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ImMUnologiCal memOry to reSpirAtory viraL infection in the airways

Submission date
12/11/2024

Recruitment status
Recruiting

Registration date
16/01/2025

Overall study status
Ongoing

Last Edited
16/01/2025

Condition category
Infections and Infestations

[_] 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
Respiratory infections are commonly caused by bacteria and viruses. Lower respiratory tract infections caused by influenza, respiratory syncytial virus (RSV), SARS-CoV-2 and human metapneumovirus (hMPV) are common in young children and older adults and the leading causes of hospitalisation. They can exacerbate morbidity, presenting an especially burdensome challenge to the quality of life and healthcare systems overall. The burden of respiratory infections, particularly in older populations, was highlighted during the COVID-19 pandemic, with increased age proving to be the biggest risk factor for morbidity and mortality. Whilst respiratory vaccines exist, they may not provide optimal immunity. In the case of COVID-19, recent data suggest that local airway adaptive immune responses could be critical in the defence against symptomatic infection in humans. In a recent study, this team demonstrated the presence of an enriched SARS-CoV-2 specific B and T cell population in BAL compared to blood. Particularly, antigen-specific T-cell responses persist in the lung mucosa for up to 7 months after infection. Data on whether such antigen-specific tissue-resident T and B cells are present in human airways after other respiratory infections are currently scanty but could be important in the rational design of new mucosal vaccines. Mucosal vaccines could provide broader and long-term protection at the site of infection to allow more efficient clearance of infection and reduce onward virus transmission. For instance, live attenuated vaccines, such as in live-attenuated influenza vaccine (LAIV) and the recent candidate pertussis-attenuated vaccine, BPZE1, have shown induction of mucosal immunity but their ability to confer long-protection is not well understood. This study aims to improve our understanding of tissue-resident immunity by collecting samples from participants who have had a recent respiratory infection, assessing breadth, longevity and cross-reactive ability. This is vital for predicting host susceptibility to future infections, and importantly, for decerning the potential target opportunities for a mucosal-delivered next-generation vaccine.

Who can participate?
Adults aged 18-85 years old with a confirmed respiratory viral infection of interest who are in good health

What does the study involve?
The study will include three groups, depending on the number of visits and subsequent viral

infection incidence. All participants will undergo a research bronchoscopy, including nasal sampling and blood collection at 35 days (± 21 days) post-confirmed respiratory viral infection with either SARS-CoV-2, hCoV RSV, influenza, rhinovirus or HMPV. Nasal samples and blood will also be collected from these participants at 126 days (±14days) post-infection. Post completion of Group A, participants will be invited to continue in the study and move into Group B for long-term assessment (a second bronchoscopy over the 9-12 months of follow-up) as well as to Group C in case a new respiratory viral infection ensues (a second bronchoscopy in case they acquire a new confirmed spontaneous infection). The total duration of the study will be approximately 5 months for participants in Group A, and up to 12 months for participants in Group B and C from the day of enrolment for each volunteer.

What are the possible benefits and risks of participating?
Participants will be helping research to understand the differences between blood and lung /nose immune responses to respiratory viral infections and how these responses behave over time. Participation will also help the research team compare these responses across different age groups in the study. Finally, they will also be helping in the development of new vaccines that can provide better and longer protection against COVID and other respiratory infections.

During the bronchoscopy, there may be some mild discomfort. After the procedure, participants may more commonly experience a sore nose/throat, cough or mild chest/back ache.

Where is the study run from?
Oxford Vaccine Group, University of Oxford, UK
Liverpool Vaccine Group, Liverpool School of Tropical Medicine, UK

When is the study starting and how long is it expected to run for?
October 2024 to December 2026

Who is funding the study?
Wellcome Trust

Who is the main contact?
Dr Carla Solórzano Gonzalez, carla.solorzanogonzalez@paediatrics.ox.ac.uk
Reyna Sara Quintero Barceinas, sara.quinterobarceinas@paediatrics.ox.ac.uk

Contact information

Type(s)
Scientific

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Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
342829

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 63937, Wellcome Trust Grant Ref: 226131/Z/22/Z

