EXAMPLE

(Name), MD/PhD

 Annotated Bibliography

(Date), 2022

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1. List All Authors with the Faculty Candidate **Highlighted**. NK cell responses to simian immunodeficiency virus exposure in naive and vaccinated rhesus macaques. *J Immunol*, 193(1):277-84, Sept 1, 2016. doi: 10.4049/jimmunol.1234567. Epub 2016 Jul 4. PMID: 12345678; PMCID: PMC1234567.

In this collaborative study we investigated activation and mobilization of NK cells in the female reproductive tract during SIV infection as well as during vaccination with the live attenuated virus vaccine SIVnef. Importantly this was one of the first studies to accurately quantify NK cells in the female reproductive tract of nonhuman primate models and indicated NK cell trafficking into the vagina occurs following virus challenge. However, these studies suggested that NK cell recruitment was not sufficient in speed or magnitude to block a take of infection, even by the live attenuated vaccine strategy. Thus, these studies served as a critical basis for subsequent research into how NK cells could be better and more rapidly harnessed by vaccine and immunotherapeutic regimens. In many ways this study helped identify critical obstacles which our laboratories have been actively and successfully targeting for the last several years to really exploit the potency of NK cells to directly or indirectly help in blocking lentivirus transmission.

This article has been cited 17 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Hypercytotoxicity and rapid loss of NKp44+ innate cells during acute SIV infection. *PLoS Pathog*, 10(12):e1234567, April 29, 2016. doi: 10.1371/journal.ppat.1234567. PMID: 12345678; PMCID: PMC1234567.

In this publication, we demonstrated that innate lymphoid cells type 3 (ILC3) are rapidly depleted in acute lentivirus infections, the first clear demonstration that this occurs early in infection. Further, we described a mechanism by which inflammatory cytokines and IDO catabolites inhibit ILC3 by directly antagonizing expression of the critical transcription factor, RORgt. The importance of these findings lies in the fact that prior to our study the kinetics and mechanism of loss which deplete ILC3 during lentivirus infections was largely unknown. This project led directly to three subsequent grants (R01 DE123456; R21 AI123456; R21 AI123456).

This article has been cited 41 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Bone marrow-imprinted gut- homing of plasmacytoid dendritic cells (pDCs) in acute immunodeficiency virus infection results in accumulation of CD4+ pDCs in the mucosae. *J Infect Dis*,

211(11):1717-25, Dec 1, 2018. doi: 10.1093/infdis/jiu671. Epub 2017 Aug 8. PMID:

12345678.

Beginning in the late 2000s multiple researchers observed that plasmacytoid dendritic cells (pDCs) are depleted from the periphery in HIV and SIV infections. However, we and others clarified several years later that pDCs are not in fact depleted, but rather accumulate in the gastrointestinal tract (GI). This manuscript teased out many facets of that mechanism by describing (i) the magnitude of GI accumulation, (ii) the fact that pDCs in the GI are hyperfunctional and contribute to immune activation, and (iii) the programming for trafficking occurs prior to egress from bone marrow.

This article has been cited 8 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Accumulation of Cytotoxic CD16+ NK Cells in Immunodeficiency Infected Lymph Nodes Associated with Functional Anergy. *J Virol*, 89(13):6887-94, Jul 2018. doi: 10.1128/JVI.00660-15. Epub 2017 Jan 22. PMID: 12345678; PMCID: PMC1234567.

In general NK cells are not found in lymph nodes, except for low frequencies of regulatory, cytokine-producing NK cells. In this study we showed that during untreated lentivirus infection, high frequencies of cytotoxic NK cells accumulate in peripheral lymph nodes. We also showed for the first time that many of the cytotoxic NK cells did not traffic to lymph nodes but rather differentiated from the less mature regulatory NK cells and demonstrated significant evidence of abnormal function. This study was significant in the description of a novel NK cell niche in lymph nodes and directly contributed to ongoing studies in my lab on exploiting NK cell mediated-clearance of HIV and SIV from lymph nodes. This study also provided fundamental data for subsequent NIH grant R01 AI143457.

This article has been cited 31 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Antigen-specific NK cell memory in macaques. *Nat Immunol*, 16(9):927-32, Dec 2019. doi: 10.1038/ni.3227. Epub 2019 Feb 20. PMID: 1234567; PMCID: PMC1234567.

