**BIOGRAPHICAL SKETCH**

NAME: Kamal Mohan Khanna

eRA COMMONS USER NAME (credential, e.g., agency login): KKHANNA

POSITION TITLE: Associate Professor, Department of Microbiology

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Youngstown State University, Youngstown, OH | B.S. | 05/1997 | Biological Sciences |
| University of Pittsburgh School of Medicine, PA | Ph.D. | 06/2004 | Immunology |
| University of Connecticut Health Center, CT | Postdoctoral Fellowship | 09/2009 | Immunology |

**A. Personal Statement**

A major focus of my lab is to identify the factors that control the activation and the anatomy of the innate and adaptive immune response to infections. My expertise lies in multi-color flow cytometry as well as single and multiphoton confocal microscopy and CODEX. Using these technologies, we study the dynamics of myeloid cells and antigen specific T cells in lymphoid and non-lymphoid tissues in response to infections and tumors.

In addition, we work extensively on the role of tissue resident macrophages in the spleen and lung in regulating pathogen clearance, tumor growth and inflammation. We recently reported the importance of CD169+ splenic resident macrophages in mediating innate immune responses by regulating pathogen localization to the splenic white pulp after infection. Furthermore, we have recently completed our study on lung resident macrophages where we describe the ontogeny and function of unique subsets of interstitial macrophages (NAMs; Nerve and Airway Associated Interstitial macropahges) and how different subsets of macrophages respond to respiratory infection and inflammation. We are now positioned very well to investigate how myeloid cells and particularly resident macrophage subsets regulate immunity and inflammation under inflammatory conditions such as infections and septic shock.

I have worked extensively with many *in vivo* infection models such as Influenza virus, SARS-CoV2, *Listeria monocytogenes*, and *Staphylococcus aureus*, to investigate the underlying mechanisms that mediate the activation, migratory and trafficking patterns of immune cells in response to infections using *in vivo* mouse models. We also use intravital imaging and other conventional methods to study the immune mechanisms that regulate mucosal homeostasis and the pathogenesis of infection induced inflammatory disorders. As a principal investigator I have continued to build upon my current research and investigate the underlying mechanisms that mediate the activation of T cells and dendritic cells in response to infections using *in vivo* mouse models. In summary, my publication track record is highly relevant to the proposed studies and I thrive on areas of research that require innovative thinking and multidisciplinary approaches. Along with my current funded grants, the following publications demonstrate my expertise.

1. Ural, BB., Yeung, ST., Devlin, JC., Vera-Licona, P., Samji, T., Sawai, CM., Perez, OP., Pham, Q., Maher, L., Loke, P., Reizis, B., **Khanna, KM**. Nerve associated lung resident interstitial macrophage subset exhibits distinct localization and polarization. (2020) *Science Immunology.* **5**, Issue 45, eaax8756. PMID: 32220976
2. Perez AO, Yeung ST, Vera-Licona PA Romagonli PA, Samji, T, Ural BB, Maher L, Tanaka M, and **Khanna KM**. Splenic CD169+ macrophages orchestrate innate immune responses by regulating bacterial localization in the spleen. (2017) *Science Immunology*. **2**: issue 16, eaah5520, PMID: 28986418. (article featured on the cover)

3. Benechet, A.P., Menon, M., Xu, D., Maher, L.A., Murooka, T.T., Mempel, T.R., **Sheridan, B.S**., Lemoine, F.M., and **Khanna, K.M.** T cell Intrinsic S1PR1 regulates endogenous CTL egress dynamics from lymph nodes during infection (2016). *PNAS* **113:** 2182-2187. PMID: 26862175
4. Romagnoli, P.A., Sheridan, B.S., Pham, Q., Lefrancois, L., and **Khanna, K.M*.** IL-17A-producing resident memory γδ T cells orchestrate the innate immune response to secondary oral *Listeria Monoctyogenes* infection. (2016). *PNAS.* **113**: 8502-8507. PMC4968747

## B. Positions, Scientific appointments and Honors

### Professional Experience

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|---|---|
| 2017-Current | Associate Professor, Department of Microbiology, NYU, Langone Health |
| 2009-2017 | Assistant Professor, Department of Immunology, University of Connecticut Health Center |
| 2004-2008 | Damon Runyon Post-Doctoral Fellow, Department of Immunology, University of Connecticut Health Center, |
| 1999-2004 | Graduate Research Assistantship, University of Pittsburgh School of Medicine, Pittsburgh, PA |
| 1997-1999 | Graduate Teaching Assistantship, Department of Biological Sciences, Youngstown State University. |

