NIH-FDA IIG

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

NEWSLETTER

SEPTEMBER 2023

PUBLICATIONS

Low cross reactivity between wild type and deamidated AAV can lead to false negative results in immune monitoring T-cell assays

Bing SJ, Warrington S, Mazor R.
Front Immunol. 2023 Jul 4;14:1211529.
PMID: 37469509 PMCID: PMC10352612 DOI: 10.3389/fimmu.2023.1211529.

We found that Adeno Associate Virus (AAV) gene therapy undergoes deamidation that can change the amino acid sequence of the capsid. This post translational modifications can cause altered T cell epitope presentation and change the immune response profile for this therapy. In this manuscript we describe how this change in sequence can compromise the performance of T cell immune monitoring assays that are performed after gene therapy and propose a simple solution to mitigate this problem.

Loss of CD4+ T cell-intrinsic arginase 1 accelerates Th1 response kinetics and reduces lung pathology during influenza infection

West EE, Merle NS, Kamiński MM, Palacios G, Kumar D, Wang L, Bibby JA, Overdahl K, Jarmusch AK, Freeley S, Lee DY, Thompson JW, Yu ZX, Taylor N, Sitbon M, Green DR, Bohrer A, Mayer-Barber KD, Afzali B, Kazemian M, Scholl-Buergi S, Karall D, Huemer M, Kemper C.
Immunity. 2023 Sep 12;56(9):2036-2053.e12.
PMID: 37572656 DOI: 10.1016/j.immuni.2023.07.014 Epub 2023 Aug 11.

Th1 cells play an important role in the control of infections, but uncontrolled/unregulated Th1 responses often result in detrimental tissue pathology. Our work shows that Th1 cells intrinsically express the enzyme arginase 1, and that loss of arginase 1 (in contrast to arginase 2) in CD4 T cells enhances the kinetics of the Th1 response (via altered glutamine metabolism), resulting in normal viral clearance and reduced pathology during influenza infection.

Transcription factor TCF-1 regulates the functions, but not the development, of lymphoid tissue inducer subsets in different tissues

Zheng M, Yao C, Ren G, Mao K, Chung H, Chen X, Hu G, Wang L, Luan X, Fang D, Li D, Zhong C, Lu X, Cannon N, Zhang M, Bhandoola A, Zhao K, O'Shea JJ, Zhu J.
Cell Rep. 2023 Aug 29;42(8):112924.
PMID: 37540600 PMCID: PMC10504686 DOI: 10.1016/j.celrep.2023.112924 Epub 2023 Aug 3.

Title explained the main findings.

GATA3 induces the pathogenicity of Th17 cells via regulating GM-CSF expression

Butcher MJ, Gurram RK, Zhu X, Chen X, Hu G, Lazarevic V, Zhao K, Zhu J.
Front Immunol. 2023 Jun 28;14:1186580.
PMID: 37449212 PMCID: PMC10337884 DOI: 10.3389/fimmu.2023.1186580.

Title explained the main findings.

Glucose-6-phosphate dehydrogenase deficiency and long-term risk of immune-related disorders

Israel A, Schäffer AA, Berkovitch M, Ozeri DJ, Merzon E, Green I, Golan-Cohen A, Ruppin E, Vinker S, Magen E.
Front Immunol. 2023 Sep 11;14:1232560.
PMID: 37753082 PMCID: PMC10518697 DOI: 10.3389/fimmu.2023.1232560.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked enzymatic disorder that is common in certain regions and populations including the Middle East and African Americans. In this large case-control study among member of an Israeli Health Maintenance Organization, we found that GP6D deficiency is associated with significantly increased incidence

of susceptibility to infections (e.g., by Staphylococcus), allergies (e.g., urticaria), and autoimmune disorders (e.g., rheumatoid arthritis).

MAVS Positively Regulates Mitochondrial Integrity and Metabolic Fitness in B Cells

Wang H, Sun W, Traba J, Wu J, Qi CF, Amo L, Kole HK, Scott B, Singh K, Sack MN.
Immunohorizons. 2023 Aug 1;7(8):587-599.
PMID: 37610299 DOI: 10.4049/immunohorizons.2300038.

MAVS is well known as a mitochondrial-tethered signaling adaptor with a central role in viral RNA-sensing pathways that induce type I IFN. We report here that MAVS plays a previously unrecognized role in controlling mitochondrial remodeling and the metabolic fitness of B cells, most noticeable in the absence of costimulatory help.

Isolation of Mouse Neutrophils

Wishart AL, Swamydas M, Lionakis MS.
Curr Protoc. 2023 Sep;3(9):e879.
PMID: 37707422 PMCID: PMC10503263 DOI: 10.1002/cpz1.879.

