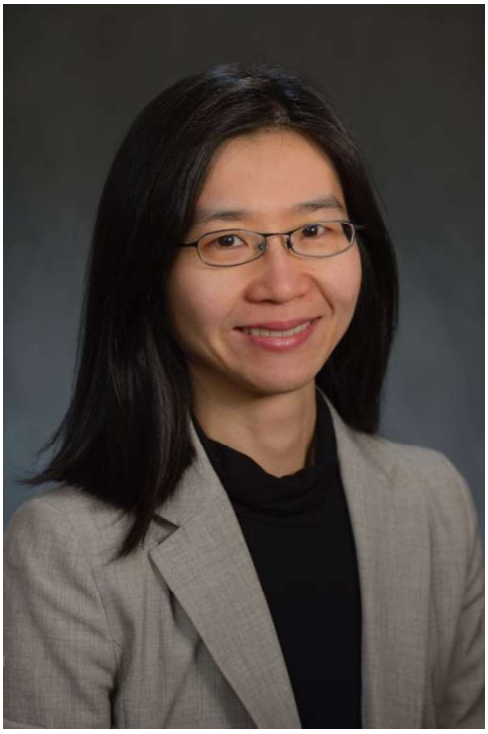
PRE-EXISTING T CELLS IN VACCINATION AND RELEVANCE TO SARS-COV-2



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Dr. Laura Su is an Assistant Professor at the University of Pennsylvania. She has a long-standing interest in understanding how exposures to noninfectious microbes impact host response to pathogens. Her work showed for the first time that individuals have expanded and functional memory T cells to pathogens to which they have never been exposed. Studies from her lab use T cell receptor sequencing, mass cytometry, and tetramer-based T cell specificity analyses to delineate the complexity of human responses to vaccines, infections, and autoimmune diseases. She was born in Taiwan, received her bachelor's degree from Massachusetts Institute of Technology, MD. She then studied her Ph.D. from New York University, and followed by postdoctoral training from Stanford University. She is also a practicing physician with specialization in Rheumatology.

ABSTRACT

The identification of memory T cells that can recognize SARS-CoV-2 before exposure has led to the speculation of pre-existing immunity, whereby memory T cells form past coronavirus infections would facilitate a faster and more robust response to SARS-CoV-2 to limit the severity of infection. However, how pre-exposure T cell characteristics impact human T cell response to a novel pathogen remains unknown. We have addressed this critical question by studying the CD4+ T cell response in unexposed individuals to live attenuated yellow fever virus (YFV) vaccine. We quantified the virus-specific population dynamics over time using class II peptide-MHC tetramers. Our data revealed that, even in the absence of known viral exposure, clonally-expanded memory phenotype T cells were found in the majority of virus-specific precursors in healthy adults. Pre-existing memory T cells can be divided into cells that were abundant before vaccination but underwent limited overall expansion and ones that generated naïve-like responses and preferentially contributed to the memory repertoire after vaccination. Single-cell T cell receptor (TCR) sequencing was used to track the evolution of immune responses to different epitopes and showed an association between the preservation of unexpanded TCRs in the pre-exposure repertoire and the robustness of post-vaccine responses. Instead of a further increase in pre-established TCR clones, vaccination boosted the representation of rare TCRs.

Thus, vaccines restructure T cell epitope specificity and clonal hierarchy. Our results linked precursor states to post-exposure response, identifying peripheral education of virus-specific repertoire as a key component of effective vaccination.