### Major Committee assignments

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|---|---|
| Oct 2013 | Ad hoc Reviewer - Cellular and Molecular Immunology - B Study Section – NIH |
| Feb 2015 | Ad hoc Reviewer - Cellular and Molecular Immunology - B Study Section – NIH |
| Oct 2015 | Ad hoc Reviewer - Cellular and Molecular Immunology - B Study Section – NIH |
| Jul 2016 | Reviewer for the special emphasis panel: ZRG1 IDM-W (51) - US- China Special Emphasis Panel study section |
| Dec 2016 | Reviewer for Immunity in Neonates and Infants UO1 study section: ZAI1-NVM-I-J1 |
| Mar 2017 | Reviewer for Special Emphasis Panel: ZRG1 IMMC02 |
| July 2017 | Reviewer for Special Emphasis Panel: ZRG1 IMM-N (02) M |
| Nov 2017 | NIH Director's New Innovator Award Review Panel – DP2 |
| Feb 2018 | Ad hoc Reviewer - Cellular and Molecular Immunology - B Study Section – NIH |
| Oct 2018 | Department of Defense Peer Reviewed Medical Research Program Study section. |
| Nov 2018 | NIH Director's New Innovator Award Review Panel – DP2 |
| Dec 2018 | Impact of Initial Influenza Exposure on Immunity in Infants: ZAI1-MFH-M-J1 |
| June 2019 | Vaccines, Host Defense, Inflammation and Immunity SEP: ZRG1 IMM-C (02) M |
| Aug 2019 | Department of Defense Peer Reviewed Medical Research Program Study section |
| Dec 2019 | NIAID Collaborative Cross Mouse Model Generation and Discovery of Immunoregulatory Mechanisms RFA study section. |
| Feb 2020 | Ad hoc Reviewer – Immunity and Host Defense – IHD study section – NIH |
| June 2020 | Reviewer for Pulmonary Host Defense Special Emphasis Panel - IMM-N (90)S |
| 2021 – 2025 | Standing member of the Immunity and Host Defense (IHD) standing study section. |

### Honors and Awards

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|---|---|
| 2021-2025 | Invited to be a Standing member of the Immunity and Host Defense (IHD) standing study section. |
| 2015-2016 | Selected as the American Association of Immunologist High School Teachers Summer Research Program in Immunology Mentor |
| 2014 | American Association of Immunologist Early Career Faculty Award |
| 2012 | American Association of Immunologist Early Career Faculty Award |
| 2011 | Chosen as an American Association of Immunologist Public Policy Fellow |
| 2010 | American Association of Immunologist Junior Faculty Award |
| 2009 | NIH Pathway to Independence Award (K99) |
| 2007 | National Institute of Allergy and Infectious Diseases, Keystone Symposia scholarship award. |
| 2004-08 | Damon Runyon Cancer Research Foundation Fellowship award |

2003 American Association of Immunologist-Huang Foundation Trainee Achievement Award
2002 University of Pittsburgh School of Medicine Travel fellowship

**C. Contribution to Science**

1. My early contributions to science consist of developing and using novel and cutting edge imaging technologies in combination with novel mouse models to visualize *endogenous* Ag-specific CD8 T cell migration and localization in virtually any lymphoid or non-lymphoid tissue, I realized that local anatomy of lymphoid tissues during steady state or during infection is a critical regulator of immunity, thus, studying the cellular choreography in context of an intact tissue environment *in-situ* was crucial. Understanding the aforementioned concepts lead to several novel findings. For example, my early work led to a paradigm shift in our concept of herpes simplex virus-1 latency (Immunity, 18; 593). The prevailing 'silent virus' model was replaced by a dynamic model of viral latency in which persistent attempts at reactivation are controlled through the constant vigilance of the immune system. Subsequently, as a Damon Runyon Fellow I modified the imaging techniques and visualized the entire kinetics of an anti-microbial immune response and the spatial relationships between T cells, antigen-presenting cells and organ structure. This work led to the publication of a ground breaking *Science* paper (Vol 318: 116) in which I described the previously unknown migratory properties of the *endogenous* primary and memory CD8 T cells responding to a bacterial infection in the spleen.

