CeMMP Centre for Cryo-electron Microscopy of Membrane Proteins

SEMINAR SERIES 2022

Assistant Prof. Christopher Barnes

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Professor Christopher Barnes is newly-appointed Assistant Professor of Biology and ChEM-H Institute Scholar at Stanford University. As a rising star in structural biology, his lab excels in leveraging interdisciplinary approaches to address fundamental principles of viral-host interactions for therapeutic benefit. His group combines biophysical methods with in vivo approaches to understand how viruses such as HIV-1 and SARS-CoV-2 infect host cells and elicit specific humoral immune responses. Over the course of the COVID-19 pandemic, Professor Barnes has made significant contributions to our understanding of antibody-spike interactions through in-depth structural analysis that detail the specificities of polyclonal antibody responses in COVID- 19-convalescent donors, and how monoclonal neutralizing antibodies or designed protein inhibitors bind spike to prevent infection. This work led to over fifteen pandemic-related publications, guiding therapeutic antibody and vaccine development. His already impressive track record in structure-guided approaches to the treatment of infectious disease has earned him such recognitions as an HHMI Hanna H. Gray Fellowship, a Burroughs Wellcome Fund PDEP award, recognition as a Norman Letvin Early Career Investigator from the Bill and Melinda Gates Foundation, and appointment as a Chan Zuckerberg Biohub investigator. Moreover, Professor Barnes is recognized for navigating challenging pandemic-related restrictions to not only contribute scientifically, but also to the national dialogue and global campaigns to educate the broader community about COVID-19 and vaccines.

Structural characterization of conserved neutralizing epitopes on the SARS-CoV-2 spike glycoprotein

SARS-CoV-2 infection or vaccination produces neutralizing antibody responses that contribute to better clinical outcomes. The receptor binding domain (RBD) and the N-terminal domain (NTD) of the spike trimer (S) constitute major neutralizing targets for the antibody system. Here we describe structures of donor-derived broadly-neutralizing antibodies bound to RBD and NTD epitopes that are conserved across the major SARS-CoV-2 variants of concern. We conclude SARS-CoV-2 infection and/or Wuhan-Hu-1 mRNA vaccination produces a diverse collection of memory B cells that produce anti-spike antibodies, some of which can neutralize variants of concern and likely contributes to the relatively benign course of subsequent infections with SARS-CoV-2 variants including omicron.