Study information

Scientific Title
A longitudinal cohort study to better understand the Immunological memory to respiratory viral infection in the upper and lower airways

Acronym
IMUCOSAL

Study objectives
This study aims to provide a better understanding of how the immune system at the nose and airways respond to various viruses, such as SARS-CoV-2, RSV, influenza etc, how long natural /hybrid immunity can last and how likely it is to confer protection against repeat respiratory viral infections.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 31/10/2024, Northwest - Greater Manchester East Research Ethics Committee (-, -, -, United Kingdom; +44 (0)207 104 8290; gmeast.rec@hra.nhs.uk), ref: 24/NW/0353

Study design
Observational longitudinal cohort study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Duration of natural and hybrid immunity in response to various viruses, including SARS-CoV-2, RSV, and influenza in the nose and airways

Interventions
This study will recruit up to 200 adults (aged 18 to 85 years) within 8 weeks following a laboratory-confirmed respiratory infection and consent them into the study. The study will include three (3) groups, depending on the number of visits and subsequent rates of respiratory infections.

Group A: All participants will undergo a research bronchoscopy, nasal sampling and blood donation between 4-6 weeks (±2 weeks) post-confirmed respiratory infection with a follow-up visit including nasal sampling and blood 4 months (±2 weeks) post-infection.
Group B: A subset of study participants from group A will be followed up to 12 months post-infection (PI). This will include an additional bronchoscopy procedure, nasal sampling and blood collection.
Group C:Any participant from group A who experiences a new respiratory infection at any time during the study, caused by the same or a new respiratory pathogen, will be invited to have another bronchoscopy 4-6 weeks (±2 weeks) post the new infection.

In a subset of study participants, nasal tissue biopsy will be collected. This procedure will be performed close to the bronchoscopy date but on a separate date and participants will be specifically consented to it. Age and other demographics will be captured in RedCap.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Frequency and breadth of antigen-specific T and B cell responses in the respiratory mucosa and blood after re-stimulation measured using flow cytometry and ELISPOTsat 35 days post infections

Secondary outcome measures
1. Sustainability of T and B cells in the respiratory mucosa and blood measured using flow cytometry and ELISPOTs for 12 months post-infection at 35,126 and 322 days post-infection
2. Assess the cross-reactive potential of T and B cells in respiratory mucosa and blood after stimulation with heterologous antigens measured using flow cytometry at 35-126 post-infection
3. Quantify antibody levels (IgA, IgG, IgM) in respiratory mucosa and blood using MSD/ELISA assays and describe their time kinetics at 35, 126 and 322 days post-infection
4. Frequency of antigen-specific T cells and antibody titres measured using flow cytometry assays, ELISA, and MSD (comparison of generated data primary and secondary objectives 1 and 2) at 35, 126 and 322 days post-infection
5. Levels and type of immunity in individuals with recurrent infection and those with only one infection within the period of participation in the study measured using flow cytometry assays, ELISA, and MSD at 35, 126 and 322 days post-infection
6. Participants age stratification in 2 groups (15-60 years of age and >60 years) measured using data collected in study records and comparison of cellular and humoral immune responsesusing flow cytometry assays, ELISA, and MSD at 35, 126 and 322 days post-infection

Overall study start date
31/10/2024

Completion date
15/12/2026

Eligibility

Key inclusion criteria
1. Adults aged 18-85 years of age (inclusive, at the time of consent)
2. Medically healthy, such that according to the investigator's judgement, hospitalisation within the study period is not anticipated, and the participant appears likely to be able to remain a study participant through the end of protocol-specified follow-up. Planned elective procedures for pre-existing conditions are allowable.
3. Fluent in English, ability to understand the procedures and convey any adverse events effectively to the research team
4. Willing and able to provide written informed consent before any study procedures are performed and can understand and comply with the requirements of the study
5. Willing to provide their national insurance number or passport number to be registered on The Over-Volunteering Prevention System (TOPS)
6. Agree to allow study staff to contact his or her GP or equivalent NHS databases to access the participant’s vaccination records, medical history