Provided are updated protocols for isolation of neutrophils from the mouse bone marrow and tissues for use in downstream functional analyses.

Evidence of a Sjögren's disease-like phenotype following COVID-19 in mice and human

Shen Y, Voigt A, Goranova L, Abed MA, Kleiner DE, Maldonado JO, Beach M, Pelayo E, Chiorini JA, Craft WF, Ostrov DA, Ramiya V, Sukumaran S, Brown AN, Hanrahan KC, Tuanyok A, Warner BM, Nguyen CQ.
JCI Insight. 2023 Sep 7:e166540.
PMID: 37676726 DOI: 10.1172/jci.insight.166540 Epub ahead of print.

This paper illustrates the association between SARS-CoV-2 infection and Sjogren's Disease (SjD). Results shows that after SARS-CoV-2 infection, mouse and humans exhibit decreased saliva flow, elevated levels of antinuclear antibodies (ANAs) with anti-SSB/La, and lymphocyte infiltration in the lacrimal and salivary glands; all markers consistent with SjD.

Co-infection of mice with SARS-CoV-2 and Mycobacterium tuberculosis limits early viral replication but does not affect mycobacterial loads

Baker PJ, Amaral EP, Castro E, Bohrer AC, Torres-Juárez F, Jordan CM, Nelson CE, Barber DL, Johnson RF, Hilligan KL, Mayer-Barber KD.
Front Immunol. 2023 Sep 1;14:1240419.
PMID: 37720210 PMCID: PMC10502726 DOI: 10.3389/fimmu.2023.1240419.

As viral coinfection can worsen the outcome of Mycobacterium tuberculosis (Mtb) infection, often through increased type-I interferon (IFN-I) production, we asked whether coinfection of mice with Mtb and SARS-CoV-2 (SCV2) would alter the outcome of either disease. We found that while SCV2 co-infection did not affect mycobacterial loads, pulmonary SCV2 titres were reduced in mice with ongoing Mtb infection compared to their SCV2-only counterparts independently of TLR2, TLR9 or IFN-I signalling.

Granulocytes subsets and their divergent functions in host resistance to Mycobacterium tuberculosis - a 'tipping-point' model of disease exacerbation

Mayer-Barber KD.
Curr Opin Immunol. 2023 Jul 10;84:102365.
PMID: 37437471 DOI: 10.1016/j.coi.2023.102365 Epub ahead of print.

Granulocytes are innate immune effector cells with essential functions in host resistance to bacterial infections. Emerging evidence is reviewed that during Mycobacterium tuberculosis infection, counter-intuitively, eosinophils are host-protective while neutrophils are host detrimental. Additionally, a 'tipping-point' model is proposed in which neutrophils are an integral part of a feedforward loop driving tuberculosis disease exacerbation.

Endogenous and Therapeutic 25-hydroxycholesterols May Worsen Early SARS-CoV-2 Pathogenesis in Mice

Fessler MB, Madenspacher JH, Baker PJ, Hilligan KL, Bohrer AC, Castro E, Meacham J, Chen SH, Johnson RF, McDonald JG, Martin NP, Tucker CJ, Mahapatra D, Cesta M, Mayer-Barber KD.
Am J Respir Cell Mol Biol. 2023 Aug 14.
PMID: 37578898 DOI: 10.1165/rcmb.2023-0007OC Epub ahead of print.

Oxysterols, derived for example from the enzyme Ch25h, have been implicated in modulating viral replication. Here we show, together with collaborators from NIEHS, that both endogenous and therapeutic 25-hydroxycholesterols do not impact SARS-CoV2 infection in mice and mice deficient in Ch25h and the oxysterol receptor GPR183 (EBI2) have similar viral titers to control mice.

Continued>>

Pyruvate dehydrogenase operates as an intramolecular nitroxyl generator during macrophage metabolic reprogramming

Palmieri EM, Holewinski R, McGinity CL, Pierri CL, Maio N, Weiss JM, Tragni V, Miranda KM, Rouault TA, Andresson T, Wink DA, McVicar DW.
Nat Commun. 2023 Aug 22;14(1):5114.
PMID: 37607904 PMCID: PMC10444860 DOI: 10.1038/s41467-023-40738-4.

Nitric oxide (NO) has been shown to be responsible for the mitochondrial rewiring resulting from macrophage polarization under pro-inflammatory stimuli. Here, the authors provide evidence for in situ production of nitroxyl (HNO) via the pyruvate dehydrogenase (PDH) cofactor lipoate, as key to sustain direct PDH inhibition.