1. Benechet, AP., Menon, M., and **Khanna, KM**. Visualizing T cell migration in situ. (2014) *Front Immunol*. **5:** 363. PMC4114210, PMCID: PMC4114210
2. Romagnoli, PA, Fu, HH, Qiu, Z, Khairallah, C, Pham, QM, Puddington, L, **Khanna, KM**, Lefrançois, L, and Sheridan, BS. (2016). Differentiation of distinct long-lived memory CD4 T cells in intestinal tissues after oral *Listeria monocytogenes* infection. *Mucosal Immunology*. **10**: 520-530. PMC5272904
3. **Khanna, K.M.,** McNamara, J.T., and Lefrançois. L. In situ imaging of the endogenous CD8 T cell response to infection. (2007) *Science.* **318:** 116-120. PMC2846662
4. **Khanna K.M.,** Bonneau R.H., Kinchington P.R., and Hendricks R.L. (2003) Herpes simplex virus glycoprotein B-specific memory $CD8^+$ T cells are activated and retained in latently infected sensory ganglia and can regulate viral latency. *Immunity*. **18**: 593-606. PMC2871305

2. Our laboratory continues to investigate the underlying mechanisms that regulate the generation of a protective innate and adaptive immune responses during infection or cancer. We have reported on the precise cellular mechanisms that lead to a protective (vs. poorly protective) immune responses in vivo. We have been using a comprehensive and innovative experimental approach which includes cutting edge imaging, flow cytometry and genomics approaches (RNA sequencing) to advance our understanding of how a productive anti-microbial immune response progresses in vivo. Using the knowledge we have gained from our aforementioned studies, we have recently developed novel vaccine vehicle against cancers. Our several funded grants, and published articles exemplify our contributions and we continue to submit several articles, which will be published in the coming months.

1. Sharma, N., Benechet, AP., Lefrancois, L., and **Khanna KM**. CD8 T Cells Enter The Splenic T Cell Zones Independently Of CCR7 But The Subsequent Expansion And Trafficking Patterns Of Effector T Cells After Infection Are Dysregulated In The Absence Of CCR7 Migratory Cues. (2015). Journal of Immunology. 195: 5227-36. PMC4655190
2. Grenier JM, Yeung ST, Qiu Z, Jellison ER, and **Khanna KM.** Combining adoptive cell therapy with cytomegalovirus-based vaccine is protective against solid skin tumors. (2018) *Frontiers in Immunology:* **8:** 1993, PMC5775971
3. Qiu, Z., Huang, H., Grenier, JM., Perez, O.A., Smilowitz, HM., Adler, B., and **Khanna, KM**. Cytomegalovirus based vaccine expressing a modified tumor antigen induces potent tumor-specific CD8+ T cell response and protects mice from melanoma (2015). doi:10.1158/2326-6066. *Cancer Immunology Research*. PMID: 25633711

4. **Khanna, K.M**., Vella, A.T., McSorley, S.J., Datta, S.K., and Lefrançois, L. (2010) T cell and antigen-presenting cell dynamics in situ control the outcome of vaccination. *J Immunol*. **185:** 239-252. PMC2997353

**Complete List of Published Work in MyBibliography:**

https://www.ncbi.nlm.nih.gov/sites/myncbi/1ZI6nzgZ3QIAk/bibliography/45907329/public/?sort=date&direction=ascending

**D. Research Support**

**Ongoing Research Support**

1R01AI143861 (Khanna, PI)
NIH/NIAID 01/01/19 – 12/31/2023
Novel lung resident interstitial macrophage subset with distinct localization and polarization
Tissue resident macrophages play critical roles in maintaining immune homeostasis in mucosal organs. Here we report the discovery of a previously uncharacterized subset of pulmonary macrophages that are exclusively found around the large bronchiole airways in mice and in humans. Understand the fundamental properties of these novel cells will help in developing new targeted strategies for preventing infection-induced inflammation

3R01AI143861-02S1 (PI: Khanna) 06/18/2020 – 12/31/2023
NIH/NIAID (COVID Supplement)
Title: Novel lung resident interstitial macrophage subset with distinct localization and polarization
The goal of this project is to model SARS-CoV2 infection and human COVID19 disease in mice using humanized ACE2 transgenic mice

R21 AI147359-02 (Khanna, PI) 01/10/2020 - 12/31/2021
The major goals of this project is to determine what the role of CX3CR1 CD4+ T cells in mediating helminth infection clearance.

