Molecular-level Antibody Repertoire Profiling and Engineering: Implications for Developing the Next-generation of Therapeutics and Vaccines

Jiwon Lee, PhD
Thayer School of Engineering, Dartmouth College, Hanover, NH 03755, USA

Email: Jiwon.Lee@dartmouth.edu | Tel: +1-603-646-3485 |
Web: https://lee-lab.engineering.dartmouth.edu/

Abstract

The repertoire of antibody molecules circulating in blood and coating mucosal surfaces is the basis for the immune system to mount protective immunity against infectious agents, and it is shaped through various exposures to pathogens and vaccines encountered during one's lifetime. While classic serology has been the standard for studying antibody responses, information on the sequence identities and abundances of the individual constituent antibody molecules remains insufficient. To address this, we combine high-resolution liquid-chromatography tandem mass-spectrometry (LC–MS/MS)-based proteomic analysis of immunoglobulins (Ig-Seq) with high-throughput sequencing of B cell receptor transcripts (BCR-Seq) to quantitatively profile immune repertoires following vaccinations and infections. Subsequently, in-depth biochemical and functional characterizations of monoclonal antibodies have resulted in clinically relevant insights regarding the precise features of immune responses that can provide effective protection and their protective mechanisms at unprecedented details. Here I will describe the integrative technologies in depth, highlight key insights gained from studying antibody repertoires to influenza and SARS-CoV-2, and demonstrate how this knowledge can guide the engineering efforts for next-generation therapeutic biologics and vaccines.

Bio

Dr. Jiwon Lee is Ralph and Marjorie Crump Assistant Professor of Engineering at Dartmouth College. Since joining Dartmouth in 2019, his overall research interest has centered on developing tools and technologies to characterize and engineer the human immune system. In particular, his group focuses on understanding how antibody molecules in circulation develop and impact human health and disease in the contexts of infectious disease, autoimmune disease, and cancer. By developing and implementing innovative high-throughput technologies, proteomic analytical methods, machine learning frameworks, big data analytics tools, and data modeling tools, his research focuses on gaining clinically relevant insights regarding the precise features of antibodies that can provide effective protection to subsequently informs the group's efforts on engineering personalized immunotherapies and preventatives. He received his B.A. in Molecular and Cell Biology from the University of California, Berkeley, and his Ph.D. in Chemical Engineering from the University of Texas at Austin. He completed a joint postdoctoral fellowship at the University of Texas at Austin and Harvard Medical School. He is also a member of the Department of Biochemistry and Cell Biology at Geisel School of Medicine at Dartmouth.