7. Willing to allow their GP and/or consultant, if appropriate, to be notified of participation in the study
8. Individuals with laboratory-confirmed respiratory viral infection of interest (swabs to be provided to volunteers by the corresponding site). The viral infections of interest are SARS-CoV-2, hCOV, RSV, Influenza, Rhinovirus and HMPV
9. Agreement to refrain from blood donation during the study
10. For participants of childbearing potential only *: willing to use effective contraception** for the duration of the study AND to have a pregnancy test at screening and bronchoscopy visits

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
85 Years

Sex
Both

Target number of participants
200; UK Sample Size: 200

Key exclusion criteria
1. Currently involved in another study unless observational or non-interventional. Exceptions may be applied at the discretion of the Chief Investigator to ensure no harm comes to the participants (e.g. excessive blood sampling or nasal sampling.
2. Participants with uncontrolled medical or surgical conditions that may preclude nasal or oral intubation with a bronchoscope or the bronchoscopy itself, in the opinion of the investigator.
3. Participants who have received anti-viral medication or convalescent plasma to treat their respiratory viral infection.
4. 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.
5. History of hereditary angioedema, acquired angioedema, or idiopathic angioedema.
6. History of any serious psychiatric condition likely to affect participation in the study.
7. Participants who have had previous adverse reactions to benzodiazepines or anaesthetic agents (lidocaine) including reversal agents such as flumazenil.
8. Participants with a full blood count, clotting or renal function level outside of local laboratory reference ranges and deemed as clinically significant by the investigator.
9. Any medication that may affect the coagulation system in the last 7 days (excluding low dose 75 mg aspirin).
10. Participants with very poor venous access.
11. Receipt of blood products or immunoglobulins within 3 months prior to screening.
12. Participants who, in the opinion of the Investigator (or designee), should not participate in

this study.
13. Participants with asthma, medicated with steroid inhalers.
14. On long term oxygen therapy (LTOT).
15. Oxygen saturations on screening of <92% on air.
16. For participants requiring spirometry^: If FEV1 is less than 50% predicted or <1 litre absolute or not able to perform the procedure. This will be assessed following spirometry on the day of the bronchoscopy.
17. Any uncontrolled medical or surgical condition as deemed clinically significant by the CI
18. For participants of childbearing potential only: participants who are pregnant, breastfeeding or lactating, or are planning pregnancy during the study.
19. Detectable circulating hepatitis B surface antigen (HBsAg).
20. Seropositive for hepatitis C virus (antibodies to HCV).
21. Seropositive for HIV (antibodies to HIV).
22. Study site staff or a partner of study site staff.
23. For nasal biopsy participants, history of a bleeding disorder (e.g factor deficiency, coagulopathy, or platelet disorder), or prior history of significant unexplained bleeding or bruising following surgical or dental procedures.
24. For nasal biopsy participants, allergy to Lidocaine local anaesthetic.

25. ^ Criteria for participants requiring spirometry
26. Medical Research Council (MRC) score >1.
27. Participants with a >20-year smoking pack history.
28. Diagnosis of chronic respiratory disease.

Date of first enrolment
15/12/2024

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
Liverpool School of Tropical Medicine
Clinical Sciences, 1 Daulby Street
Liverpool
United Kingdom
L7 8XZ

Study participating centre
University of Oxford
Department of Paediatrics, Oxford Vaccine Group, Headington

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United Kingdom
OX3 7LE

Study participating centre
John Radcliffe Hospital
Headley Way
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OX3 9DU

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Governance, Ethics & Assurance Team (RGEA)
Joint Research Office, 1st Floor, Boundary Brook House
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United Kingdom
OX3 7GB
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RGEA.Sponsor@admin.ox.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.ox.ac.uk

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

Participants will not be identifiable from shared or published data. De-identified participant data will be made available upon requests directed to the chief investigator. Proposals will be reviewed and approved by the sponsor, chief investigator, and collaborators on the basis of scientific merit. After approval of a proposal, data can be shared through a secure online platform after signing a data access agreement.

Intention to publish date
15/12/2027

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date