Boosting NAD preferentially blunts Th17 inflammation via arginine biosynthesis and redox control in healthy and psoriasis subjects

Han K, Singh K, Meadows AM, Sharma R, Hassanzadeh S, Wu J, Goss-Holmes H, Huffstutler RD, Teague HL, Mehta NN, Griffin JL, Tian R, Traba J, Sack MN.
Cell Rep Med. 2023 Sep 19;4(9):101157.
PMID: 37586364 PMCID: PMC10518596 DOI: 10.1016/j.xcrm.2023.101157 Epub 2023 Aug 15.

To uncover mechanisms whereby NAD+-boosting blunts inflammation, we explored how the NAD+ precursor nicotinamide riboside (NR), regulated immune function in healthy subjects and in the inflammatory disease psoriasis. NR promotes arginine and fumarate biosynthesis, which in turn activates NRF2-orchestrated anti-oxidant defense pathways, resulting in amelioration of CD4+ Th17 immune responsiveness.

Cell surface nucleocapsid protein expression: A betacoronavirus immunomodulatory strategy

López-Muñoz AD, Santos JJS, Yewdell JW.
Proc Natl Acad Sci U S A. 2023 Jul 11;120(28):e2304087120.
PMID: 37399385 PMCID: PMC10334784 DOI: 10.1073/pnas.2304087120 Epub 2023 Jul 3.
This study is also featured in the PNAS showcase on "Kudos": https://www.growkudos.com/publications/10.1073%25252Fpnas.2304087120/reader

We reported that SARS-CoV-2 Nucleocapsid (N) protein is abundantly expressed on the surface of both infected and neighboring uninfected cells, where it is a target for antibody-based immunity and inhibits leukocyte chemotaxis by binding chemokines. In this study, we extend these findings to N from the common cold human coronavirus (HCoV)-OC43. This protein also inhibits CXCL12-mediated leukocyte migration in chemotaxis assays, as do all highly pathogenic and common cold HCoV N proteins.

The emerging importance of lymphatics in health and disease: an NIH workshop report

Mehrara BJ, Radtke AJ, Randolph GJ, Wachter BT, Greenwel P, Rovira II, Galis ZS, Muratoglu SC.
J Clin Invest. 2023 Sep 1;133(17):e171582.
PMID: 37655664 PMCID: PMC10471172 DOI: 10.1172/JCI171582.

This Review summarizes the outcomes of the NIH workshop entitled "Yet to be Charted: Lymphatic System in Health and Disease," held in September 2022, with emphasis on major areas for advancement. International experts showcased the current state of knowledge regarding the lymphatic system and highlighted remaining challenges and opportunities to advance the field.

*In our "**Science as Art**" section, please see a beautiful illustration of key milestones that punctuate the centuries-long pursuit to map the lymphatic system, metaphorized by the life cycle of water lilies.*

Advances and prospects for the Human BioMolecular Atlas Program (HuBMAP)

Jain S, Pei L, Spraggins JM, Angelo M, Carson JP, Gehlenborg N, Ginty F, Gonçalves JP, Hagood JS, Hickey JW, Kelleher NL, Laurent LC, Lin S, Lin Y, Liu H, Naba A, Nakayasu ES, Qian WJ, Radtke A, Robson P, Stockwell BR, Van de Plas R, Vlachos IS, Zhou M; HuBMAP Consortium; Börner K, Snyder MP.
Nat Cell Biol. 2023 Aug;25(8):1089-1100.
PMID: 37468756 DOI: 10.1038/s41556-023-01194-w Epub 2023 Jul 19.

The Human BioMolecular Atlas Program (HuBMAP) aims to create a multi-scale spatial atlas of the healthy human body at single-cell resolution by applying advanced technologies and disseminating resources to the community. As the HuBMAP moves past its first phase, creating ontologies, protocols and pipelines, this Perspective introduces the production phase: the generation of reference spatial maps of functional tissue units across many organs from diverse populations and the creation of mapping tools and infrastructure to advance biomedical research.

*In our "**Science as Art**" section, we are featuring the Nature Cell Biology cover in August 2023 that accompanies this perspective on HuBMAP.*

Continued>>

Organ Mapping Antibody Panels: a community resource for standardized multiplexed tissue imaging

Quardokus EM, Saunders DC, McDonough E, Hickey JW, Werlein C, Surrette C, Rajbhandari P, Casals AM, Tian H, Lowery L, Neumann EK, Björklund F, Neelakantan TV, Croteau J, Wiblin AE, Fisher J, Livengood AJ, Dowell KG, Silverstein JC, Spraggins JM, Pryhuber GS, Deutsch G, Ginty F, Nolan GP, Melov S, Jonigk D, Caldwell MA, Vlachos IS, Muller W, Gehlenborg N, Stockwell BR, Lundberg E, Snyder MP, Germain RN, Camarillo JM, Kelleher NL, Börner K, Radtke AJ.

