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Lymph node flu and COVID-19 vaccine responses in younger or older adults

Submission date 05/09/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 15/09/2023	**Overall study status** Completed	
Last Edited 17/11/2026	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
This study investigates how lymph nodes cells respond to vaccines and how this changes as we age. Older people typically respond less well to vaccines than younger adults, and they are more affected by diseases such as flu and COVID-19, so it is important to understand how age influences the immune system. This will help us develop age-bespoke vaccines for younger and older people. Lymph nodes are small bean-shaped organs present all over the body. After a vaccine is given in the arm, the lymph nodes in the armpit swell in response. Inside the lymph nodes are cells that develop antibodies and cells in response to the vaccine. These antibodies and cells protect us from infection after we have had a vaccine. Lymph node cells can be sampled using a needle under ultrasound guidance. This is called fine needle aspiration (FNA) and it is a well-established test in the clinic; in research it enables direct testing of immune cells. This information will help design future vaccines for different populations, e.g., younger or older people.

Who can participate?
Healthy adults in two age groups: 18-45 years and 65 years and over

What does the study involve?
All participants will receive one dose of COVID-19 booster vaccination and one dose of seasonal influenza vaccine into the opposite arm. Participants will be randomly allocated to have a fine needle aspiration (FNA) biopsy of axillary lymph nodes on both sides at two timepoints; either 7 days, 14 days, or 28 days (determined by randomisation) and at 84 days after the study injections. Each study visit will consist of a blood draw and collection of information on serious adverse events.

What are the possible benefits and risks of participating?
The recruitment population may directly benefit from participation in the study. This is because the individuals will be vaccinated with licensed vaccines against influenza and COVID-19. No specific additional medical care will be provided through participation, and medical procedures are performed with the aim of determining eligibility and safety during the study. The risks are limited to localised bruising and discomfort can occur at the site of blood sampling and fine needle aspiration of lymph nodes.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
August 2023 to September 2026

Who is funding the study?
1. Medical Research Council (UK)
2. UK Research and Innovation (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
328280

Central Portfolio Management System (CPMS)
56845

Study information

Scientific Title
An experimental medicine study of influenza and COVID-19 vaccine immune challenge responses in Lymph nodE single-cell Genomics in AnCestrY and ageing (LEGACY03)

Acronym
LEGACY03

Study objectives
This study aims to understand how we respond to vaccines and how this changes as we age. This information will be valuable for developing vaccines against commonly circulating viruses and future pandemics.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/08/2023, North East – Newcastle & North Tyneside 2 REC (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8086, +44 (0)207 104 8140, +44 (0)207 104 8016; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 23/NE/0154

Primary study design
Interventional

Study design
Non-randomized; Interventional; Design type: Prevention, Vaccine

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Flu and COVID-19 vaccine responses

Interventions
1. Fine needle aspiration (FNA) of axillary lymph nodes
2. Non-diagnostic ultrasound

3. Study injection: seasonal influenza vaccine, COVID-19 vaccine given contemporaneously as intramuscular injections into the right and left arms. The influenza vaccine is given into the right arm and the COVID-19 vaccine into the left arm

All participants will receive one dose each of the two vaccines in different arms. Participants will be randomly allocated to undergo FNA to collect lymph node cells from both armpits at either 7 or 14 or 28 days, with another FNA for all participants at 84 days after study injections (vaccination). Participants will be assessed for eligibility at a screening visit; those eligible to take part will attend a further 7 visits over 13 weeks. Blood samples will be taken at each visit.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Seasonal influenza vaccine, COVID-19 vaccine

Primary outcome(s)
The frequency, phenotype, and function of immune cells in axillary secondary lymphoid tissue and blood after intramuscular immunisation, measured using single-cell ribonucleic acid sequencing (scRNA-seq) to measure cell-by-cell transcriptomes in lymph node cells and/or multiparameter flow cytometry, at Day 0, 7, Day 14 and Day 28 and Day 84 after the study injection

Key secondary outcome(s)
Reactive lymph nodes defined using ultrasound measurements of secondary lymphoid tissue at Day 0, 7, Day 14, Day 28, and Day 84 after study injection

