Infectious Diseases Labs

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11:00am to 12:00pm (SGT)

Join Zoom Meeting here
Meeting ID: 942 3250 8297
Passcode: 621655

Engineer next-generation vaccine using human spleen organoids.

Effective vaccine responses require the presence of a "danger signal" alongside the antigen. Commonly used vaccine adjuvants such as alum, MF59, and AS01/02 have been pivotal in enhancing vaccine efficacy. However, these adjuvants (aluminum salt, shark liver oil, tree extracts) lack specificity. In my research, I propose a strategy that focuses on targeting specific cytokine signaling pathways to achieve high vaccine efficacy and safety profiles. Traditionally, the screening of molecular adjuvants in mice is resource-intensive and may not translate effectively to humans.

Mark Davis lab demonstrated that the in vitro organoid cultures derived from human lymphoid organs (tonsil or spleen) can recapitulate all major components of vaccine responses. Collaborating with lab members, I developed a high-throughput human spleen organoid screening and phenotyping platform.

Using this platform, I screened 12 cytokines and assessed their capacity to augment plasmablast formation 7 days after in vitro influenza vaccination. Among these cytokines, interferon beta emerged as the only significant enhancer of the vaccine response in both spleen and tonsil organoids. Furthermore, I investigated the correlation between cytokine serum levels and influenza vaccine responses in human cohorts. I analyzed data from 4 independent influenza vaccination cohorts spanning five different flu seasons administered at Stanford Clinics, where 77 cytokines were profiled across baseline samples (sample N>600). Our meta-analysis revealed that serum interferon beta levels, as well as its downstream effectors IL18, CXCL10, and IL1RA, predicted the antibody titer 28 days after influenza vaccination, particularly in a vulnerable subgroup with low baseline titers. Additionally, our findings suggested that interferon beta directly stimulates B cells during vaccination.

Through an investigation integrating human organoid modeling and human cohorts, we demonstrated that Type I interferon signaling is a rate-limiting factor for vaccine responses in the population, thus presenting a promising target for molecular adjuvants.

Dr. Chen is an Eli Lilly Fellow of the Life Science Research Foundation from Mark Davis's lab at Stanford University. He completed Ph.D. studies with Dr. Rong Li at Stowers Institute for Medical Research, where he studied the adaptive role of aneuploidy (chromosomal copy number variations), a hallmark of cancer. His graduate work was awarded First Place in the Kaluza Prize by the American Society of Cell Biology (one person per year). During postdoc, he studied human immunology. His research on autoimmune lung diseases was highlighted in the 2021 treatment guideline issued by the American College of Rheumatology. For vaccine research, he analyzed big data in human cohorts and verified the causative associations using the cutting-edge human spleen organoids platform. The studies revealed a rate-limiting factor for vaccine responses in the human population.

Hosted by : Prof Lisa Ng

Webinar is open to all. No registration required

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