NIH-FDA IIG

National Institutes of Health // Food and Drug Administration // Immunology Interest Group

NEWSLETTER

SEPTEMBER 2022

PUBLICATIONS

Intranasal inoculation of an MVA-based vaccine induces IgA and protects the respiratory tract of hACE2 mice from SARS-CoV-2 infection

Americo JL, Cotter CA, Earl PL, Liu R, Moss B
Proc Natl Acad Sci USA. 2022 Jun 14; 119(24) e2202069119
DOI: 10.1073/pnas.2202069119. PMID: 35679343. PMCID: PMC9214525

Current vaccines have greatly diminished the severity of the COVID-19 pandemic, even though they do not entirely prevent infection and transmission, likely due to insufficient immunity in the upper respiratory tract. Here, we showed that intranasal administration of a replication-deficient modified vaccinia virus Ankara (MVA)-based SARS-CoV-2 spike vaccine raised protective immune responses in the K18-hACE2 mouse model and prevented or rapidly reduced replication of SARS-CoV-2 in the upper and lower respiratory tract.

Single-Cell Analysis Reveals the Range of Transcriptional States of Circulating Human Neutrophils

Wigerblad G, Cao Q, Brooks S, Naz F, Gadkari M, Jiang K, Gupta S, O'Neil L, Dell'Orso S, Kaplan MJ, Franco LM
J Immunol. 2022 Jul 20:ji2200154.
DOI: 10.4049/jimmunol.2200154. PMID: 35858733.

In We describe a data analysis pipeline that can significantly increase the detection of human neutrophils in scRNA-seq and apply this pipeline to the study of human peripheral blood neutrophils. Our findings indicate that circulating human neutrophils are transcriptionally heterogeneous cells, which can be classified into one of four transcriptional clusters that are reproducible among healthy human subjects.

High-throughput imaging of mRNA at the single-cell level in human primary immune cells

L Gadkari M, Sun J, Carcamo A, Alessi H, Hu Z, Fraser IDC, Pegoraro G, Franco LM
RNA. 2022 Sep;28(9):1263-1278.
DOI: 10.1261/rna.079239.122. PMID: 35764396. PMCID: PMC9380748.

We describe a method for High-Content Imaging (HCI)-based quantification of relative changes in transcript abundance at the single-cell level in human primary immune cells. We anticipate that this method, which we abbreviate as hcHCR, will be a suitable assay for low- to medium-throughput chemical, genetic or functional genomic screens in primary human cells, with the possibility of performing personalized screens or screens on cells obtained from patients with a specific disease.

Preclinical and clinical studies of bintrafusp alfa, a novel bifunctional anti-PD-L1/TGFBβRII agent: Current status

Gameiro SR, Strauss J, Gulley JL, Schlom J
Exp Biol Med (Maywood). 2022 Jul;247(13):1124-1134.
DOI: 10.1177/15353702221089910. PMID: 35473390. PMCID: PMC9335510.

This article reviews recent preclinical data interrogating the mode of action of bintrafusp alfa and the potential role of TGFβB in human papillomavirus (HPV)-associated malignancies and presents a comprehensive overview of recent bintrafusp alfa clinical studies in a range of malignancies.

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Tumor-targeted interleukin-12 synergizes with entinostat to overcome PD-1/PD-L1 blockade-resistant tumors harboring MHC-I and APM deficiencies

Minnar CM, Chariou PL, Horn LA, Hicks KC, Palena C, Schlom J, Gameiro SR
J Immunother Cancer. 2022 Jun;10(6):e004561.
DOI: 10.1136/jitc-2022-004561. PMID: 35764364. PMCID: PMC9240938.
Murine studies showed that the combination of entinostat and NHS-IL12 therapy elicits potent antitumor activity and survival benefit through prolonged activation and tumor infiltration of cytotoxic CD8+ T cells in three αPD-1/αPD-L1) refractory models. These findings provide a rationale for this combined use in the clinical setting for patients whose tumors have innate or acquired αPD1/αPD-L1 resistance and/or defects in APM.

Immune correlates of clinical parameters in patients with HPV-associated malignancies treated with bintrafusp alfa

Tsai YT, Strauss J, Toney NJ, Jochems C, Venzon DJ, Gulley JL, Schlom J, Donahue RN
J Immunother Cancer. 2022 Apr;10(4):e004601.
DOI: 10.1136/jitc-2022-004601. PMID: 35418484. PMCID: PMC9014099.
Interrogation of both cellular and soluble components of the peripheral immunome, either prior to therapy for HPV-associated malignancies, or early in the therapeutic regimen, can help define which patients are most likely to benefit clinically from the novel immunotherapeutic agent bintrafusp alfa, as well as aid in defining the mechanism of action of a given immunotherapeutic and potentially provide valuable prognostic information.

