Immune cells present long before infection can predict flu symptoms

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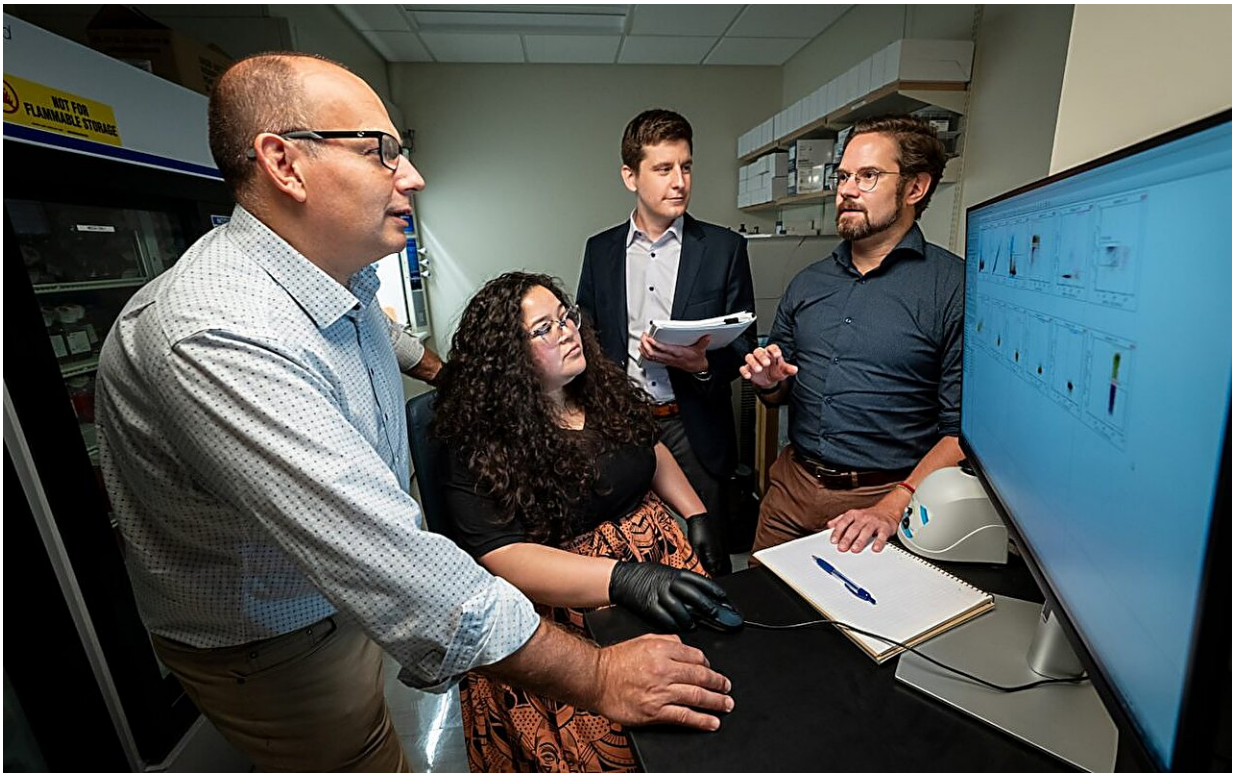


(L to R) Co-corresponding author Richard Webby, Ph.D., St. Jude Department of Host-Microbe Interactions, co-first author Aisha Souquette, Ph.D., co-first author Robert Mettelman, Ph.D., and senior corresponding author Paul Thomas, Ph.D., St. Jude Department of Immunology. Credit: St. Jude Children's Research Hospital

St. Jude Children's Research Hospital scientists, in collaboration with the

Institute of Environmental Science and Research (ESR) Limited, found that immune cells present in people months before influenza (flu) infection could more accurately predict if an individual would develop symptoms than current methods which primarily rely on antibody levels.

The study found certain immune cells were associated with increased protection, while other immune cells were associated with increased susceptibility to developing symptoms after catching the virus. The findings have implications for new approaches to public health and were published today in *Nature Immunology*.

"We've been struggling for decades, if not centuries, with why some people get sick with infections and some don't," said co-corresponding author Richard Webby, Ph.D., St. Jude Department of Host-Microbe Interactions. "This is one of the best attempts to try and figure that out for influenza. We were able to measure many different immune parameters from a single blood draw and correlate them with protection from, or susceptibility to, infection symptoms."