In this publication, we demonstrated the first evidence that NK cell memory could be generated in any primate species by showing splenic and liver NK cells can mediate antigen-specific recall responses against SIV and SHIV infections. We further showed that infection was not required and memory could be elicited by adenovirus vaccination, and also demonstrated the response was dependent on NKG2C expression. These findings made a major impact on the NK cell field in that prior to our work, this phenomenon was thought to only occur in mice, but has now been repeated in other primate and human studies validating our findings. Multiple NIH grants have been awarded to my laboratory directly related to this research (R01 AI123456; R56 AI123456; R21 AI123456).

This article has been cited 145 times.

1. List All Authors with the Faculty Candidate **Highlighted**. SIV-induced Translocation of Bacteria in the Liver Mobilizes Myeloid Dendritic and Killer Cells Associated With Kidney Damage. *J Infect Dis*, 213(3):361-9, Jan 1, 2020. doi: 10.1093/infdis/jiv404. Epub 2019 Sept 3. PMID: 12345678; PMCID: PMC1234567.

A major etiology of HIV and SIV disease is related to the phenomenon of microbial translocation (MT) whereby the gastrointestinal tract breaks down releasing microbial products into the periphery. MT promotes activation of peripheral lymphocytes and exacerbates disease progression, but the impact of MT on blood filtering organs (i.e., liver) was previously unknown. Herein we described a massive accumulation of microbial products in the liver resulting in myeloid dendritic and NK cell activation and subsequent liver damage. This study was a direct precursor to NIH grant R01 DE026327 and collaborative immunomodulation studies with Novartis, Inc.

This article has been cited 11 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Enhancement of Microbiota in Macaques Results in Modulation of Mucosal Immune Function. *J Immunol*, 196(5):2401-9, May 1, 2020. doi: 10.4049/jimmunol.1234567. Epub 2019 Aug 29. PMID: 12345678; PMCID: PMC1234567.

Mucosal surfaces have a critical in modulating susceptibility to infectious diseases. Thus strategies to enhance mucosal immunity or tune the local microflora are of significant interest for vaccines and immunotherapeutics. In this collaborative study we showed that probiotic therapy increased B cell expression of IgA, T follicular helper cells in the lymph nodes, and expanded the number of innate lymphoid cells type 3 in the mucosae in rhesus macaques. The findings published herein largely served as the basis for awarding of grant DE123456 which is a collaborative effort between my lab and Dr. Platt’s lab.

This article has been cited 37 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Acute Liver Damage Associated with Immune Activation in a Nonhuman Primate Model of Hepacivirus Infection. *J Virol*, 90(20):9153-62, Mar 10, 2020. doi: 10.1128/JVI.01051-16. PMID: 1234567; PMCID: PMC1234567.

In this publication, we described acute hepatitis and liver damage in common marmosets during GBV-B infection with a model we developed. Disease occurred very early after infection and mimicked pathologic and immunologic changes similar to human HCV disease. This study was important since prior to our work, GBV-B models of HCV had not been shown to induce the full spectrum of pathology or potential for chronicity that our model provides.

This article has been cited 11 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Persistent Low-Level Replication of SIV Drives Maturation of Antibody T Cell Responses to Induce Protective Immunity against SIV Infection. *PLoS Pathog*, 12(12):e1234567, Jul 13, 2021. doi: 10.1371/journal.ppat.1234567. PMID:12345678; PMCID: PMC1234567. \*Co-first authors

To date, the most effective vaccine strategy against a lentivirus has been the live attenuated virus, SIV, which readily protects against intravenous and mucosal challenge of macaques. However, the correlates of protection have been and partially remain unclear. In this comprehensive study, we evaluated mucosal and systemic cellular and humoral responses that were associated with protection against virus challenge. Importantly, a transient low-level replication of the attenuated vaccine was the major stimulus to mature T cell and antibody responses in the mucosae and secondary lymphoid organs. Indeed these critically matured responses were most associated with protection against virus entry and dissemination. The findings herein have continued to inform development of HIV and SIV vaccine strategies.

This article has been cited 16 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Natural killer cells migrate into and control immunodeficiency virus replication in lymph node follicles in green monkeys. *Nat Med*, 23(11):1277-1286, Jun 2021. doi: 10.1038/nm.4421. Epub 2020 Sept 16. PMID: 12345678; PMCID: PMC1234567.

In this study, we demonstrated that NK cells can independently clear SIV (replicating and latent) from virus reservoirs (B cell follicles) in the lymph nodes of Green Monkeys. In this species of primate, SIV is nonpathogenic and has long been known to induce persistent infection, but not induce disease. These data provide the first demonstration of a mechanism by which NK cells are specifically involved in virus clearance from a reservoir site, and was the first major collaboration between my laboratory and the Institute. This fruitful collaboration has resulted in additional collaborative studies and awarding of an NIH grant (R01 AI143457) to our teams specifically focused on extending this research.

