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A study of immune memory responses across tissues

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06/10/2026

Recruitment status
Recruiting

Registration date
20/11/2026

Overall study status
Ongoing

Last Edited
20/11/2026

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Faulty regulation of the immune system contributes to multiple diseases including inflammatory arthritis, cardiovascular disease and cancer, and as such represents a leading cause of disability and death worldwide. Whilst there have been revolutionary advances in our understanding of how to use drugs to target abnormal immune responses or harness the immune system's ability to fight disease, there remains huge unmet need for both new agents and the repurposing of established drugs.

Unfortunately, as many as 9 in every 10 promising drugs studied in human clinical trials ultimately fail and are abandoned prior to regulatory approval, stifling innovation and contributing to increased costs for the drugs that do make it to market. A significant number of these failures can be attributed to incorrect decision making early in development, where information gained in the laboratory or in animal studies fails to translate to intended effects in patients.

One approach to improve the efficiency of the drug development process is the use of human immune challenge studies. In these studies, healthy volunteers are given small amounts of substances which are foreign to their immune system to provoke a temporary response: the 'challenge'. Depending on the nature and dose of the challenge, the body's immune system will react in a different but predictable way, elements of which mimic those seen in disease, thereby 'modelling' them. These models can help safely bridge the gap between animal experiments and patient groups and, if sufficiently understood, test the effect of new drugs without exposing patients to risk. Sadly, whilst immune challenge models have been used in drug development for many years, the approach is greatly limited by our lack of understanding of the stability and longevity of immune responses over extended periods of time.

The purpose of this research is to better understand and describe the long-term stability of a common method of immune challenge which uses a protein called 'Keyhole Limpet Haemocyanin' (KLH). KLH is available as a highly-purified formulation, and because it is not usually encountered by the human immune system (it is derived from an inedible shellfish), it allows us to study the development of immune responses right from the time it is administered. We plan to give groups of healthy volunteers a set dose of KLH alongside an 'immune-boosting' agent (Montanide ISA™51, commonly referred to as an adjuvant). We will then re-challenge all the volunteers by injecting a set dose of KLH into the skin on their forearms, similar to an allergy test, taking images, blood samples and skin biopsies. By rechallenging participants up to three

times over the course of 3 months, we aim to understand the nature, time course, and variability of the immune response in each individual. We will also assess the impact of rechallenging at spatially distinct locations on the skin, and whether this impacts the response to KLH. In addition, in some participants, we will assess the responses in axillary lymph nodes (small organs in the armpit which coordinate the immune response), through the use of a technique called fine needle aspiration. No previous studies have directly explored the impact of repeated local rechallenge on KLH immune responses. The results will help us describe the variability of KLH memory responses over time, which will inform pharmacological studies aiming to compare responses before and after drug treatment, within an individual. In turn, we hope this will help improve the percentage of drugs progressing from concept to clinical therapy, addressing unmet health needs.

Who can participate?
Healthy volunteers aged 18 - 45 years old

What does the study involve?
1. You will be given injections of keyhole limpet haemocyanin (KLH; trade name: Immucothel) into the muscle or skin, on three occasions, with or without a medicine ('adjuvant') which helps the immune response (Montanide ISA-51). All these products are used clinically and are manufactured to the standard of medicines.
2. You will have to attend a screening visit, where we will ask questions about your health, perform a physical examination, and take a blood sample. If you are eligible based on the screening assessment and decide to take part, you will have to attend the research facility a further 5 to 7 occasions over up to 91 days, for 30 mins to two hours per visit.
3. You will be closely monitored by the study team with a range of tests and procedures, including questionnaires, physical examinations, blood tests, skin imaging using Laser Speckle Imagers.
4. For Group 1, on four of the visits (visits 1, 3, 5, and 7) we will take a tiny sample of skin (punch skin biopsy) from your forearm (four samples total), using local anaesthetic.
5. For Group 2 and Group 3, on the final visit (visit 6) we will take a tiny sample of skin (punch skin biopsy) from your forearm (four samples total), using local anaesthetic.
6. For Group 4 and Group 5, on two of the visits (visits 3 and 5) we will take samples of the lymph nodes in your armpits (left and right) using a very thin needle, using local anaesthetic. On the final visit we will take a tiny sample of skin (punch skin biopsy) from your forearm (two samples total), using local anaesthetic.
7. You will be free to withdraw from the study at any time you wish.