Neoantigen Presentation and IFNgy Signaling on the Same Tumor-associated Macrophage are Necessary for CD4 T Cell-mediated Antitumor Activity in Mice

Perez-Diez A, Liu X, Matzinger P
J Cancer Res Commun. 2022 May;2(5):316-329.
DOI: 10.1158/2767-9764.crc-22-0052. PMID: 35903540. PMCID: PMC9321644.
We and others have previously shown that tumor specific CD4 T cells can be very efficient rejecting tumors in both animal models and clinical settings. Mechanistically, we show here the cellular and molecular changes that CD4 T cells induce on tumor associated macrophages (TAM) for full anti-tumor effect, mainly through cognate interaction and IFN-g signaling on the same TAM.

Cell surface SARS-CoV-2 nucleocapsid protein modulates innate and adaptive immunity

López-Muñoz AD, Kosik I, Holly J, Yewdell JW
Sci Adv. 2022 Aug 5;8(31):eabp9770.
DOI: 10.1126/sciadv.abp9770. PMID: 35921414. PMCID: PMC9348789.
SARS-CoV-2 Nucleocapsid Protein, considered to be localized in the cytosol, is abundantly expressed on the cell surface during infection. This work characterizes the mechanisms governing Nucleocapsid cell surface binding, transference to neighboring cells, and immunomodulation.

Rapid GPR183-mediated recruitment of eosinophils to the lung after Mycobacterium tuberculosis infection

Bohrer AC, Castro E, Tocheny CE, Assmann M, Schwarz B, Bohrnsen E, Makiya MA, Legrand F, Hilligan KL, Baker PJ, Torres-Juarez F, Hu Z, Ma H, Wang L, Niu L, Wen Z, Lee SH, Kamenyeva O; Tuberculosis Imaging Program, Kauffman KD, Donato M, Sher A, Barber DL, Via LE, Scriba TJ, Khatri P, Song Y, Wong KW, Bosio CM, Klion AD, Mayer-Barber KD
Cell Rep. 2022 Jul 26;40(4):111144.
DOI: 10.1016/j.celrep.2022.111144. PMID: 35905725. PMCID: PMC9460869.
Here we show that eosinophils are among the earliest cells from circulation to sense and respond to Mycobacterium tuberculosis (Mtb) infection, as early as one week after Mtb exposure. In mice this influx is CCR3 independent and instead requires cell-intrinsic expression of the oxysterol receptor GPR183, which is highly expressed on human and macaque eosinophils.

Dual B-cell targeting therapy ameliorates autoimmune cholangitis

Zhang W, Shao T, Leung PSC, Tsuneyama K, Heuer L, Young HA, Ridgway WM, Gershwin ME
J Autoimmun. 2022 Aug 24;132:102897.
DOI: 10.1016/j.jaut.2022.102897. PMID: 36029718.
Utilizing a mouse model of primary biliary cholangitis developed at the NIH, the authors demonstrate that depletion of B cells with anti-BAFF and anti-CD20 results in significant clinical improvement. The authors identified a specific IgM+ FCRL5+ B cell subset as the primary target of depletion.

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Treatment with a JAK1/2 inhibitor ameliorates murine autoimmune cholangitis induced by IFN overexpression

Shao T, Leung PSC, Zhang W, Tsuneyama K, Ridgway WM, Young HA, Shuai Z, Ansari AA, Gershwin ME

Cell Mol Immunol. 2022 Aug 30.

DOI: 10.1038/s41423-022-00904-y. PMID: 36042351.

In this manuscript the authors demonstrate that, in a mouse model of autoimmune cholangitis induced by chronic IFN-g expression, treatment of female mice with the JAK1/2 inhibitor ruxolitinib reversed disease. Interestingly peritoneal and liver macrophages were polarized from an M1 to an M2 phenotype and that correlated with an increase in IRF4 and STAT6 expression

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SPOTLIGHT

Dr. Carlson is a Principal Investigator in the Division of Bacterial, Parasitic and Allergenic Products, Office of Vaccines Research and Review in CBER FDA. To learn more about his work visit: https://www.fda.gov/vaccines-blood-biologics/biologics-research-projects/identification-targets-development-vaccines-and-biological-therapies-against-gastrointestinal

Paul Carlson, Ph.D.