This article has been cited 40 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Hepatic immunopathology during occult re-infection. *Virology*, 512:48-55, May 2021. doi: 10.1016/j.virol.2017.08.037. Epub 2020 Sep 13. PMID: 12345678; PMCID: PMC1234567.

A major question regarding HCV infections is whether or not re-infection occurs and, if so, can additional measures of new liver damage be detected. Using our nonhuman primate model of cleared hepacivirus (GBV-B) infection, we re-challenged animals that had previously cleared virus and evaluated systemic and local measures of hepatic pathology. Although not surprisingly viremia was blunted or absent altogether upon re-challenge, animals showed significant evidence of fibrosis and local inflammation in the liver. This confirmed that even an occult re-infection

can induce new liver pathology even in the presence of previous antiviral responses and absence of viremia.

This article has been cited 6 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Markers associated with immune activation in HIV patients on antiretroviral therapy. *Sci Rep*, 8(1):7227, May 5, 2021. doi: 10.1038/s12345-018-25515-4. PMID:12345678

Most cell types, including immune cells, release nanovesicles referred to as exosomes. Previous studies suggested a role for exosomes in HIV pathogenesis, but this study sought to better characterize the cargo of exosomes and how it impacts oxidative stress and subsequently overall immune activation and immunomodulation of myeloid cell populations. This series of experiments showed an increase in exosomes in persons living with HIV, even on ART, and that expansion correlated with generalized markers of oxidative stress and immune activation. Further, Notch4 was specifically shown as a major mediator of the effect. Overall, this collaborative study filled an important niche in the field and elucidated potential pathways that could be targeted to reduce inflammation in HIV infection.

This article has been cited 48 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Tracking KLRC2 (ABC2C)+ memory-like cells in and rhMCM+ rhesus macaques. *PLoS Pathog*, 14(5):e1234567, Jul 31, 2021. doi: 10.1371/journal.ppat.1234567. PMID: 12345678; PMCID: PMC1234567.

We described herein an expansion of rhesus CMV (rhCMV)-specific NKG2C+ NK cells in rhesus macaques and how this population is further modulated by co-infection with SIV. This study used a novel technique of RNA probe flow cytometry developed in our lab to detect mRNA of the NKG2C gene (KLRC1) because no faithful antibodies for this model exist for rhesus macaques. This study was significant to the field since it validated that rhCMV induced a virus-specific cell population of NK cells. This study also served as partial basis for pending grants R01AI123456 and R01HD123456 to study NK cell memory and NK cell responses against CMV infection.

This article has been cited 16 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Progressive infection induces natural cell receptor-expressing T cells in the gastrointestinal tract. *AIDS*, 32(12):1571-1578, Mar 31, 2020. doi: 10.1097/QAD.0000000000001234. PMID:12345678; PMCID: PMC1234567.

Conceptually, NK cell receptor-expressing B cells (NKB) have been quite controversial due to conflicting evidence in both mice and humans by multiple groups. Our team’s studies have tried unbiasedly approach this research by using advanced immunological methods to quantify phenotypically and functionally this putative cell type in humans and rhesus macaques. Initial

results revealed a systemically distributed cell population in both species fitting the description previously put forward for both mice and humans. Specifically, stable expression of surface IgM and IgA and IL-18 production was part of the unique cellular phenotype. Further, we found this population was significantly expanded during SIV infection, particularly in the gut, thus offering the first and only comprehensive characterization of this novel cell population in two species and during lentivirus infections. These findings are highly significant for the confirmation of a rare innate cell phenotype and directly led to funding of the current grant R21AI123456 for which additional studies remain ongoing.

This article has been cited 3 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Intestinal damage precedes immune dysfunction in HIV infection. *Mucosal Immunol*, 11(5):1429-1440, Oct 2021. doi: 10.1038/s41385-018-0032-5. Epub 2021 Jun 1. PMID: 12345678

HIV and SIV infections are characterized by persistent inflammation driven by microbial translocation and immune dysfunction. This is largely due to a loss of IL-17/22-producing cells in the mucosae and a breakdown of the GI mucosae. However, the kinetics of these events have been largely unclear. In this comprehensive analysis of acute SIV infection with intensive sampling of the mucosae we investigated measures of T cell activation and loss, epithelial breakdown, microbial translocation, neutrophil infiltration, as well as the colonic proteome. Largely this study revealed that both structural and functional damage occurs in epithelial cells before immune dysfunction and systemic activation. These findings clarified a missing scientific gap and offered new insights for potential immunotherapies.