What are the possible benefits and risks of participating?
We will reimburse £710 to £890 for completing all study procedures and follow-up, depending on the group allocation. This amount is calculated based on the estimated cost of travel to attend the visits, total number and type of study procedures performed, and the duration of each study visit. The participant will not gain any direct benefit from the study. We hope that the information we gather from this and future studies will help us to develop new treatments for diseases caused by, or affecting the immune system.
Keyhole Limpet Haemocyanin (Immucothel) is a highly purified protein obtained from the blood of an inedible shellfish. It
has been used for over 50 years for challenge studies similar to ours, at doses up to 5 times greater than those used in our study. The specific product we are using (Immucothel) is a registered medicine in some countries. Expected common (more than 1 in 10 risk) adverse effects are limited to mild responses at the injection site e.g. pain, redness, warmth, swelling, tenderness or itching. Other potential foreseeable risks (less than 1 in 10 risk) would be similar to those seen with standard vaccinations, including mild systemic reactions e.g. flu-like illness

with feverishness, fatigue, malaise, arthralgia, sore muscles and headache. In almost all cases we would expect these to last no more than a few days. In very rare cases (less than 10,000 risk), local reactions could be more severe. If this were to occur we would not give any further injections and would withdraw you from the study, while also providing any appropriate medical care that you might need, or referring you to your GP or other NHS service as required. There are some very rare but serious adverse effects that can occur with commonly used vaccinations. Although KLH is not a vaccine, it is similar to a vaccine in that it is foreign to the body and provokes an immune response, and it is therefore reasonable to expect a similar potential for these adverse effects. These include severe allergy (anaphylaxis) and problems with nerves such as Guillain-Barre Syndrome. The risk of these is extremely low (1 to 2 in a million risk).
Montanide ISA-51 is a mineral oil-based adjuvant, extensively studied for enhancing vaccine responses. Montanide ISA-51 can cause transient local skin reactions, including swelling, redness, pain, and itch (approximately 1 in 10 risk). Occasionally
(less than 1 in 100 risk) Montanide ISA-51 has been associated with systemic effects such as fatigue, and fever, which would be expected to disappear in no more than a day or two. In rare situations (less than 1 in 1000 risk), more severe local
reactions have been observed. These side effects were not reported in the two previous studies which combined KLH with Montanide ISA-51 at the same doses used in this study, thus the risk of these more severe side effects is considered to
be low (less than 1 in 1000 risk).
To minimize the risk of problems all study procedures will be performed by experienced professionals using appropriate precautions and equipment.
If you take part in the study and complete all follow-up the total amount of blood taken will be between 173 to 203 mL, depending on your group allocation which is less than half of a standard blood donation. As such it would not be expected to cause problems for an otherwise healthy volunteer. The blood donation itself requires the use of a needle into a vein of the arm, and this can cause minor bruising and tenderness in around 1 in 10 people, and occasionally feeling faint or actually fainting (in around 1 in 20 to 1 in 100 people). We will provide food and water following blood donation. Very rarely, in less than 1 in 10,000 people, sites of blood tests can become infected and require antibiotic treatment (we will provide these, unless you require treatment outside of normal working hours, at which point we would direct you to normal NHS services). The blood tests will be taken by experienced members of the study team which should minimize the risks of side effects.
Intramuscular injection is a commonly performed procedure for the administration of medicines, including vaccines. The potential risks commonly include (1 in 10 likelihood) minor discomfort on injection, minor bruising, tenderness, and
occasionally feeling faint or actually fainting (1 in 20 to 1 in 100 people). There can also be discomfort for a few days afterwards due to bruising related to the injection, and due to the body's response to the KLH (+/- adjuvant) injection. Very rarely sites of injections can become infected and require antibiotic treatment (less than 1 in 10,000 risk). The injections will be performed by experienced members of the study team which should minimize the risks of side effects.
The risks of intradermal injection are similar to those of intramuscular injection. Intradermal injections can cause stinging at the time of injection. There can also be discomfort, redness, and itching for a few days afterwards. Very rarely (in less than
1 in 10,000 people) a small sore can form at the time of injection which can longer to heal or cause scarring.
Skin punch biopsy is a commonly performed diagnostic procedure. The potential risks (1 in 10 people) include minor bruising, bleeding, and skin discomfort. A 4-6mm punch biopsy will be performed using local anaesthetic to reduce discomfort. The injection of anaesthetic can cause stinging during injection which fades quickly as the anaesthetic takes effect. It is common (in at least 1 in 10) for a small scar or persistent skin discoloration to be visible once the skin has

