**Docket #:** S23-361

# Pathogen-agnostic Vaccine Harnessing Integrated Organ Immunity

Researchers at Stanford have found that a vaccine, enhanced with adjuvants that imprint an antiviral state on innate immune cells and non-hematopoietic organ cells, could confer lasting nonspecific protection against diverse pathogens.

Conventional vaccines are designed to produce antigen-specific antibodies or cytotoxic T cell responses against specific pathogens. However, some inadvertently invoke heterologous immunity against non-targeted antigens. This can be leveraged to design pathogen-agnostic universal vaccines. Recent studies suggest that both immunological memory in the adaptive immune system and trained immunity of innate immune system are involved. However, further investigation is needed to identify specific mechanisms to modulate to induce nonspecific immunity.

Stanford researchers have found that the interaction between the adaptive and innate immune systems and non-hematopoietic cells in tissues is key to antigen-agnostic protective immunity. Based on their previous finding that BCG vaccine induces heterologous immunity via CD4 T-cell derived IFN-gamma, which imprints an antiviral state on the innate immune system and epithelial cells, they developed a vaccine containing antigen ovalbumin and GLA/3M-052 adjuvants, which elicit IFN-gamma responses. In vaccinated mice, antigen-stimulated T cells imprinted prolonged and broad innate-mediated antiviral resistance in myeloid and epithelial cells, protecting mice against SARS-CoV-2 and influenza viruses, unrelated to the administered antigen.

**Figure**

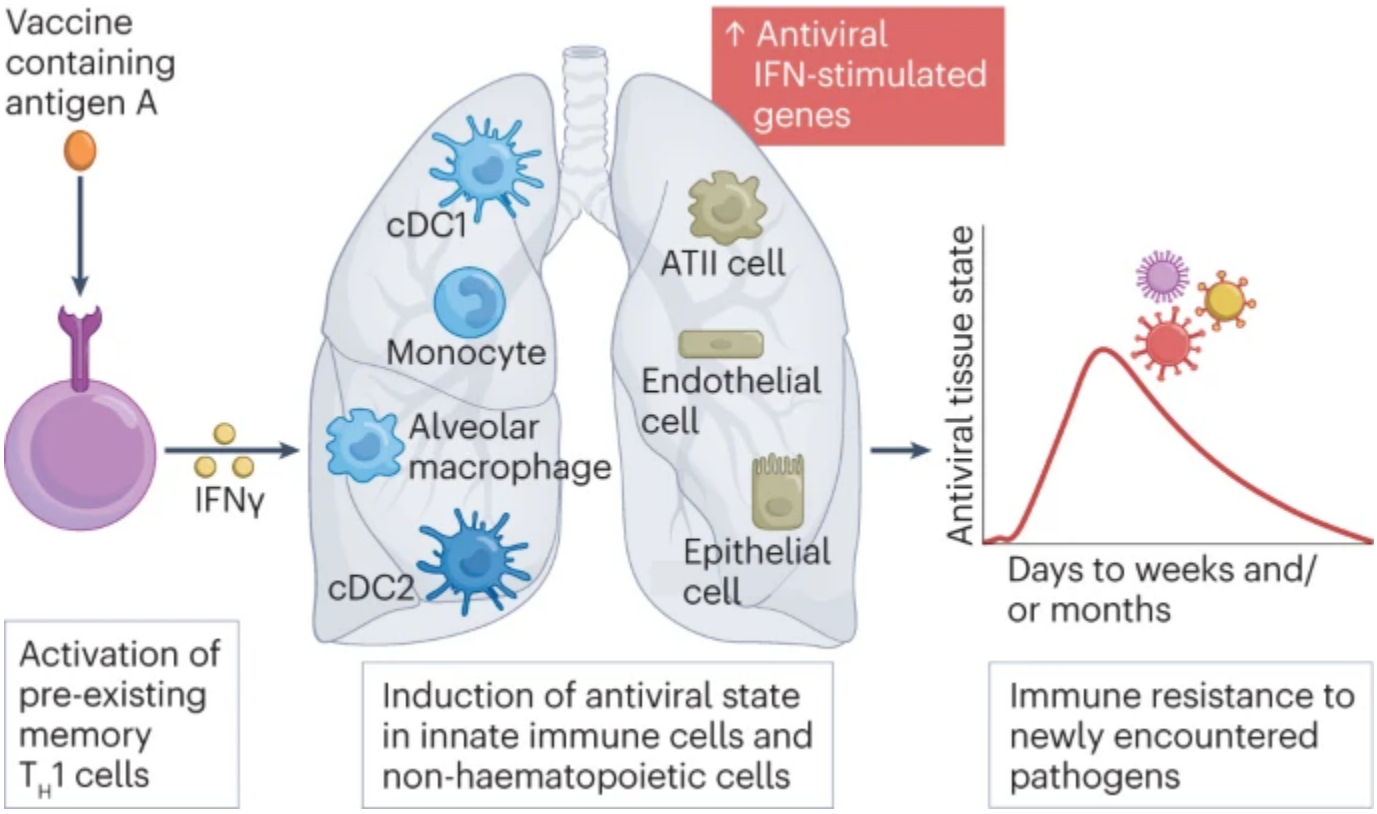



*Figure Description:* Harnessing integrated organ immunity for universal vaccines (Pulendran, 2024).

**Stage of Development**
Proof of concept - in vivo

## Applications

- Stop-gap measure to prevent infection upon emergence of a new pathogen
- Vaccines against prototype pathogens
- Prophylactic treatment when anticipating increased exposure to pathogens

## Advantages

- Broad protection against diverse pathogens
- Lasting effects (on the order of weeks as of now)

## Publications


- Lee, A., Floyd, K., Wu, S., et al. (2024). BCG vaccination stimulates integrated organ immunity by feedback of the adaptive immune response to imprint prolonged innate antiviral resistance. *Nature Immunology, 25*(1), 41–53.
- Pulendran B. (2024). Integrated organ immunity: a path to a universal vaccine. *Nature Reviews Immunology, 24*(2), 81–82.


## Patents

- Published Application: WO2025043016

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