Nat Methods. 2023 Aug;20(8):1174-1178.
PMID: 37468619 PMCID: PMC10406602 DOI: 10.1038/s41592-023-01846-7 Epub 2023 Jul 19.

Multiplexed antibody-based imaging enables the detailed characterization of molecular and cellular organization in tissues. Advances in the field now allow high-parameter data collection (>60 targets); however, considerable expertise and capital are needed to construct the antibody panels employed by these methods. Organ mapping antibody panels are community-validated resources that save time and money, increase reproducibility, accelerate discovery and support the construction of a Human Reference Atlas.

*This article was part of the special Human BioMolecular Atlas Program (HuBMAP) Nature Collection, featured on the cover of Nature in July 2023 and Nature Cell Biology in August 2023. Collection: https://www.nature.com/immersive/d42859-023-00019-y/index.html. In our "**Science as Art**" section, we are also showcasing the cover of Nature in July 2023 - a stunning "Body image" that highlights this initiative.*

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ANNOUNCEMENTS

IIG-FAES SYMPOSIA on BARRIER IMMUNITY

NOV 15-17, 2023
NIH-BETHESDA MD (NATCHER)
Registration link - https://faes.org/IIG

Day 1

Session 1: The Epithelial Barrier
Session 2: Inflammation and Myeloid Cells at the Barrier
Poster Session: Epithelia, Innate and Adaptive Immunity and Systems Immunology
Workshop 1: Epithelia, Innate and Adaptive Immunity and Systems Immunology
Session 3: Adaptive Immunity at the Barrier

Day 2

Session 4: Pathobionts at the Barrier
Session 5: Viral Immunity at the Barrier
Poster Session: Pathobionts, Neuro-immune Axis and Tumor Immunity
Workshop 2: Pathobionts, Neuro-immune Axis and Tumor Immunity
Session 6: Neuro-Immune Axis at the Barrier

Day 3

Session 7: Systems Immunology at the Barrier
Session 8: Metastasis at the Barrier
Closure

Image source: https://www.elveflow.com/microfluidics-beta-innovation/beta-packs/gut-on-a-chip

2023 William E. Paul lecture

On September 13, 2023, Dr. Diane Mathis, professor of Microbiology and Immunobiology at Harvard Medical School, delivered the eighth annual William E. Paul lecture in the Lipsett Auditorium. Marilyn Paul (left) and Stefan Muljo (right) presented Dr. Mathis with a certificate of recognition afterwards.

Photo credit: Christopher Wanjek
(NIH, Office of the Director)

For more information on Dr. Mathis and the William E. Paul Lecture, please visit https://oir.nih.gov/wals/named-honorific-lectures/william-paul-lecture

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MEMBER NEWS

Kudos to the newly-elected IIG Steering Committee members!

Tenured investigators
Ron Germain (NIAID)
Naomi Taylor (NCI)
Daniela Verthelyi (FDA/CDER)

Tenure-track investigators
Mia Sung (NIA)
Han-Yu Shih (NEI/NINDS)
Eric Dang (NIAID)

Staff scientists/clinicians
Lydia Roberts (NIAID)
Joanna Bandola-Simon (NCI)
Dragana Jankovic (NIAID)

Post-doc fellows/graduate students
Sanghyun (Peter) Kim (NCI)
Julia Gross (NIAID)
Grozdan (Gogi) Cvijetic (NIDCR)
Valentina Ottaviani (NIDCR)

Image source: https://www.freepik.com/free-photo/bokeh-background-perfect-canva_33572018.htm#query=celebration%20background&position=0&from_view=keyword&track=ais

SITC-Genentech Women in Cancer Immunotherapy Fellowship

Award Amount: $100,000 (one-year)

Awardee: Kylynda C. Bauer, PhD
Institution: National Cancer Institute
Project Title: "Vagal-CD8+ T cell axis: Harnessing neuroimmune circuits to alter anti-tumor immunity in liver cancer"

Congratulations!

