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# Immunity to liver-stage Plasmodium falciparum malaria parasites

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| **Submission date**<br>27/10/2022 | **Recruitment status**<br>Recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>07/11/2022 | **Overall study status**<br>Ongoing | |
| **Last Edited**<br>10/06/2025 | **Condition category**<br>Infections and Infestations | |

**Plain English summary of protocol**

Background and study aims
Malaria is a major cause of death in endemic regions of the world. The malaria parasite Plasmodium falciparum has an initial asymptomatic (without symptoms) life stage within the human host (liver stage). Further development of the parasite at the liver stage would prevent progression into the pathogenic (disease-causing) blood stage. As a result, the liver stage is a target for many current malaria vaccine candidates, but immunity against this stage is not well understood. This study aims to provide further insights into immunity to liver-stage Plasmodium falciparum.

Who can participate?
Patients aged over 18 years undergoing medically-indicated partial liver resection (surgery to remove part of the liver) for underlying disease

What does the study involve?
1. 6 ml blood will be drawn for HLA-A2 phenotyping
2. 24 ml blood will be drawn before liver surgery through an existing line
3. Liver tissue will be obtained that is not required for diagnostic purposes and would otherwise be considered medical waste, which will be processed to obtain hepatocytes (liver cells) and liver-resident immune cells

What are the possible benefits and risks of participating?
There is no direct benefit to study participation. The risks associated with blood samples are minor and there is no additional risk to patients associated with the processing of already-removed liver tissue.

Where is the study run from?
Radboud University Medical Center (Netherlands)

When is the study starting and how long is it expected to run for?
December 2019 to June 2026

Who is funding the study?
Radboud University Medical Center (Netherlands)

Who is the main contact?
Dr Matthew B.B. McCall, matthew.mccall@radboudumc.nl

# Contact information

### Type(s)
Principal investigator


### Contact name
Dr Matthew B. B. McCall

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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
NL72410.091.19

# Study information

### Scientific Title
Immunity to liver-stage Plasmodium falciparum in peripheral and tissue-resident immune cells

### Acronym
LYTIC

### Study objectives
In this study the researchers will establish an in vitro assay using leukocytes (CD8+ T cell line, fresh peripheral blood mononuclear cells [PBMCs] and liver-resident lymphocytes) in combination with freshly isolated human hepatocytes to study respectively cytolytic T cell and innate immune recognition and killing of P. falciparum-infected hepatocytes

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 18/05/2020, METC Oost-Nederland (Postbus 9101, 6500 HB Nijmegen, Netherlands; +31 (0)24 361 31 54; metcoost-en-cmo@radboudumc.nl), ref: 2019-6064

## Study design
Single-centre investigator-initiated exploratory study

## Primary study design
Observational

## Study type(s)
Other

## Health condition(s) or problem(s) studied
Antimalarial immune response to liver-stage P. falciparum

## Interventions
An observational study applying HLA-A2 phenotyping; isolation of hepatocytes and intrahepatic immune cells; expansion of a circumsporozoite protein (CSP)-specific CD8+ T cell line; antimalarial immune response to liver-stage P. falciparum

1. 6 ml blood will be drawn by venepuncture upon receipt of informed consent for HLA-A2 phenotyping
2. 24 ml blood will be drawn prior to liver surgery via an existing intravenous or arterial line
3. Liver tissue will be obtained from the recruited patients undergoing medically-indicated partial liver resection for underlying disease, that is not required for diagnostic purposes and would otherwise be considered medical waste, and processed to obtain hepatocytes and liver-resident immune cells

## Intervention Type
Other

## Primary outcome(s)
Measured at the surgery visit:
1. Recognition of P. falciparum-infected hepatocytes by CSP-specific cytolytic CD8+ T cells and hepatic and peripheral innate/innate-like lymphocytes measured using flow cytometry
2. Killing of P. falciparum-infected hepatocytes by CSP-specific cytolytic CD8+ T cells and hepatic and peripheral innate/innate-like lymphocytes measured using fluorescence microscopy

## Key secondary outcome(s))
Measured at the surgery visit:
1. Recognition and killing of P. falciparum-infected hepatocytes by CSP-specific cytolytic CD8+ T cell line measured using flow cytometry and fluorescence microscopy
2. Differences in recognition and killing of P. falciparum-infected hepatocytes between liver-resident and peripheral lymphocytes measured using flow cytometry and fluorescence microscopy
3. The individual lymphocyte (sub-)populations which contribute to the recognition and killing of P. falciparum-infected hepatocytes, identified using flow cytometry

### Completion date
30/06/2026

## Eligibility

### Key inclusion criteria
1. Aged 18 years and above
2. Scheduled for partial liver resection for underlying disease
3. Signed written informed consent

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Sex
All

### Key exclusion criteria
1. Known receipt of immunosuppressive or cytostatic agents within the past 3 months, except the use of topical and inhaled steroids
2. Known human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV) infection, or other known clinically-relevant immunodeficient state

### Date of first enrolment
14/11/2022

### Date of final enrolment
31/05/2026

## Locations

### Countries of recruitment
Netherlands

### Study participating centre
**Radboud University Medical Centre**
Department of Medical Microbiology
Geert Grooteplein Zuid 28
Nijmegen

Netherlands
6525 GA

# Sponsor information

**Organisation**
Radboud University Nijmegen Medical Centre

**ROR**
https://ror.org/05wg1m734

# Funder(s)

**Funder type**
University/education

**Funder Name**
Radboud Universitair Medisch Centrum

**Alternative Name(s)**
Radboudumc, Radboud University Medical Center, Radboud University Nijmegen Medical Center, RUNMC

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Universities (academic only)

**Location**
Netherlands

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated and/or analysed during the current study will be available upon request from the Principal Investigator (Matthew B.B. McCall, MD PhD; matthew.mccall@radboudumc.nl). Requests will be reviewed by a Data Access Committee and data sharing conditions agreed upon in a Data Use Agreement. Identifiable data will not be shared.

The type of data that will be shared: anonymised immunological data that are generated in the study (identifiable data will not be shared)

Timing for availability: data will be available after the publication of primary and secondary outcomes in a peer-reviewed journal (latest 1 year after the end of the study)
Whether consent from participants was required and obtained: written consent from all study participants will be obtained; consent includes permission to use data for other purposes related to liver-stage immunity
Comments on data anonymization: data will be pseudonymised: Study participants will be assigned a study identification code (LYTIC001, LYTIC002, etc). Study identification codes will be assigned by the study nurse in a chronological order where 001 will be assigned to the first study participant being enrolled and 002 to the second study participant. Study identification codes do not contain identifying elements. Study identification codes will be documented on the subject identification log which will be stored separately from all study documents containing identifiable data.
Any ethical or legal restrictions: Export of data outside the EU may be subject to restrictions; human tissue samples shall be stored for a maximum of 15 years; study data shall be stored for a minimum of 20 years.
Any additional comments: Data will be shared upon reasonable request, as assessed by the principal investigator and sponsor

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | version 3 | 27/03/2020 | 04/11/2022 | No | Yes |
| Participant information sheet | version 4 | 07/11/2022 | 17/04/2023 | No | Yes |
| Participant information sheet | version 6 | 07/06/2024 | 30/10/2024 | No | Yes |
| Protocol file | version 3.0 | 21/04/2020 | 04/11/2022 | No | No |
| Protocol file | version 4 | 31/10/2022 | 17/04/2023 | No | No |
| Protocol file | version 6 | 07/06/2024 | 30/10/2024 | No | No |