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Creating and studying a group of yellow fever-vaccinated individuals to discover factors affecting the immune response to vaccination and acute viral infections

Submission date
17/07/2023

Recruitment status
No longer recruiting

Registration date
26/08/2023

Overall study status
Completed

Last Edited
17/09/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This study, conducted by the Division of Clinical Pharmacology at the University Hospital, LMU Munich, in Germany, aims to understand how people's immune system responds to the yellow fever vaccine and to identify biomarkers - indicators in the blood that might explain the differences in response to the yellow fever vaccine. Yellow fever is a serious disease spread by mosquitoes and is common in parts of Africa and South America. While there is a vaccine to prevent this disease, the human immune response can vary.

Who can participate?
Healthy men and women aged between 18 and 55 years old who are planning to travel to areas where yellow fever is common and have not received a yellow fever vaccine before

What does the study involve?
These participants, who are free from any chronic diseases or acute infections and with women not being pregnant, are asked to receive the yellow fever vaccine, which will be administered according to the recommendation for travelers. The study involves five visits for each participant, one just before the vaccination and four on days 3, 7, 14, and 28 after the vaccination. During these visits, blood samples are collected and the participant is asked questions about their health and background.

What are the possible benefits and risks of participating?
Participants gain dual benefits from this study. Firstly, they receive the yellow fever vaccine, protecting them against the disease in case of travel to affected areas. Secondly, their participation helps further the understanding of the body's response to this vaccine, contributing to future improvements in vaccine development.

However, participation did involve some risks, including mild side effects from the vaccine such as a mild fever or a sore arm at the injection site. Rarely, some individuals might have a serious

reaction to the vaccine, but the study team will closely monitor all participants for any signs of adverse effects.

Where is the study run from?
LMU Munich (Germany)

When is the study starting and how long is it expected to run for?
January 2015 to April 2023

Who is funding the study?
1. iMed program of the German Helmholtz societies (Germany)
2. German Research Foundation (Deutsche Forschungsgemeinschaft) ANR/DFG grant FlavImmunity/ANR-17-CE15-0031-01 (Germany)

Who is the main contact?
Prof. Dr. Simon Rothenfusser, simon.rothenfusser@med.uni-muenchen.de (Germany)

Contact information

Type(s)
Principal investigator

Contact name
Prof Simon Rothenfusser

ORCID ID
https://orcid.org/0000-0003-1151-7614

Contact details
Lindwurmstr. 2a
Munich
Germany
80337
+49-89-4400-57321
simon.rothenfusser@med.uni-muenchen.de

Additional identifiers

Study information

Scientific Title
Establishment and analysis of a yellow fever vaccination cohort for the identification of individual prognostic factors in vaccinations and acute viral infections

Study objectives
The study hypothesizes that there are identifiable biomarkers that correlate with the magnitude and quality of the immune response following yellow fever vaccination. These biomarkers could improve vaccine development and understanding of factors that influence vaccine response.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 26/08/2015, Ethics Committee of the Medical Faculty of the LMU Munich (Pettenkoferstr. 8a, Munich, 80336 München, Germany; +49894400 55191; ethikkommission@med.uni-muenchen.de), ref: 86-16

Study design
Prospective cohort study

Primary study design
Observational

Study type(s)
Prevention, Efficacy

Health condition(s) or problem(s) studied
The condition under investigation is the immune response to yellow fever vaccination in healthy individuals.

Interventions
The yellow fever vaccination with the attenuated YF17D virus is a model system to examine the individual immune response of adult participants exposed to a viral infection under controlled conditions. In addition, it is a paradigm of a successful live vaccine that induces long-time /lifelong protection after a single injection.

The study has three aims. Firstly, an in-depth characterization of the innate and adaptive immune response to YF17D to understand why it is such an effective vaccine. Second, to identify genetic and non-genetic host factors, that influence inter-individual differences in the response to the virus, and third, to identify predictors, including early response parameters, of the individual long-term immune response.

This is a prospective cohort study that includes healthy individuals who received the yellow fever vaccine 17D for travel purposes between 2015 and 2019. After vaccination, participants were invited to take part in five additional visits on days 0, 3, 7, 14, and 28 to collect samples as well as comprehensive demographic and clinical history data.