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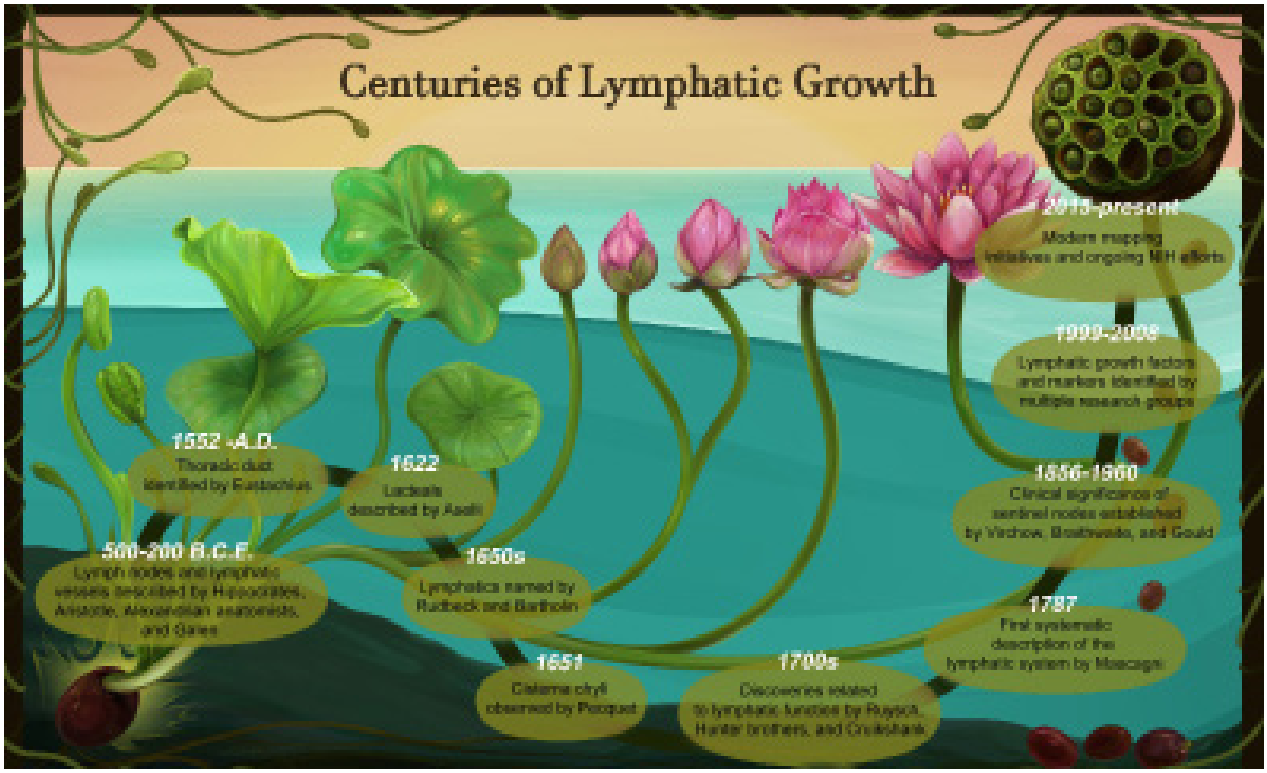

"Centuries of lymphatic growth"

Ten important events in the history of lymphatic research that occurred between 500 BCE and the present day, depicting the water lily life cycle as a metaphor for the growth and promise of the field. Water lilies, genus Nymphaea, and the lymphatics system were both named for the nymphs of Greek and Latin mythology. See Supplemental Table 1 of the NIH lymphatics workshop report (PMID: 37655664) for a comprehensive timeline of lymphatic discoveries and NIH-led activities and funding opportunities. Illustration by Autumn Yarmosh and David M. Sullivan.

