QUANTITATIVE & SYSTEMS BIOLOGY SEMINAR: Identification of novel Toxoplasma virulence factors using CRISPR/Cas9 screens

Jeroen Saeij
Professor Pathology, Microbiology & Immunology
University of California, Davis

Date:
9/10/2021

Time:
2:30 PM-3:45 PM

Location:
COB2 140

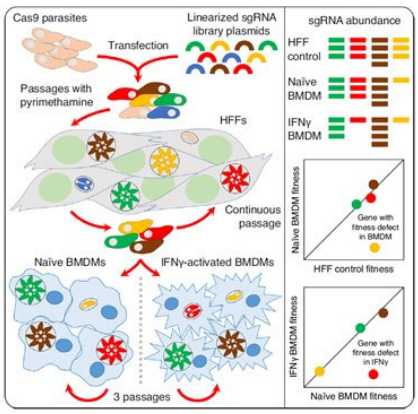
About The Speaker:

I have a broad background in immunology, parasitology, and genetics with specific training in the genetics of host-parasite interactions. As a PhD student, I studied the genetics of the innate immune response of inbred carp that differed in resistance to trypanosomes. I also received comprehensive training in animal models and immunology. As a postdoctoral fellow at Stanford in John Boothroyd's lab, I used forward and reverse genetic tools to identify Toxoplasma genes involved in strain differences in virulence and modulation of the host cell. I also studied the effect of these genes on the mouse immune response both in vivo and in vitro.

My major contributions to the field as a postdoctoral fellow were showing that Toxoplasma rhoptry proteins were the major determinants of strain differences in virulence and modulation of the host cell. A major effort of my lab is to identify Toxoplasma genes that mediate its co-option of the host cell, to characterize the proteins encoded by these Toxoplasma genes, their host cell interaction partners and their role in virulence. We demonstrated that also dense granule proteins (GRAs) are involved in the modulation of host cell signaling pathways. We have recently used focused in vivo CRISPR/Cas9 Toxoplasma loss-of-function screens to identify novel Toxoplasma genes that mediate in vivo fitness. We also study host genetic factors involved in resistance to Toxoplasma. Thus, the overarching goal of the lab is to understand Toxoplasma-host cell interactions. To achieve our goals, we use a combination of genomics, biochemistry, genetics, microscopy, immunology and computational tools.

Abstract:

Toxoplasma gondii is a model apicomplexan that also causes severe disease in fetuses and immuno-compromised individuals. Many Toxoplasma genes likely evolved to modulate the host immune system, overcome in vivo nutrient deficiencies, and disseminate to distant organs. The key to Toxoplasma's successful co-option of the host are proteins secreted from its rhoptry and dense granule secretory organelles, named ROPs and GRAs, respectively. To systematically analyze Toxoplasma genes that contribute to in vivo fitness and virulence we have performed genome-wide and focused CRISPR/Cas9 loss-of-function screens. These screens identified Toxoplasma genes that are important for survival in naïve and activate macrophages, at the site of infection, or required to reach organs.



For more information, contact : Kirk Jensen
Kjensen5@ucmerced.edu