A novel method of measuring neutralizing antibodies was developed and validated using this cohort. Blood samples are collected and used for high-dimensional immunophenotyping of peripheral blood mononuclear cells (PBMCs) with a spectral analyzer; plasma and serum samples are used to analyze the cytokine and antibody response and the kinetics of replication of the vaccine virus. The study also aims to characterize the immune response of individuals after yellow fever vaccination, investigate the influence of individual genotypes on immune responses, and gain general knowledge about immunological processes in acute viral infection.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
YFV17D vaccine (Stamaril)

Primary outcome(s)
Magnitude and durability of the immune response to the yellow fever vaccine measured by developing and validating a novel method to quantify neutralizing antibodies against the yellow fever virus in participants 14 and 28 days after vaccination

Key secondary outcome(s))
1. Inter-individual variability in antibody response measured by comparing the robustness of the immune response among individuals after vaccination
2. Correlation of biomarkers with vaccine response measured by identifying biomarkers, such as lymphocyte count at day 7 and basophil absolute count, that correlate with the magnitude of the immune response
3. Characterization of peripheral blood mononuclear cells (PBMCs) measured using high-dimensional immunophenotyping with a spectral analyzer, which may provide insight into individual immune responses
4. Evaluation of the cytokine response and the kinetics of vaccine virus replication measured using plasma samples from participants

Completion date
28/04/2023

Eligibility

Key inclusion criteria
1. Male or female individuals between the ages of 18 and 55 years old
2. Healthy with no acute infections or chronic diseases
3. Women must have a negative pregnancy test
4. Willingness to provide written informed consent after being thoroughly informed of the risks and benefits of the study
5. Availability for all study time points (i.e., able to attend all study visits)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
All

Total final enrolment
250

Key exclusion criteria
1. Pregnant or lactating women
2. Previously received a yellow fever vaccination
3. Pre-existing flaviviral diseases such as dengue fever or West Nile virus infection
4. Known allergies to egg or egg components or aminoglycosides
5. A temperature greater than 38°C on the day of study entry or an acute illness (with or without fever) on the same day
6. Receipt of any other vaccination less than 30 days before the study
7. A history of autoimmune diseases or immunosuppression
8. Known anaphylactic or allergic reactions
9. Using unregistered drugs or drugs in clinical trials
10. Clinically significant mental illness
11. Receipt of immunoglobulins or blood products within three months of the study or are planning to do so during the study
12. Injection drug users
13. Ongoing tumor diseases
14. Past or current manifestations of haematological, renal, hepatic, pulmonary, CNS, cardiovascular, or gastrointestinal diseases
15. Anyone deemed by the investigator to not be compliant with the study objectives and protocol
16. A foreseeable absence from the study center during the study period, such as due to a planned vacation

Date of first enrolment
01/10/2015

Date of final enrolment
31/07/2019

Locations

Countries of recruitment
Germany

Study participating centre
LMU Munich, Division of Clinical Pharmacology
University Hospital
Lindwurmstrasse 2a
Munich
Germany
80337

Study participating centre

LMU Munich, Division of Infectious Diseases and Tropical Medicine
University Hospital
LMU Munich
Leopoldstrasse 5
Munich
Germany
80802

Sponsor information

Organisation
Ludwig Maximilian University of Munich

Funder(s)

Funder type
Research organisation

Funder Name
Helmholtz Association

Alternative Name(s)
Helmholtz-Gemeinschaft, Объединение имени Гельмгольца, , Helmholtz Association of German Research Centres

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Germany

Funder Name
Deutsche Forschungsgemeinschaft

Alternative Name(s)
German Research Association, German Research Foundation, Deutsche Forschungsgemeinschaft (DFG), DFG

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Dr. Simon Rothenfusser, simon.rothenfusser@med.uni-muenchen.de; data requestors must sign a data access agreement to gain access. De-identified individual participant data that underlie the results reported in articles, including tables, figures, and appendices, can be provided after publication. Please note that privacy and ethical restrictions may apply.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/02/2024	17/09/2024	Yes	No
Preprint results		07/05/2023	24/07/2023	No	No