



QUANTITATIVE & SYSTEMS BIOLOGY COLLOQUIUM:

Imprinting Durable Antibody-mediated Immunity

Deepta Bhattacharya
University of Arizona

About the Speaker:

Dr. Bhattacharya received his PhD from the University of California, Berkeley studying NF- κ B in B cell biology and conducted his postdoctoral research at Stanford University on hematopoietic stem cells. He began his independent research career in 2008 at Washington University in St. Louis where he remained through tenure until, as a Tucson native, he moved home to UArizona in 2017. Over the past 16 years, his work has focused on the basic biology of antibody responses to infections and vaccines, including mRNA vaccines, and on regenerative medicine and immunological transplantation barriers. Dr. Bhattacharya is the recipient of numerous awards including the New York Stem Cell Foundation Robertson Investigator Award in 2012. Dr. Bhattacharya directed the graduate program in molecular medicine, the departmental promotion, tenure, and evaluation committee at UArizona, the graduate admissions committee at Washington University in St. Louis, and chaired the public communications committee and is a member of the nominating committee for the American Association of Immunologists. Since 2020, Dr. Bhattacharya has been regularly interviewed by major media outlets including The New York Times, The Washington Post, and The Wall Street Journal to provide his perspectives on the pandemic and his group's research. Dr. Bhattacharya is a scientific co-founder of Clade Therapeutics and Aleutian Therapeutics and was on the founding team for Sana Biotechnology. Dr. Bhattacharya's intellectual property has been licensed by established companies including Gilead Sciences, and several startups including FortySeven Inc, Jasper Therapeutics, and Inograft Biotherapeutics. He has served on the scientific advisory boards for GlaxoSmithKline on COVID-19 therapeutics and for HilleVax on norovirus vaccines. He is currently the executive director of the Center for Advanced Molecular and Immunological Therapies at The University of Arizona.

Abstract:

The duration of antibody production varies across different infections and vaccines. To define molecular programs that promote durable humoral immunity, we used mice deficient in ZBTB20, a transcription factor that is highly expressed by plasma cells and is required to maintain antibody production. However, genetic deletion of Zbtb20 in long-lived plasma cells had no impact on the duration of antibody production. Instead, deletion of Zbtb20 in B cells only within the first week after immunization caused a subsequent failure to maintain plasma cells. Through single cell ATAC-sequencing, we observed elevated IRF8- and Ets-dependent epigenetic programs in ZBTB20-deficient B cells at 7 days post-immunization, whereas the corresponding transcriptional changes manifested ~1 week later. Switching the adjuvant from alum to an oil-in-water formulation suppressed Ets-dependent epigenetic programs and rescued ZBTB20-deficient plasma cell survival and antibody production. Genetic deletion of Irf8 also rescued ZBTB20-deficient antibody responses following alum-adjuvanted immunizations. We conclude that B cell-intrinsic epigenetic programs begin to imprint durable antibody production prior to obvious transcriptional consequences and act weeks before most long-lived plasma cells are formed.



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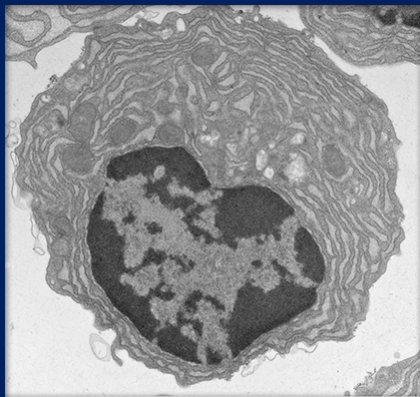
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Time:

10:30 AM - 11:45 AM

Location:

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For more information, contact: Kirk Jensen
kjensen5@ucmerced.edu