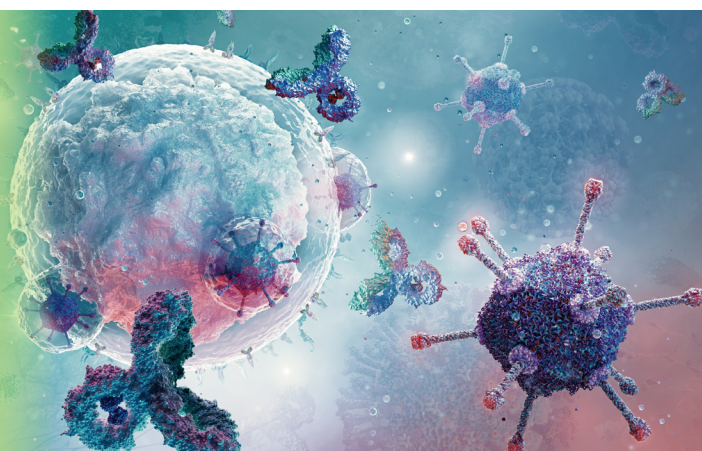


Immune Challenge Models For Drug Development



During an immune challenge test, a stimulus (e.g. an allergen, endotoxin, viral agent, pollutant or drug substance) is administered to a healthy subject or patient to trigger local or systemic inflammatory processes to mimic a diseased state. With a stimulated inflammatory response in a controlled setting, drug efficacy can be evaluated over a shorter period of time compared to a traditional Phase II study in patients. A challenge/re-challenge test with a neoantigen, an antigen for which healthy volunteers are immunologically naïve, allows for the assessment of both innate and adaptive primary and memory immune responses.

Extensive Respiratory, Nasal and Systemic Challenge Model Experience

Challenge Assay	Model Description	Challenge Agent Administration	Study Population	Outcome Assessments
Respiratory Challenge Models				
Lipopolysaccharide (LPS)	Endotoxin administration to evaluate anti-inflammatory effect of study drug. Valuable for disorders like asthma, ARDS and ALI.	Breath-activated dosimeter	Healthy volunteers, COPD patients	Sputum obtained to assess cellular composition and biomarker expression
Allergen	Assessment of the effect of study drug on inflammatory pathways triggered by an inhaled allergen (ex. ragweed, animal dander, pollen, etc.). Valuable for allergic asthma.	Three-step process: (i) identify subject-specific allergen via skin prick test (ii) inhaled allergen dose via breath-activated nebulizer (dosimeter) (iii) re-challenge with allergen	Allergic asthma patients	Early and late asthmatic responses defined as a reduction in FEV1 of at least 15-20% compared to baseline, 0-3 and 3-8 hours respectively, after the allergen challenge
Capsaicin	Administration of tussive agent to assess drug effect on cough reflex. Valuable for coughing disorders.	Nebulizer	Healthy volunteers, chronic cough patients	Maximal cough response (Emax) and concentration of tussive agent causing 50% of the maximal cough response (ED50)
Methacholine	Direct stimulus to assess bronchial hyperresponsiveness in asthma. Valuable for assessment of (reversibility of) bronchoconstriction.	Nebulizer	Healthy volunteers, asthma patients	The provocative concentration causing a 20% fall in FEV1 (PC20)
Adenosine (UK only)	Indirect stimulus to assess bronchial hyperresponsiveness in asthma. Valuable for Proof of Concept studies in asthma.	Nebulizer	Healthy volunteers, asthma patients	The provocative concentration causing a 20% fall in FEV1 (PC20)

ALI, acute lung injury; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; FEV, forced expiratory volume

Challenge Assay	Model Description	Challenge Agent Administration	Study Population	Outcome Assessments
Nasal Challenge Models				
Allergen	To evaluate anti-inflammatory effects and/or bioavailability of intranasal drugs. <i>Valuable for all intranasally administered drugs as well as for allergies specifically.</i>	Three-step process: (i) identify allergen via skin prick test (ii) intranasal allergen challenge to select subject-specific allergen dose and confirm nasal congestion (iii) re-challenge with allergen	Healthy volunteers, allergic asthma patients	Nasal symptoms and nasal airflow
Histamine	To assess the effect of decongestant or evaluate effect of congestion on intranasal absorption. <i>Valuable for ALL intranasally administered drugs as well as for allergies specifically.</i>	Spray or nebulizer	Healthy volunteers	Nasal symptoms or nasal airflow
Rhinovirus	To assess the preventative or therapeutic effectiveness of anti-viral treatment on lower airway infection. <i>Valuable for rhino-viral infections.</i>	Intranasal instillation for viral inoculation	Healthy volunteers	Presence and severity of cold symptoms as well as lung function tests, biomarkers
Systemic Challenge Models				
Lipopolysaccharide (LPS)	To evaluate the anti-inflammatory effects of an investigational product in response to an endotoxin. <i>Valuable for (bacterial) infections and inflammatory diseases.</i>	Intravenous	Healthy volunteers	Changes in immune cell populations and inflammatory cytokines
Keyhole limpet hemocyanin (KLH)	To assess the effect of anti-inflammatory drugs on the immunological response to a xenogeneic allergen. <i>Valuable for autoimmune diseases.</i>	Intramuscular	Healthy volunteers	Changes in immune cell populations, inflammatory cytokines, anti-KLH antibodies and immune receptor occupancy

ALI, acute lung injury; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; FEV, forced expiratory volume

Why Choose Celerion Belfast, UK?

At Celerion, we believe in working together to create a healthier world. From study startup to closeout, we are with you every step of the way.

- ▶ **Clinical Facilities:** MHRA-accredited clinical facility includes 78 beds across 4 wards
- ▶ **Personalized Study Design:** tailored study designs and protocols to optimize clinical trials
- ▶ **Participant Recruitment:** vast database of healthy volunteers and access to exploratory patient cohorts within 4 respiratory disease areas: asthma, chronic cough, COPD and cystic fibrosis
- ▶ **Clinical Laboratory Testing:** on-site, fully dedicated MHRA-accredited Clinical Laboratory
- ▶ **Quality Management:** highly experienced team will help ensure your study is conducted ethically, reliably and in compliance with regulatory standards avoiding unnecessary delays
- ▶ **Data Management and Biometrics:** bridging the gap between medical practice and laboratory science to support informed go/no-go decisions earlier
- ▶ **Client Data Portal:** real-time data access via Celerion's proprietary client portal, Celexus®

RESOURCES:

[Nasal Challenge Studies](#)

[Respiratory Disease Expertise](#)

[Your Partner for High-Quality PBMC Processing & Clinical Site Training](#)

[Pulmonary Sampling Techniques and Sample Analysis](#)

Dedicated Rooms and Capabilities to Support Respiratory Challenge Studies

Our purpose-built clinical facility in Belfast, UK, has state-of-the-art, dedicated allergen testing rooms for respiratory and nasal challenge studies, and are equipped with extract air filters to avoid distribution of inhaled allergens, toxins, drugs and other particulates. Moreover, our Belfast clinical team can support a full range of respiratory assessments including whole body plethysmography, spirometry, bronchoalveolar lavage (BAL) and sputum sampling.