This article has been cited 23 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Hallmarks of primate immunodeficiency infection recapitulate loss of lymphoid cells. *Nat Commun*, 9(1):3967, Jun 10, 2021. doi: 10.1038/s41467-018-05528-3. PMID:1234567; PMCID: PMC1234567.

This collaborative study was a direct follow-up, scientifically, to our 2014 PLoS Pathogens paper where we continued to explore mechanisms of ILC loss in HIV and SIV infections. Importantly, this study clarified that ILC could be partially preserved with antiviral therapies, and that experimental CD4 T cell depletion in the absence of infection also resulted in ILC loss. This confirmed a previous hypothesis that CD4 T cell numbers and ILC were directly linked. Indeed we further confirmed this phenomenon in persons living with HIV and also showed that in patients with idiopathic lymphopenia, ILC were also concomitantly lost. Collectively, these studies provided new mechanisms for ILC loss during lentivirus-induced disease.

This article has been cited 17 times.

1. List All Authors with the Faculty Candidate **Highlighted**. CMV Primes Functional Signaling in Adaptive NK Cells but Is Subverted by Infection in Rhesus Macaques. *Cell Rep*, 25(10):2766-2774.e3, Jan 1, 2022. doi: 10.1016/j.celrep.2021.11.020. PMID:1234567; PMCID: PMC1234567.

In this study, we provided the mechanistic basis for enhanced ADCC responses observed in gamma-chain deficient NK cells. Specifically, we showed that this cell population uses an alternative signaling pathway using the zeta chain, rather than traditional gamma-chain signaling. Further we found that lentivirus infection causes a disruption of this pathway. This study is a major component of a larger ongoing collaboration within our program project, P01AI123456, and also contributed to pending grants R01 AI123456 and R01 HD123456. Further, the study of this cell type is of significant interest for targeted immunotherapies and development of these concepts with industry partners is ongoing.

This article has been cited 11 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Semaphorin 7A modulates cytokine- induced responses by human killer cells. *Eur J Immunol*, 49(8):1153- 1166, Jan 2022. doi: 10.1002/eji.123456789. Epub 2021 May 5. PMID:1234567; PMCID: PMC1234567.

Cytokine-induced memory NK cells are one of the 4 major groups of adaptive NK cells and are currently being studied in the context of anti-cancer therapies with industry partners. However, one of the primary deficits in studying this cell population has been a lack of mechanism and lack of biomarkers. This study partially filled both these gaps by identifying Semaphorin 7A as a primary modulator of the response. This is important as it gives a targetable molecule that could be exploited in immunotherapeutics. This research is also part of a long-term and productive collaboration with Dr. Jost who works within my larger group.

This article has been cited 9 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Delineation of the Killer Cell Transcriptome in Rhesus Macaques During SIV Infections. *Front Cell Infect Microbiol*, 10:194, Apr 29, 2022. doi: 10.3389/fcimb.2020.00194. PMID:12345678; PMCID: PMC1234567.

Nonhuman primate models are critical to the study of many infectious diseases and NK cells play a major role in modulating the immune responses therein. However, despite significant investigation of NK cells in nonhuman primate models (largely by our group) the transcriptional profile of nonhuman primate NK cells had previously remained unstudied. In this publication we described in significant detail the macaque NK cell transcriptome and evaluated similarities and differences with the transcriptional profiles of human NK cells. We anticipate the publication and deposition of the raw data to serve as a resource for future NK cells studies in macaques and that was a primary goal for this study. Further, as a test-case we applied this NK cell transcriptomic signature to SIV and ZIKV datasets and successfully detected important changes in NK cell biology, confirming the utility of this approach. This was a collaboration

between our group and the Barouch and Bosinger research laboratories and provided critical data for pending grant R01AI1234567.

This article has been cited 3 times.

1. List All Authors with the Faculty Candidate **Highlighted**. Single-shot Ad46 vaccine protects against SARS-CoV-2 in rhesus macaques. *Nature*, 586(7830):583-588, Oct 2022. doi: 10.1038/s41586-020-2607-z. Epub 2022 Feb 28. PMID: 1234567; PMCID: PMC1234567.

This was a large collaborative study to provide the initial in vivo efficacy of Ad46 vaccines in protecting against SARSCoV2 in macaques. The further extension of these studies has led to the current Johnson and Johnson vaccine. Our laboratories provided analysis of innate immune cell responses for the projects, and these studies laid the foundation for two pending grants focused on NK cell biology and SARSCoV2, R01 DK123456 and R01 AI123456.

This article has been cited 132 times.