Tell us about your science.

My laboratory works on a wide range of topics including bacterial pathogenesis (Clostridioides difficile iron acquisition and oxygen resistance), Fecal Microbiota Transplantation (safety, manufacturing methods, and biomarkers of potency), assay development for Live Biotherapeutic Products (LBPs), and bacteriophage therapy. Currently, the phage therapy project is the primary immunology project in the laboratory. We are working to understand the host immune response mounted against a phage during therapeutic use and how that could impact reuse of a given phage product in the same individual. We, like others, have seen significant host responses targeting the phage, particularly antibody responses. Interestingly, we are seeing different levels of antibody neutralization against different families of phage, indicating that understanding the immunogenicity of a given phage may warrant consideration in phage cocktail design.

What event(s) lead to your career in science and interest in immunology?

For as long as I can remember, I have had an interest in science and biology in particular. Gradually that grew more specific, into an interest in immunology and infectious disease. For my PhD, I worked on innate immune responses to the intracellular bacterium, Francisella tularensis, and its ability to shut down those responses. While this lead to a greater focus on how pathogens respond to and alter their environments during infection, the role of the immune system has always been in the back of my mind. More recently, after starting my lab at FDA, we started studying various aspects of bacteriophage therapies and one immediate question was whether the immune system would have an impact on use of this therapeutic modality. This question brought a renewed interest in immunology to the laboratory. We are now working to elucidate both innate and adaptive immune responses to bacteriophage therapy to better understand how to improve the effectiveness of this novel therapeutic.

How has a mentor or colleague substantially influenced your career trajectory?

Throughout my career I have been lucky to have supportive mentors that inspired and challenged me. My grad school and postdoc mentors were at very different stages of their careers, one just starting his assistant professor position and the other an established full professor. While I obviously benefited from their unique experiences, they both supported and encouraged independent exploration which allowed me the freedom to pursue interesting and important research questions. Looking back, I recognize that the support from my mentors and their encouragement to explore were invaluable.

In what area(s) do you expect significant research/medical advances in the next 5-10 years?

I would expect to see both the microbiome and bacteriophage therapy fields to see significant advances in the next decade. In terms of therapeutic potential, these fields are still in their infancy. I expect significant advances in our understand of the contribution of members of the human microbiota, and their components/products, to overall health and disease. I also expect the phage field to grow significantly as more clinical usage is seen and more questions arise regarding ways to improve these therapeutic viruses.

What do you value most about the NIH-FDA Immunology community?

Due to the diverse scientific focus of my laboratory, which is made up of mainly microbiologists, IIG has been vital in providing scientific expertise and resources lab members working on immunology based projects. We have especially benefitted from the weekly seminar series, IIG workshop, and emergency reagents listserv.

How do you spend your free time?

I enjoy fishing, hiking and other activities with my wife and daughter.

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SPOTLIGHT

Dr. Jigar Desai just completed his postdoctoral fellowship under Dr. Michail Lionakis' mentorship and started his own lab at Hackensack Research Institute. IIG congratulates Dr. Desai as a new faculty and alumnus of NIAID/NIH. To learn more about his work visit:
https://hmh-cdi.org/our-team/desai-lab/

Jigar V. Desai, Ph.D.

Tell us about your science.

My research focuses on defining organ-specific mechanisms involved in regulating the innate immune response, with an emphasis on invasive fungal infections such as invasive candidiasis and aspergillosis. During my postdoctoral fellowship with Dr. Lionakis at the NIAID, I uncovered a novel role for the complement system protein- C5 in antifungal host defense. Building upon this work, I aim to decipher the tissue-specific interplay between proteins of the complement system and fungi and its impact on local and systemic immunity. To this end, my lab at the Center for Discovery & Innovation (CDI at Hackensack Meridian Health, NJ) utilizes in vivo murine infection/colonization models, genetically engineered mouse/fungal strains, primary-cells/cell lines for in vitro assays, real-time intravital microscopy, and host/pathogen-directed organ-specific transcriptomics. Through this work, I anticipate providing novel insights into organ-specific regulation of antifungal immune response and elucidating previously uncharacterized mechanisms of complement biology.

What event(s) lead to your career in science and interest in immunology?

Atop my childhood fascination with basic sciences, I had the fortune of having exceptionally brilliant scientists as my mentors who have guided me to where I am currently. My interest in immunology started growing as I was completing my Ph.D. As a graduate student, I was investigating the genetic and biophysical basis of fungal pathogenesis; increasingly, I wanted to understand the mechanistic basis of how the host dealt with the fungus, which itself is a commensal but can be a deadly opportunistic pathogen. To that end, I joined the Fungal Pathogenesis Section as a postdoctoral fellow with Dr. Lionakis, where my fascination with immunology increased by leaps and bounds.

