QUANTITATIVE AND SYSTEMS BIOLOGY COLLOQUIUM:
Leveraging genetic screens and mRNA vaccines to protect against *Toxoplasma gondii*

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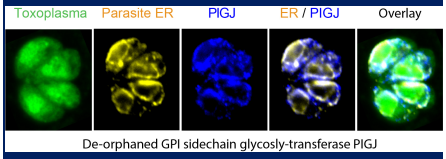

De-orphaned GPI sidechain glycosly-transferase PIGJ

About the Speaker:

Dr. Jensen grew up in Southern California with aspirations of becoming a physical therapist for the Los Angeles Lakers, initially enrolling in Human Anatomy and Physiology classes at a community college. However, his career trajectory shifted dramatically after contracting malaria, a life-threatening parasitic disease, particularly for young children. This experience ignited his curiosity about parasites and immunology, leading him on a lifelong pursuit of the immunology of infectious diseases. Dr. Jensen completed his graduate studies under the mentorship of Eli Sercarz at the La Jolla Institute for Allergy and Immunology, UCSD (Masters) and Yueh-hsiu Chien at Stanford University (Ph.D.). His contributions to γδ T cell biology during this time demonstrated that 'antigen experienced' cells become IFNγ producers, while 'antigen naïve' cells produce IL-17 during thymic development, uniquely positioning them for inflammatory regulation. For his postdoctoral work, Dr. Jensen joined Jeroen Saeij's lab at MIT, where he focused on the impact of *Toxoplasma gondii* virulence factors on macrophage function and intestinal inflammation. Over the past decade at the University of California, Merced, his lab has pioneered research on immunological memory against *T. gondii* infection, leveraging the genetic diversity of *Mus musculus* and *T. gondii* to uncover novel pathways for protective immunity, including that by vaccination. Currently, Dr. Jensen serves as the Chair of the Molecular & Cell Biology (MCB) Department and was the inaugural Chair of Admissions for the Quantitative Systems Biology (QSB) graduate program (2015-18). He has served on 32 Ph.D. thesis committees within this program and graduated 4 Ph.D. QSB students through his lab. His accolades include UC Merced's Academic Senate Award for Distinguished Early Career Research, the School of Natural Sciences (SNS) Award for Distinction in Undergraduate Research Mentoring and is an editor at Infection and Immunity.

Abstract:

Parasites cause 96 million Disability Adjusted Life Years (DALYs) and 2 billion new infections every year. And yet, a fully protective vaccine to prevent human parasitic disease has remained elusive. Solving the problem of parasite vaccines underpins the research in the Jensen lab. Specifically, we study requirements for immunity to highly virulent strains of the widespread intracellular parasite of animals, *Toxoplasma gondii*. In this seminar, I would like to discuss how we have leveraged the genetic diversity of both *T. gondii* and one of its hosts, *Mus musculus*, to understand mechanisms of acquired immunity to *T. gondii* that follow natural infection or vaccination. First, a genetic screen using a large recombinant inbred mouse panel called the Collaborative Cross (CC) revealed a significant contribution from a single locus centered on the Wnt-signaling pathway transcription factor, Tcf7 or TCF-1. In resistant mice, enhanced central memory CD8 T cell responses via TCF-1 expression underlie the success of attenuated *T. gondii* vaccines against highly virulent South American strains. Second, exploring the genetic diversity of parasite strains that differ in virulence led us to reconsider the role of glycosylphosphatidylinositols (GPIs) in parasite pathogenesis and vaccination. GPIs are highly conserved anchors for eukaryotic cell surface proteins and parasite membranes are highly decorated with GPI-anchored proteins, and free GPIs called GIPLs. We show that antigens targeted by antibodies appear extremely sensitive to the GPI-anchor and when modified in *T. gondii* by the de-orphaned glycosyltransferases, PIGJ and PIGE, it significantly alters host survival following infection. Finally, we have assessed immunization of surface antigens with and without GPI attachment through mRNA vaccination, which revealed a fundamental requirement for the GPI in eliciting humoral responses to GPI-anchored proteins. We reason vaccination strategies aimed at *T. gondii* prevention, and other parasites, should target these signaling pathways and the GPI to achieve immunity.

Date:

10/17/2024

Time:

10:30 AM - 11:45 AM

Location:

SSM 104

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