Completion date
01/09/2026

Eligibility

Key inclusion criteria
1. Adults aged between 18 to 45 years (inclusive) OR aged 65 years and over
2. Medically stable (i.e., according to investigator's judgement, it is not anticipated that the participant will require hospitalisation within the study period or that they will need to withdraw from the study for medical reasons before completion of protocol-specified follow-up). A stable medical condition is defined as disease not requiring significant change in therapy or hospitalisation for worsening disease during the 90 days prior to enrolment.
3. Able to attend the scheduled visits and to comply with all study procedures, including internet access for the recording of electronic diaries
4. Willing and able to give informed consent for participation in the study
5. Agree to allow study staff to contact his or her GP or equivalent NHS databases to access the participant’s vaccination records and medical history
6. Willing to allow their GP and/or consultant, if appropriate, to be notified of participation in the study
7. Willing to provide their national insurance number or passport number to be registered on The Over-Volunteering Prevention System (TOPS)

8. Agree to refrain from blood donation whilst in the study
9. For participants of childbearing potential only (as defined by protocol). Willing to use effective contraception established for the duration of enrolment in the study AND have a negative pregnancy test on the days of screening and study injections.
10. Have received at least a primary (two-dose) schedule of any MHRA, UK-authorised or licenced COVID-19 vaccine.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
53

Key exclusion criteria
1. Participation in another research study involving an investigational product, or which includes procedures that could compromise the integrity of this study (such as significant volumes of blood already taken), within the 12 weeks prior to enrolment, or planned participation in such a study within the study period.
2. Body mass index >=35 kg/m²
4. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate.
5. Administration of regular anticoagulation medication likely to induce bruising or bleeding on fine needle aspiration.
6. Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; severe infection(s); receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months, or long-term systemic corticosteroid therapy (including for more than 7 consecutive days within the previous 3 months).
7. History of anaphylaxis in relation to vaccination, or local anaesthetic such as lidocaine.
8. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine including hypersensitivity to the active substance or to any of the excipients of the experimental vaccine or to local anaesthetic such as lidocaine.
9. History of hereditary angioedema, acquired angioedema, or idiopathic angioedema.
10. History of cancer that is not resolved (except basal cell carcinoma of the skin and cervical carcinoma in situ).
11. History of any serious psychiatric condition likely to affect participation in the study.

12. For participants of childbearing potential only: participants who are pregnant, breastfeeding or lactating, or are planning pregnancy during the study.
13. History of a bleeding disorder (e.g., factor deficiency, coagulopathy, or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture.
14. History of confirmed major thrombotic event (including cerebral venous sinus thrombosis, deep vein thrombosis, pulmonary embolism); history of antiphospholipid syndrome, or history of heparin-induced thrombocytopenia.
15. History of episodes of capillary leak syndrome.
16. Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, or neurological illness, as judged by the Investigator (note, mild/moderate well-controlled co-morbidities are acceptable)
17. Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 42 units per week.
18. Suspected or known injecting drug use within the 5 years preceding enrolment.
19. Detectable circulating hepatitis B surface antigen (HBsAg).
20. Seropositive for hepatitis C virus (antibodies to HCV).
21. Seropositive for HIV.
22. A history of pericarditis, myocarditis or other cardiac inflammation deemed significant by the investigator
23. Any clinically significant finding on screening investigations, that are either unlikely to resolve or do not resolve on repeat testing (at the discretion of an Investigator) within the recruitment timeline of the study.
24. Member of the study team. This is deliberately loosely defined, but at a minimum will include: anyone on the delegation log; anyone who might be anticipated to be placed onto the delegation log in the course of the study; anyone who has access to personal data on study participants (beyond name, contact details, DOB); and anyone who attends meetings where details of the study are discussed, for example safety updates.

Date of first enrolment
01/10/2023

Date of final enrolment
31/01/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Medical Research Council; Grant Codes: MR/W024977/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	24/10/2023	01/11/2023	No	No
Protocol file	version 1.2	15/12/2023	20/12/2023	No	No
Protocol file	version 1.3	24/01/2024	26/01/2024	No	No
Protocol file	version 1.4	15/04/2024	21/05/2024	No	No
Protocol file	version 1.5	06/06/2024	18/06/2024	No	No
Protocol file	version 1.6	19/08/2024	12/09/2024	No	No
Protocol file	version 1.7	22/11/2024	02/12/2024	No	No
Protocol file	version 1.8	17/01/2025	30/01/2025	No	No
Protocol file	version 2.0	25/02/2025	07/05/2025	No	No