healed—this usually fades over time but may be permanent. In rare cases (less than 1 in 1000), certain individuals can develop more prominent scars (called keloids). We will exclude people from the study who are known to have developed keloids previously, or have a family history of this, because we know this increases the risk of keloids. There is a very small risk (1 in 50) of infection following skin biopsy—this is minimized by use of skin antiseptic at the time of biopsy, and careful technique of the doctor performing the biopsy.
Lymph node fine needle aspiration is a safe, minimally invasive procedure performed in routine clinical diagnostic practice – but as with any medical intervention, it carries some risk. The procedure should not be any more uncomfortable than a blood test and commonly results in mild discomfort, bruising, or swelling in at least 1 in 10 people. Any tenderness afterwards will resolve. You can take a simple painkiller like paracetamol if you need it; avoid taking aspirin, as this may increase the risk of bruising. The needle used is fine, but bleeding under the skin may sometimes occur after the procedure in around 1 in 100 people. It usually stops quickly by itself. Any bruising will fade within 2 weeks. The risk of bleeding is higher if you are taking any medications that make your blood thinner such as warfarin, aspirin or clopidogrel. If you regularly take any of these medications you will not be able to participate in the study. If you take any aspirin or blood thinning medication in the 7 days before the FNA procedure please let us know.
Infection after FNA is rare (less than 1 in 1000 risk). If you get redness, pain and/or tenderness in the days afterwards you may need antibiotic treatment. It is possible for the needle used in a fine needle aspiration (FNA) procedure to damage underlying structures; however, such occurrences are extremely rare (occurs in less than 1 in 10,000 people). Among these, a rare (less than 1 in 10,000 risk) but potential complication of FNA of axillary (armpit) lymph nodes is a pneumothorax.
This occurs when air leaks into the space between the lung and chest wall, which can cause pain and, in some cases, difficulty breathing. A small pneumothorax can heal by itself with rest. Fine needle aspiration procedures are conducted under ultrasound guidance to prevent this from happening. If the doctor is not able to collect enough sample, he/she may decide to repeat the FNA with your permission.

Where is the study run from?
Oxford Experimental Medicine Clinical Research Facility (EMCRF) (UK)

When is the study starting and how long is it expected to run for?
September 2026 to December 2028

Who is funding the study?
UCB Biopharma SRL

Who is the main contact?
Dr Rajalakshmi Punampalam, translationalpharmacology@ndorms.ox.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Integrated Research Application System (IRAS)
370141

National Institute for Health and Care Research (NIHR)
PID19708

Study information

Scientific Title
Investigating the human biology of resident immunity in tissue via neoantigen challenge (INHABIT)

Acronym
INHABIT

Study objectives
Primary objective:
To enumerate T cells in the skin following successive rechallenges with KLH

Secondary objective:
To describe the degree of T-helper cell skewing following multiple KLH rechallenge

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 01/07/2026, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (2 Redman Place, London, EC20 1JQ, United Kingdom; +44 (0)207 104 8000; cambsandherts.rec@hra.nhs.uk), ref: 26/EE/0143

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Basic science

Study type(s)

Health condition(s) or problem(s) studied
Basic science study of neoantigen and recall immune responses in healthy volunteers

Interventions
Part A (serial rechallenges) - Group 1 (n = 18):
IM dose subunit KLH 1000 µg plus Montanide ISA-51 day 0, followed by ID KLH 10 µg at days 28, 56, and 84.

Part B (multi-site multiple rechallenge) - Group 2 (n = 6):
IM dose subunit KLH 1000 µg plus Montanide ISA-51 day 0, followed by injections at 4 sites on forearms on days
28 and 56 with either 10 µg KLH or 0.9% saline.

ID injections (day 28, day 56):
1. KLH, KLH
2. KLH, Saline
3. Saline, KLH
4. Saline, Saline

Part B (Multi-site multiple rechallenge) - Group 3 (n=6):
IM dose subunit KLH 1000 µg plus Montanide ISA-51 day 0, followed by injections at four sites on forearms on days
56 and 84 with either 10 µg KLH or 0.9% saline.