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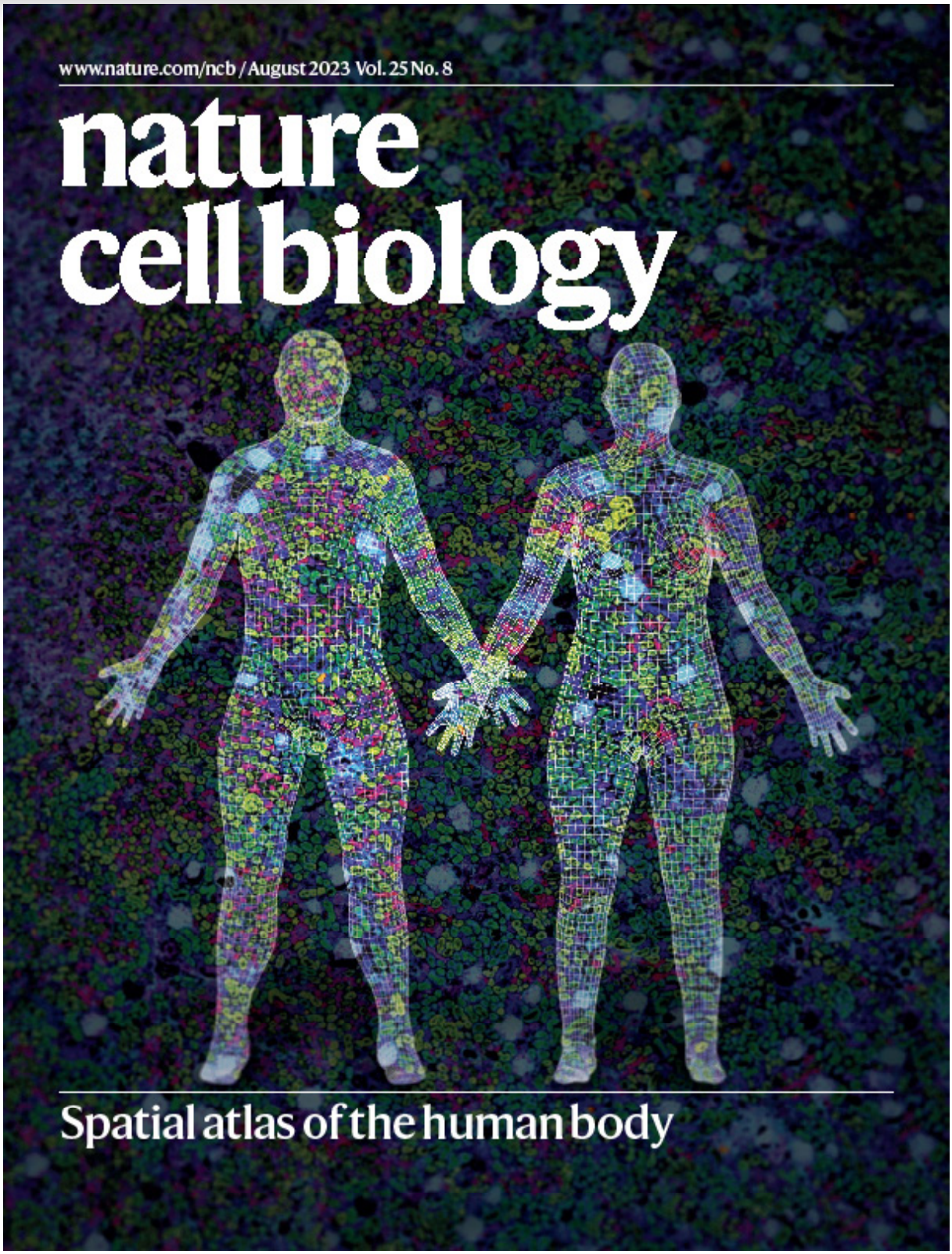

"Spatial atlas of the human body"

The Human BioMolecular Atlas Program (HuBMAP) presents its production phase — the generation of spatial maps of functional tissue units across organs from diverse populations and the creation of tools and infrastructure to advance biomedical research (PMID: 37468756). *Image: Heidi Schlehlein. Cover Design: Lauren Heslop. Source: https://www.nature.com/ncb/volumes/25/issues/8.*

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"Body image"

Launched in 2018, the Human Biomolecular Atlas Program (HuBMAP) aims to map how cell types are arranged in the human body. The initiative is both developing and then deploying the necessary technology to create maps of organs at single-cell resolution. In this week's issue, three papers reveal early fruits of these labours. In the first paper, Michael Snyder and his colleagues use an imaging technique called CODEX and single-cell technologies to map the human intestine. In a second paper, Sanjay Jain and colleagues use spatial transcriptomics to map the human kidney. And in the third paper, Michael Angelo and co-workers use another imaging technique, called MIBI, to map the maternal–fetal interface. Together, these three maps at single-cell resolution hint at the power of spatial analyses in understanding human biology and disease. Cover image: Heidi Schlehlein. Source: https://www.nature.com/nature/volumes/619/issues/7970.

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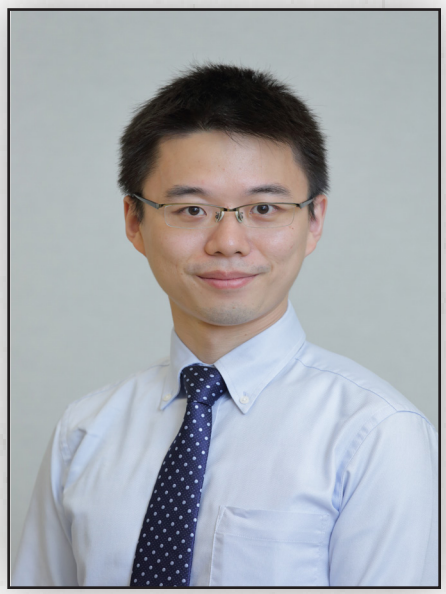
Immunology Interest Group

SPOTLIGHT

Dr. Zhao is a Stadtman Investigator in the Thoracic and Gastrointestinal Malignancies Branch, Center for Cancer Research, NCI. To learn more about his work visit: https://irp.nih.gov/pi/chen-zhao



Chen Zhao, M.D.

