

# Immunity to liver-stage Plasmodium falciparum malaria parasites

<b>Submission date</b> 27/10/2022	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 07/11/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 10/06/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## 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

**ORCID ID**  
<https://orcid.org/0000-0002-2473-0943>

**Contact details**  
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## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
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

### **Secondary study design**

Immunological study

### **Study setting(s)**

Hospital

### **Study type(s)**

Other

### **Participant information sheet**

See study outputs table

### **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<sup>+</sup> 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 measure**

Measured at the surgery visit:

1. Recognition of *P. falciparum*-infected hepatocytes by CSP-specific cytolytic CD8<sup>+</sup> 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

### **Secondary outcome measures**

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

### **Overall study start date**

23/12/2019

### **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

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

45

### **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

**Sponsor details**

Department of Medical Microbiology,

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6525 GA

+31 (0)24 361 3663

malariavaccin@radboudumc.nl

**Sponsor type**

University/education

**Website**

<https://www.radboudumc.nl/en/research/departments/medical-microbiology>

**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

**Publication and dissemination plan**

A final report will be prepared by the investigators at the Radboudumc and will be signed by the investigator. The investigator and sponsor will make every effort to publish the results in a peer-reviewed journal.

**Intention to publish date**

30/06/2026

**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?
<a href="#">Participant information sheet</a>	version 3	27/03/2020	04/11/2022	No	Yes
<a href="#">Protocol file</a>	version 3.0	21/04/2020	04/11/2022	No	No
<a href="#">Participant information sheet</a>	version 4	07/11/2022	17/04/2023	No	Yes
<a href="#">Protocol file</a>	version 4	31/10/2022	17/04/2023	No	No
<a href="#">Participant information sheet</a>	version 6	07/06/2024	30/10/2024	No	Yes
<a href="#">Protocol file</a>	version 6	07/06/2024	30/10/2024	No	No