ID injections (day 56, day 84):
1. KLH, KLH

2. KLH, Saline
3. Saline, KLH
4. Saline, Saline

Part C (mapping memory T cell responses across multiple tissues) - Group 4 (n = 8):
IM dose subunit KLH 1000 µg plus Montanide ISA-51 day 0, followed by ID KLH 10 µg and 0.9% saline injections at two sites on forearms at day 28.

Part C (mapping memory T cell responses across multiple tissues) - Group 5 (n = 8):
IM dose subunit KLH 1000 µg plus Montanide ISA-51 day 0, followed by ID KLH 10 µg and 0.9% saline injections at two sites on forearms at day 28.

Additional study procedures occurring following main study participation (all groups, optional for all study participants)
Repeat re-challenge ID dose subunit KLH 10 µg.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Subunit KLH (Immucothel ™, Biosyn Corporation, Fellbach, Germany), Montanide ISA™-51 VG adjuvant (Seppic, Paris, France) – referred to throughout as Montanide ISA-51

Primary outcome(s)
1. T cell enumeration measured using T cell number per gram of cutaneous tissue after each rechallenge at day 0, 35, 63 and 91 (study part A)

Key secondary outcome(s)
1. Degree of T-helper cell skewing following multiple KLH rechallenge measured using the number of IFN- γ (TH1) and IL-4 (TH2) producing PBMCs in response to KLH stimulation by ELISpot in each group (cells per 10e6 PBMC), and ratio of TH1:TH2 antigen responsive cells at day 0, 28, 35, 56, 63, 84 and 91 (study part A)

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study and is able to comply with the study protocol
2. Male or female, 18—45 years of age inclusive, at the time of signing the informed consent
3. Healthy as determined by a physician, based on a detailed medical history and a complete physical examination, including vital signs and laboratory measurements
4. Body mass index (BMI) within the range 18 to 35 kilogram/meter squared (inclusive)
5. Females of childbearing potential are eligible to enter if they are not pregnant (negative pregnancy test on the day of both screening and vaccination) and willing to use effective methods of contraception to prevent pregnancy from the time of first dose to 60 days after the

last dose
6. Male participants with female partners of child-bearing potential: must agree to use effective methods of contraception from the time of the first dose of challenge agent to 60 days afterwards
7. Sufficient English language ability to enable appropriate informed consent procedures to be conducted in English

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Antibiotics or antiviral therapy after a serious illness within 30 days of study entry
2. Any use of immunosuppressant or immunomodulatory agents (systemic or topical) in 3 months prior to study entry, including anticoagulant or antiplatelet drugs
3. Chronic medical conditions with potential effect on immune responses including diabetes, significant history of atopy, or any condition that, in the opinion of the investigator, would interfere with the study
4. Presence of tattoos, naevi or other skin abnormalities such as keloids (or history of keloids) that may, in the opinion of the investigator, interfere with study assessments or increase the risk of an adverse outcome from study procedures (e.g. skin biopsy healing)
5. Pregnant or breastfeeding (lactating) females, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
6. Allergy to KLH, Montanide ISA-51, related vaccine adjuvants, or components of the study challenge agents
7. Allergy to shellfish
8. History of schistosomiasis (confirmed or highly suspected based on clinical history or epidemiological risk factors, or due to potential cross-reactive immune responses to KLH)
9. Previous exposure to Keyhole Limpet Haemocyanin, e.g. in the context of a previous study, except for existing KLH-exposed participants who have been recalled for optional KLH rechallenge in the skin
10. Participants participating, within 60 days of screening, in recreational sun-bathing, or use of a sunbed, on the area of the skin from wrist to shoulder inclusive
11. Received phototherapy within 4 weeks prior to screening visit and 6 weeks of the baseline visit
12. Phobia of needles or minor surgical procedures

13. Current smoker or using nicotine replacement therapy
14. Participants receiving any vaccinations within 30 days prior to screening visit, or will require vaccination prior to the end of study follow-up
15. Any other significant disease, disorder, or finding, which, in the opinion of the investigator, may either put the participant at risk, affect their ability to participate in the study or impair interpretation of the study data

Date of first enrolment
21/09/2026

Date of final enrolment
30/09/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Experimental Medicine Clinical Research Facility (EMCRF)
Churchill Hospital, Headington
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OX3 7LE

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type

Funder Name
UCB Pharma

Alternative Name(s)
UCB Pharma Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available