test B) of individual *Mtb* colonies after

bacterial culturing on solid growth media. The purpose is to be able to directly compare the *Mtb* bacteria in the sputum to those isolated from the lung tissue. All bacterial *Mtb* isolates will be genetically characterized by whole genome sequencing (molecular test C).

All collected patient data and samples (bacterial *Mtb* isolates and blood) will be coded (pseudonymised) before shipment to research group at Swiss Tropical and Public Health Institute (Swiss TPH) in Basel for further processing.

In summary, if you agree to take part in this study and you sign this consent form the following will be done:

- Doctor will ask your health related questions and will specific forms for the study;
- You will be asked to provide a phone number to contact you in case you need a follow-up visit, which you can refuse to provide without excluding from the study; Your contact information will be kept separately from the research related information and will not be entered into the electronic database;
- Additional sputum sample will be collected right before lung surgery;
- Resected lung tissue will be used for experimental tests in the laboratory;
- All bacterial *Mtb* isolates recovered from all sputum samples and lung resections will be used for laboratory testing;

What are the benefits of this study?

This project provides overall benefit to global scientific community to understand mechanisms of the bacterial and human organism interaction better. It will also directly benefit the National TB Program (NTP) of Georgia, by supporting epi-surveillance of disease. The knowledge gained from the project can lead to better understanding of the *Mtb* strains circulating in the country and identification of transmission hot-spots.

You might also directly benefit from some of the additional molecular analyses performed on samples provided by you (e.g. detection of additional drug resistance) which will help your treating physician to provide better clinical care to you. In case you agree, such additional, incidental findings will be shared with your doctor who will contact you. You can refuse to get any additional information by ticking the "No" box on pg.6, without withdrawal from the study.

Are there any risks and / or burdens?

This study will include several experimental approaches carried out **on the Mtb bacteria** isolated from TB patients in Georgia (as opposed to the patients themselves) in the laboratory. Therefore, risk to the patient is minimal. Obtaining sputum can be considered no more than minimal risk.

Any unforeseen event posing a risk to the participants will be communicated to the ethical committees.

What are my rights if I do choose to participate?

Your participation is completely voluntary, and you have the right to refuse to be in this study. You can stop at any time after giving your consent. This decision will not affect in any way your current or future medical care or any other benefits, to which you are otherwise entitled.

The study doctor/investigator and/or sponsor may stop you from taking part in this study at any time if they decide it is in your best interest, or if you do not follow study instructions. You will be informed of any test results and any other findings relevant to your health that may help you prevent, diagnose and treat existing or future diseases. If you do not wish to be informed, please talk to the study doctor.

Confidentiality

We respect your privacy and we will keep all your information private. No information, that identifies you, will be released without your written permission unless required by law. Your study records will identify you by a subject identification number (numerical code) and not by your name. Any information that identifies you, will not be shared with anyone else (including your spouse or family or health providers) without your written permission. If a research article or publication comes from this study, you will not be identified by name.

The research personnel will not have access to your identifying information. Only coded (pseudonymised) patient data relevant to the project will be transferred to the project personnel. The study-related data will be used by Swiss TPH in accordance with local and EU data protection law. Your medical records may be examined by quality assurance auditors or other authorized personnel appointed by the sponsor, by the appropriate ethics review board members, and by inspectors from regulatory authorities.

Retention and destruction of study data and biological material

The bacterial samples and coded (pseudonymised) data collected during this study will not be destroyed at the end of the project as we are planning to pursue this study long-term in the frame of our on-going collaboration between NCTBLD and Swiss TPH with future funding. Your de-identified data and bacteria extracted from your sputum samples stored on site, as a database/biobank for research purposes, can be sent in encrypted form to another database/biobank in Switzerland as part of this study. Health related data will be stored indefinitely after publication of the research findings. Biological material (bacteria extracted from your sputum) will also be partially stored (backup sample) indefinitely after data collection.

Compensation

We will ask you to conduct additional study related visit to NCTBLD. In relation to these extra visits, we will provide you with transportation. We will not provide any additional incentives for your participation in the study.

It is unlikely that you will suffer any physical harm caused by one of our sample collection procedures. Should this ever occur, you will be treated and fairly compensated for it according to local laws and the liability insurance policy in effect.

Contacts

If you have any questions, concerns or complaints about the research, you may call the Chair of the National Center for Tuberculosis and Lung Disease Ethics Committee: Dr. Paata Aladashvili on his personal phone +995 599559103 or visit him at 50 Maruashvili str, 0101, Tbilisi, Georgia.

Regarding your personal data handling, you can contact Mr. David Leladze (david.leladze@tbgeo.ge), Head of the IT Services.

Consent

We will give you a copy of this consent form to keep. Please read this form carefully. Please ask if you do not understand or want to know something. Your written consent is required for study participation. Nothing in this form can make you give up any legal rights. By signing this form, you will not give up any legal rights. You are free to take home an unsigned copy of this form and talk it over with family or friends.
Please tick the appropriate box if you agree with the statement or not.

Yes/No

- ☐ ☐ I confirm that I have read and understood the content of this document;
- ☐ ☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without medical care or legal rights being affected;
- ☐ ☐ I understand that participation in the study might require to provide an additional sputum sample and blood withdrawal;
- ☐ ☐ I agree to share my contact details (phone number) and outcomes of the tests performed in the study with the National TB Program and the Ministry of Health;
- ☐ ☐ In case of any additional drug resistance findings (incidental findings), I agree for the information to be shared with my doctor and me.
- ☐ ☐ I agree that responsible individuals of the study team, monitors, regulatory authorities or the health professionals responsible for my care, may look at my medical records and data;
- ☐ ☐ I understand that the information that I provide will be stored electronically and will be used for research purposes now or at a later stage in accordance to national guidelines;
- ☐ ☐ I agree to take part in the above study;

_____
Name of Participant (please print)

_____ _____
Signature of Participant Date Time

If the participant cannot read

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

_____

Name of Witness (please print)

_____ _____

Signature of Witness Date Time

_____

Name and role of Person Conducting Informed Consent Discussion (please print)

_____ _____

Signature of Person Conducting Informed Consent Discussion Date Time