Tell us about your science.

My group has been focusing on using advanced tissue imaging, including multiplex imaging, spatial transcriptomics and intravital imaging, and genetically engineered mouse models to understand the three-way interactions among tumor cells, the immune system, and the microbiota in the tumor microenvironment of lung cancer.

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

I decided to pursue biomedical research after spending a summer in a genetics lab looking for SNPs as a summer high school intern. Then, I went to medical school in China and did my internal medicine resident at Memorial Sloan Kettering Cancer Center where I took care of CAR-T patients. The magic power of immunotherapy led me to immunology.

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

My mentor, Ron Germain, taught me how to think as an immunologist… especially how to choose appropriate controls.

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

Tumor immunology.

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

The IIG email list.

How do you spend your free time?

Painting.

Continued>>

Immunology Interest Group

SPOTLIGHT

Dr. Amy Rosenfled is a principal investigator in the Division of Viral Products, Office of Vaccines Research and Review, FDA.

Tell us about your science.

My laboratory studies enteroviruses, in particular those enteroviruses that associate with the development of acute flaccid myelitis (AFM), a childhood polio-like paralysis. These viruses include enterovirus D68, A71, C99, D94, D111 and echovirus B29. Projects ongoing in the laboratory include but are not limited to the identification of the cell surface proteins required for enterovirus entry, uncoating and genome release; the antigenic structure of members of the genus; and the establishment of immune competent animal models of the pathologies associated with enterovirus infection.

Amy B. Rosenfeld, Ph.D.

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

My parents are biochemists and I always enjoyed 'playing' in their laboratories as a kid. During senior year in high school I participated in a science program that allowed me to spend half of my time doing research for a pharmaceutical company, where I had my own little laboratory. At the end of graduate school, a paper suggesting that type 1 interferon restricted poliovirus tissue tropism was published. These data combined with the observation that not everyone infected with a poliovirus developed paralysis suggested that host's responses significantly influenced infection outcomes.

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

I completed my PhD with Vincent Racaniello at Columbia University studying translation initiation mediated by the Internal Ribosome Entry Site (IRES) of poliovirus and hepatitis C virus using the budding yeast S. cerevisiae. By allowing me to undertake a project that was outside the scope of his expertise and focus of his laboratory, he fostered my scientific growth, independence, and creativity. While our weekly meetings were designed to discuss the problems my research encountered, more often than not the conversation focused on the history of molecular biology and virology. It is through these conversations that I developed a great appreciation of the history of science and enterovirus research. I continue to use this appreciation and knowledge of history to expand our scope of understanding of enterovirus biology.

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

I think that the use of collaborative cross and outbred mice for studying viral pathogenesis will significantly expand our understanding of the mechanisms for disease associated with viral infection, especially those with a broad spectrum of pathologies.

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

I appreciate the diversity of interests that my colleagues who participate in the NIH-FDA immunology community have.

How do you spend your free time?

I spend my free time with friends and family, most of who are not scientists.

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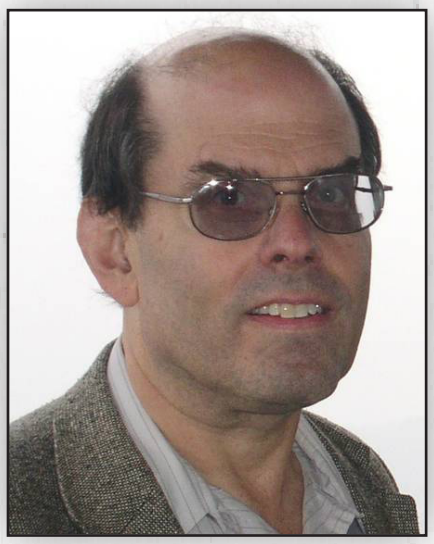
Immunology Interest Group

SPOTLIGHT

Dr. Howard Young is a senior investigator in the CCR Cancer Innovation Laboratory, NCI. To learn more about his work visit: https://ccr.cancer.gov/staff-directory/howard-a-young

What sparked your interest in science, and how did you choose your area of research/scientific questions at different stages of your career?



Howard Young, Ph.D.

My grammar school and high school teachers were always very supportive of my interest in science so that was one motivating factor. I also had a small microscope and I loved looking at at the creatures in pond/stream water. I was a microbiology major all through college and I did well in the microbiology courses so I thought that I should stick with it. I also worked in the lab of the Microbiology chair the summer after my junior year and during my senior year. My grad school project was more biochemistry than immunology but I was given a lot of independence, so I figured research was a career for me. Had I started grad school one year later, I might well have been a plant molecular biologist as that was when Gene Nester started his pioneering work on Agrobacterium.