2R37AI038446-26 (PI: Weiser) 04/01/1996-06/30/2025
Title: Mechanisms of Pneumococcal Persistence during Carriage
This project is focused on cellular immunity in the clearance of colonization by Streptococcus pneumonia.
Role: Co-Investigator

**Completed Research Support**

W81XWH-17-1-0480 (Khanna, PI) 09/30/17 – 09/29/20
DOD
Mechanisms and Therapeutic Implications of the Pregnane X Receptor Targeting Indole Bacterial Metabolites in Inflammatory Bowel
The goals of this proposal are to utilize mechanistic studies designed to understand how enteric infection may trigger inflammatory bowel diseases and target the pregnane X receptor (PXR) for therapy against infection induced inflammation in the intestinal mucosa.

5U01-AI095544 (Khanna, PI) 07/01/2011-06/30/2016
Role of TCR γδ cells in the mucosal response to intestinal infection
The aims of this proposal are focused on understanding the induction and function of TCR γδ memory T cells in the intestinal mucosa in response to oral bacterial infection.

1R21-AI109188 (Khanna, PI) 07/11/2014 – 06/30/2016
NIH/NIAID
Mechanisms controlling memory CD8 T cell recognition of autoantigen

The goal of this project is to determine how peripheral tolerance is maintained in the wake of autoantigen expression and how these tolerance mechanisms control memory CD8 T cell responses in the mucosal tissues.

1R01AI097375 (Khanna, PI) 09/01/13 - 01/31/17
NIH/NIAID (Diversity Supplement)
Visualizing the Innate and adaptive Immune response to Listeria Monocytogenes
In this proposed study we will use three different immunization models to determine the mechanisms responsible for mounting a protective anti-microbial immune response. By identifying the specific immune mechanisms that are either disrupted or poorly activated by co-immunization or immunization with attenuated bacterial vaccines in vivo, we will better understand the factors that regulate the generation of protective innate and adaptive immune responses.

1R01AI097375 (Khanna, PI) 02/01/12 - 01/31/18 (NCE)
NIH/NIAID
Visualizing the Innate and adaptive Immune response to Listeria Monocytogenes
In this proposed study we will use three different immunization models to determine the mechanisms responsible for mounting a protective anti-microbial immune response. By identifying the specific immune mechanisms that are either disrupted or poorly activated by co-immunization or immunization with attenuated bacterial vaccines in vivo, we will better understand the factors that regulate the generation of protective innate and adaptive immune responses.

PO1-AI056172 (Khanna, Core PI) 05/15/13 – 04/30/18
NIH/NIAID
Modulation of Biodefense Responses to Microbial Pathogens
Core C (fluorescence Microscopy Core) Director
The major goal of this project is to define the parameters for development of protective immunity against viral and bacterial pathogens and their products. The central hypothesis is that early events in T cell activation determine whether or not long-term immunity is induced in response to vaccination, or whether damage is initiated in response to a bacterial toxin

2R01AI041576 (Khanna, PI) 08/16/13 - 7/31/17
NIH/NIAID
CD8 T Cell Activation and Migration in vivo
The major goals of this proposal is to identify the checkpoints in memory CD8 T cell development after infection. In this proposed study we will determine how external milieu affects CD8 T cell differentiation and identify the metabolic, and molecular mechanisms that influence the developmental potential of early effector CD8 T cells into memory T cells.

W81XWH-14-1-0342 (Khanna, PI) 09/30/14 – 03/29/17
DOD
Development of Cytomegalovirus Based Vaccines Against Melanoma
The major goal of this proposal is to develop virus vectors that express melanoma antigens as prophylactic and therapeutic vaccines to treat melanoma.

U01AI095776 (Khanna) 07/01/15 – 06/30/17
Human MAIT Cells in Airway Mucosal Immune Responses to Intracellular Infections
The major goal of this grant is to determine how pregnane X receptor (PXR) regulates inflammation in the gut mucosa after enteric infections.