Prophylactic Strategy to Prevent Inflammatory Lung Injury from Diverse Respiratory Viruses via NAM Reprogramming

A lung-targeted, resistance-proof prophylactic that prevents inflammatory lung injury from respiratory viral infections without systemic immunosuppression and pathogen clearance.

Technology

Dr. Khanna's lab at NYU has developed a novel host-directed prophylactic approach that leverages the body's own immune regulatory mechanisms to protect against acute respiratory disease. The invention centers on training a newly discovered subset of lung-resident nerve- and airway-associated interstitial macrophages (NAMs) to suppress inflammation and enhance survival in severe respiratory infections. Rather than targeting the pathogen, this platform primes NAMs to adopt a tissue-protective phenotype that improves disease tolerance during lethal infections such as influenza (e.g., 100% survival in trained mice versus 100% mortality in controls) without reducing viral burden. Mechanistically, type 2 immune conditioning is required for this protective state, and recombinant type 2 cytokines (e.g., IL-4 complex and IL-5) can recapitulate protection from influenza-induced morbidity (weight loss), providing a clinically actionable path to implementation. This first-in-class NAM-training immunomodulatory approach has shown promising efficacy in preclinical models.

Background

Influenza, SARS-CoV-2, and other respiratory pathogens can cause lifethreatening lung inflammation and acute respiratory distress syndrome (ARDS), especially in vulnerable populations. Most current interventions focus antivirals, vaccines, or symptomatic support, leaving a major gap in prophylactic tools that modulate local host immunity and prevent immunopathology. NAMs are an immunoregulatory macrophage population situated near airways and nerves in the lung that suppress damaging inflammation during infection. This methodology is the first to demonstrate that durable local innate memory in NAMs can be established and exploited prophylactically to protect lung tissue from severe inflammation associated with viral respiratory infections, and that type 2 immune conditioning (IL-4/ IL-5) is a key driver of this program.

Development Stage

Preclinical proof-of-concept has been established in mouse models of lethal influenza infection using IL-4/anti-IL-4 complex and IL-5. Current efforts focus on optimizing dosing, expanding efficacy studies to additional respiratory disease models such as SARS-CoV-2, and confirming translational applicability using single-cell RNA-seq data from human lungs.

Technology ID

KHA02-03

Category

Life Sciences/Therapeutics/Inflammat Disease

Doug Brawley

Life Sciences/Therapeutics/Infectious Disease/HIV

Sofia Bakogianni

Authors

Kamal M. Khanna

View online

Applications

- **Prophylactics:** Inhalable or locally delivered immune-conditioning agents (e.g., IL-4/IL-5 cytokine combinations, agonists/mimetics, or immunomodulatory cocktails) to train NAMs in situ for patients at risk of ARDS or viral pneumonia.
- **Cell therapy:** Ex vivo autologous or allogeneic NAM conditioning followed by adoptive transfer for lung injury.
- **Biomarkers:** NAM-specific markers (e.g., Chil3, CD200R2) for patient stratification and monitoring reprogramming and treatment response.
- **Research tool:** NAM-DTR mouse model to test training stimuli and small-molecule modulators.

Advantages

- **Potential first-in-class approach:** Protects lung tissue without reducing viral burden (disease tolerance), enabling a differentiated therapeutic mechanism.
- **Pan-viral potential:** Host-directed NAM reprogramming may provide broad protection against inflammatory lung injury across respiratory viruses, independent of antigenic drift.
- **Limited off-target effects:** Local (e.g., inhaled) conditioning concentrates effects at the site of injury, minimizing systemic exposure while promoting immune tolerance.
- **Durable protection:** Rapid induction of longlasting innate memory in NAMs (2–4 weeks post-conditioning) may reduce dosing frequency.
- **Flexible delivery:** Compatible with in vivo inhalation/local delivery and ex vivo NAM reprogramming with reinfusion.
- **Low resistance risk:** Tissue protection strategy avoids resistance driven by pathogen mutation.

Intellectul Property

NYU has filed a U.S. provisional patent application covering compositions and methods of use for training NAMs (including cytokine-based conditioning strategies) to induce disease tolerance in respiratory infections and other inflammatory pulmonary conditions.

Explore other available products test at NYU TOV Licensing