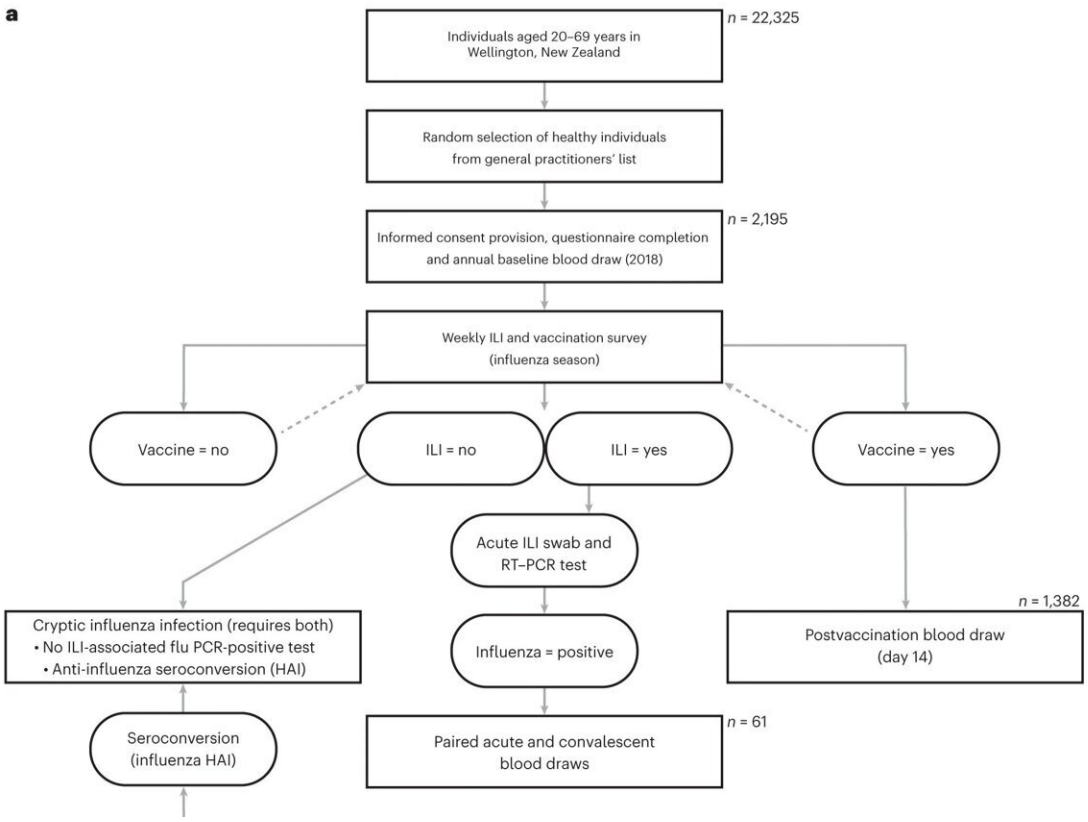
Functional diversity improves anti-influenza immune performance

The researchers found that having a more functionally diverse set of immune cells was correlated with increased protection from flu symptoms. The group identified these cells by comparing the immune cells present in the blood of patients who had symptoms from flu infection to those who were asymptomatic or uninfected. The blood samples, taken up to six months before that flu season, showed very different sets of immune cells in the two groups.

Those without symptoms not only had a more functionally diverse set of immune cells but those cells were also associated with an influenza-

specific long-term response, sometimes called the memory response. Patients with symptoms tended to have a more similar set of inflammatory immune cells, which are more likely to be involved in a nonspecific, functionally narrow and short-term response.

The analysis included volunteers in the surveillance for a community cohort-based influenza-like illness (SHIVERS-II) study in New Zealand. SHIVERS-II includes a unique cohort of volunteer patients that the study tracks over time, including their health information. For this study, the volunteers regularly had their blood drawn so the scientists could characterize their immune cells and find which were associated with protection from flu symptoms.



SHIVERS-II study design, participant enrollment, sample collection and participant demographics. **a**, Schematic depiction of the SHIVERS-II study

design and participant numbers for year 1 (2018). RT–PCR, reverse transcription followed by PCR. **b**, Following consented enrollment, demographic information and whole blood samples were collected from all vaccinated and unvaccinated participants in the preseason period (nonvaccinated baseline) and 14 days after vaccination (vaccinated baseline). Participants meeting the WHO-defined criteria for ILI were tested for influenza viruses by PCR, and confirmed cases were sampled further during acute infection. All enrolled participants were sampled after the season. Cryptic infections were adjudicated in the postseason period from ILI- and PCR-negative participants with a fourfold or greater increase in HAI antibody titers without postvaccination HAI seroconversion. Right, 206 enrolled participants were selected for study inclusion from four baseline comparator groups (unvaccinated–uninfected, unvaccinated–infected, vaccinated–uninfected and vaccinated–infected) based on age- and sex-matching. **c**, Sex (assigned at birth) of $n = 206$ participants stratified by vaccination status and age (years) and compared by two-sided Wilcoxon rank-sum test (unvaccinated female ($n = 58$) versus unvaccinated male ($n = 42$), $P = 0.07$; vaccinated female ($n = 66$) versus vaccinated male ($n = 42$), $P = 0.63$). Boxes represent the median and 25th–75th percentiles; whiskers indicate the minimum (left) and maximum (right) values no further than 1.5 times the interquartile range (IQR); notches extend to 1.58 × IQR/sqrt(n), providing the 95% confidence interval (CI). *P*