Immune Response to Microbial Pathogens

**Jason Cyster**

Antibody responses are important for protection from extracellular pathogens. The Cyster lab studies the induction of germinal center and plasma cell responses to various antigens and to influenza virus, as well as the mechanisms guiding the trafficking of effector lymphocytes. The lab is also exploring how gut commensals shape the mucosal IgA response and how innate lymphocytes position at epithelial surfaces (intestine and skin) to provide barrier immunity.

**Other Research in Dr. Cyster’s Lab:**

Diabetes and Autoimmunity
Development and Differentiation
Immune Regulation
Immune Receptors and Signaling

**Joanne Engel**

The Engel lab is interested in the interactions between microbial pathogens and host cells. We use genetic, cell biologic, genomic, and immunologic techniques to study two important bacterial pathogens, Pseudomonas aeruginosa and Chlamydia trachomatis.

**Margaret Feeney**

The Feeney Lab is interested in the immunopathogenesis of HIV and malaria in childhood. The broad goals of our research program are to elucidate the developmental differences between T cell responses in children and adults, and to identify correlates of protective immune responses to HIV and malaria in order to guide the rational design of vaccines and immunomodulatory therapies.

**Judith Hellman**

We are studying the role of TLR2 and ERK5 in bacterial sepsis caused by peritonitis (cecal ligation and puncture), primary bacteremia (Staph aureus, E. coli), and pneumonia (Staph aureus, E. coli).

**Other Research in Dr. Hellman's Lab:**

Immune Receptors and Signaling
Inflammation

**Richard Locksley**

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We use a variety of microbial pathogens, including Leishmania, Listeria and Nippostrongylus, to model the acquisition of stable cytokine phenotypes by helper T cells in vivo. Our interests involve unraveling mechanisms that position cells in critical areas together and the orchestration of their effector function.

**Other Research in Dr. Locksley's Lab:**


**Averil Ma**[11]

Our work on intracellular mechanisms of coordinating signal transduction events has focused on the molecule A20. Tumor necrosis factor (TNF) is a pleiotropic pro-inflammatory cytokine that stimulates multiple cellular activation and survival signaling pathways. By targeting the TNF induced A20 gene, we found that A20 deficient mice develop profound autoimmunity coupled with an inability of A20 deficient cells to terminate TNF induced NF-kB responses (Lee et al., Science, 2000[12]). We subsequently generated A20 TNF and A20 TNFR double mutant mice, and found that A20 is critical for regulating toll-like receptor (TLR) induced NFkB signals that commit both innate and adaptive immune responses (Boone et al., Nature Immunology, 2004[13]). Moreover, we have found that A20 is also critical for terminating JNK signals. Thus, A20 mediates cross-talk between NFkB and JNK signaling pathways. Moreover, we have found that A20 is a unique ubiquitin modifying enzyme that regulates both the activity and stability of signaling proteins (Wertz et al., Nature, 2004[14]; Boone et al., Nature Immunology, 2004[13]). A20 is thus a biochemically unique molecule that is critical for regulating multiple signaling pathways and biological processes that depend on these pathways. Recent studies indicate A20 is expressed in T cells and dendritic cells, and may play critical roles in regulating both innate and adaptive immune responses. Ongoing studies focus on the physiological targets of A20’s enzymatic activity, the biochemical mechanisms by which A20 functions, the regulation of A20 activity, and the roles of A20 in regulating T cell and dendritic cell activation and survival. Experiments related to microbiology will examine the role of A20 in regulating macrophage and dendritic cell response to model infectious organisms (e.g., Listeria).

**Other Research in Dr. Ma's Lab:**


**James McKerrow**[15]

My laboratory is interested in the interaction between eukaryotic parasites and the host immune system. We are focusing on two classes of organisms. The first are intracellular parasites exemplified by Leishmania and Trypanosoma cruzi. We are defining how they evade the host immune response during their residence in host macrophages. Our second area of interest is how the complex schistosome blood fluke alters its developmental program depending upon the status of the host immune response.

**Ari Molofsky**[16]

Immune responses to bacteria, viruses, fungi, and helminths elicit distinct classes of immunity that can persist long after pathogen clearance. We have described how transient helminth or bacterial infection provokes persistent alterations in adipose tissue immune cells and metabolic function. We are broadly interested in how diverse infections alter tissue resident immune cells and impact subsequent tissue homeostasis and pathology.

**Other Research in Dr. Molofsky's Lab:**
Nadia Roan

In addition to characterizing the molecular interplay between HIV and CD4+ T cells in various tissue microenvironments, we are using mass cytometry to define the signatures of innate and adaptive immune cells at different stages of HIV disease progression, and using this information to identify predictors of clinical outcome following treatment.

Other Research in Dr. Roan's Lab:

HIV and Viral Immunity

Shomyseh Sanjabi

Our lab focuses on immune responses that are elicited against sexually transmitted pathogens in mucosal tissues, including female reproductive tract and large intestine. TGFβ is an immunosuppressive cytokine that is present at high concentrations in the mucosal tissues. During systemic infections, TGFβ is induced at the peak of the immune response in mice. We are interested in identifying the source of this TGFβ and to also understand how signaling by this cytokine may shape effector immunity and memory T cell development and function. We are also interested in the impact of seminal fluid components and female sex hormones on mucosal immunity against viral transmission, innate and adaptive immune activation, and viral pathogenesis and clearance.

Other Research in Dr. Sanjabi's Lab:

HIV and Viral Immunity

William Seaman

We demonstrated that TREM-2, a receptor that is induced during macrophage activation, binds broadly to bacteria and to some fungi. We are therefore studying the role of this recognition in host defense against pathogens.

Other Research in Dr. Seaman's Lab:

Immune Receptors and Signaling

Anita Sil

[23]
H. capsulatum survives and replicates in the phagosome or phagolysosome of macrophages. How this fungus colonizes an intracellular niche that is normally hostile to microbes is a mystery. The ability of H. capsulatum to prevent acidification and maturation of the phagosome is thought to play an important role in survival in macrophages. We hypothesize that H. capsulatum produces gene products that block phagosome maturation and acidification. One of our main research goals is to use molecular genetic approaches to uncover which pathogen molecules are required to inhibit phagosome maturation. We are also using functional genomics to decipher which host genes are manipulated by the pathogen. We are part of a program project grant to study the immune response to intracellular pathogens, so this work is informed and influenced by studies of the interaction of host cells with Listeria monocytogenes, Mycobacterium tuberculosis, and Francisella tularensis in the laboratories of Dan Portnoy (UC Berkeley), Jeff Cox (UCSF), and Denise Monack (Stanford), respectively. A comparative analysis of approaches employed by these four intracellular pathogens will allow us to contrast strategies employed by a diversity of microbes.

Other Research in Dr. Sil's Lab:

Immune Receptors and Signaling