How has a mentor or colleague substantially influenced your career trajectory?

I began my postdoctoral fellowship as a novice in immunology. Still, by the end of my fellowship, I was able to secure a K99/R00 Pathway to independence award and successfully transition to establish my lab. All these wouldn't have been possible without the active support of my postdoctoral mentor, Michail S. Lionakis. Additionally, I was exceptionally fortunate to be surrounded by highly creative clinical and postdoctoral fellows at the Fungal Pathogenesis Section, many of whom actively assisted me in my journey; I can't thank them enough!

In what area(s) do you expect significant research/medical advances in the next 5-10 years?

For my general research area, I expect significant advancement in understanding how the commensal mycobiome and common environmental fungi condition the local and systemic immune response and impact overall human health.

What do you value most about the NIH-FDA Immunology community?

I truly appreciate the collaborative nature and generosity of the NIH-FDA Immunology community. From a trainee's perspective, I believe that the community is one of the most valuable resources from the standpoint of career development/advancement and a reinforcer of truly collaborative science.

How do you spend your free time?

I enjoy cooking, running, biking and board games.

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2022 IIG Workshop

December 8–9, 2022 - Natcher Conference Center - BG 45

The planning effort for the 2022 FDA-NIH IIG Workshop held on December 8 – 9, 2022 at the Natcher Conference Center continues!

Thank you to all who registered for this year's workshop. Now that the registration period has closed, the Workshop Committee will review the submitted abstracts and create the scientific program. As in the past, some abstracts will be selected for short talks and the rest will be considered for in-person poster presentations at Natcher. Posters will also be available on-line as static presentations (but will not be interactive).

Natcher Conference Center (Building 45), National Institutes of Health (NIH)

As a reminder, we expect this to be a hybrid meeting, with space for ~200 people in-person and the remainder as virtual only. We'll update the plans if conditions dictate a change to an all-virtual format.

Our 2022 workshop gurus will be Erika Pearce, from Johns Hopkins University, and NIAID's own Yasmine Belkaid. We hope that journal editors will again be our guests, and planning for special sessions (over and above the science driven by your great data) is underway as well. So, get ready!

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Your Votes Are In!

We're pleased to announce the election of the newest members to join the IIG Steering Committee!

Tenured PI (2 year term)
- Gregoire Altan-Bonnet (NCI)
- Li Yang (NCI)
- Michael Sack (NHLBI)

Tenure-track Investigator / Assistant Clinical Investigator (2 year term)
- Christian Mayer (NCI)
- Julie Fox (NIAID)

Staff Scientist / Staff Clinician (2 year term)
- Amy Hsu (NIAID)
- Sabina Kaczanowska (NCI)
- Masashi Watanabe (NCI)

Postdoctoral Fellow / Graduate Student (1 year term)
- Amy Zhang (NEI)
- Alexandria Wells (NIAID)
- Susannah Shissler (NCI)
- Oyebola (Bola) Oyesola (NIAID)

FDA Liaison (2 year term)
- Ha-Na Lee (FDA)

Thank you to the entire IIG community for participating in the elections!

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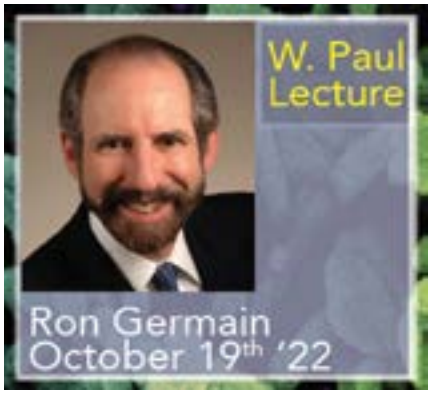
SEMINAR SERIES

Upcoming seminars



Missed a seminar?

Catch up on prior talks at...

https://www.niaid.nih.gov/research/immunology-seminars

FDA: http://web.microsoftstream.com/channel/5c371a75-2d56-45d3-9f86-7bacc3015066

*Recordings are generally available 1-2 weeks after the pre-

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Join the Listserv!

Immunology Interest Group

Share with new colleagues and trainees that join the lab:

Please visit the IIG website and (re)subscribe to the IMMUNI-L NIH Listserv with your NIH or FDA email address:

https://www.niaid.nih.gov/research/immunology-interest-group

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