One of the grad students in the lab I worked in as an undergrad was at the NIH and with his help I came to the NCI as a postdoc at a salary of $11,000/year. After 5 years at NCI, I got my own lab in Frederik and was focused on characterizing the RAS oncogene and cloning the Rasheed Rat Sarcoma virus. However, I did not feel that I was competitive, so I became Director of Technical Services at Bethesda Research Labs. After my first year, I knew that I really missed research and Joe Oppenheim took a chance by hiring me in the Biological Response Modifiers Program. The program needed someone with expertise in molecular biology and although I did not even give a recruitment seminar, I was hired as a Cancer Expert for one year. I asked for 2 years and because of the willingness of other PIs to collaborate with me and the aggressiveness of my first postdoc, Dr. Elizabeth Kovacs, I was able to secure a long term position. That is where I became interested in cytokines and in the regulation of IFN-g gene expression. As might be expected, there have been hills and valleys in my career and while it is hard to believe that my research career is soon ending, I am very grateful for all the support I have received over the years from many in the NIH/FDA immunology community. It has been a wonderful place to work.

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

Regenerative medicine will explode as replacement organs using stem cells will become more readily available. Also personalized medicine will become standard and treatments will be based on the metabolome, microbiome and immunobiome of patients.

What do you feel is one of the most challenging events in your career, and how did you cope with the difficulty?

Without a doubt, the most challenging event has been my decision to close my lab. Given that I have been doing research since 1968, it is hard to imagine not doing so. There are many factors that led to my decision, but I realize that it is really the best time to turn off the lights. I want to make sure that the members of my lab are placed in positions that will help them meet their career goals.

Another difficult time was the passing of Joost Oppenheim. By hiring me, Joe gave me the opportunity to continue in a research career and I am not sure where I would be, had he not supported me.

As a final example, when I worked at BRL, I was told on a Thursday afternoon, that on Friday morning I would have to tell 8 people that they are being let go immediately. It was very hard to do that given that I worked closely with them. Those of us that were not let go had very mixed feelings as we felt very bad for our co-workers but also we were relieved that we still had a job. I then became the recipient of every phone call into the company other than orders or if someone specific was requested. I tried to treat every customer well (I spoke to over 3000) and I helped them as much as possible.

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Could you share your mentoring experience? What do you think contributed to the fulfillment of your mentorship?

As a mentor I treat everyone as an individual with their own specific needs (e.g. how often they want to meet with me). I find it important to listen carefully to their ideas and I give them as much independence as they desire. I always told new lab members that, at the end of their time in the lab, it is my hope that they felt the time in my lab was worthwhile and helped them advance their career. Can't say that I have been 100% successful, but that is always my objective.

The covid pandemic reminded us of the importance of science literacy among the general public. What do you think we could do to help improve science education?

We have to be more aggressive about communicating science to the public. The NIH used to have a Speaker's Bureau where staff could volunteer to speak to different groups (high school classes, adult education, Lion's Club, etc). It proved to be very successful but once the individual who organized the effort retired, the program disappeared. I have tried to get the bureau reinstated but with no luck.

Also, I have worked with Dr. Louis Catania to create a website focused on educating the public and scientists who are not immunologists about the immune system (see www.immuneparadox.com) and this effort has met with interest. This is a completely free website and while we have seen consistent usage from individuals around the world, we need help in advertising the effort through social media.

How to you spend your free time? What time management experience you would like to share?

With regards to time management at the NCI, I have some recommendations that I have lived by:

1) When an administrator requests something from you, get the required information/forms back to them immediately. It will cut down on emails and make their job easier and faster.

2) When it is time to complete a required course (e.g. yearly IT security review), do so immediately!!! Otherwise, you may well forget about it and then be constantly reminded that you have to complete the training. This just wastes everyone's time and ignoring the requirement will not make it go away.

3) When a colleague asks for your feedback about their manuscript, do so in a timely manner. As a PI, I always made reviewing papers from my lab my top priority. Over the years, trainees have told me how frustrated they become when their paper sits on the desk of their boss for an extended period of time.

4) Trainees should meet with their mentors on a very regular scheduled basis.

5) Attend seminars even outside your direct interests with 2 questions in mind. "How can the speaker help me with my research and how can I help them with their research". Unexpected collaborations may result (e.g. I got involved with Ebola virus research after hearing a seminar about the virus).

6) Make sure you take a moment to express your appreciation to the workers and your co-workers that make the NIH/FDA work. A "Thank You" can mean more than you might imagine.

7) Only work with people who like chocolates because you will always know how to make them happy :-)

I am not sure how I will deal with the additional time I will have after the closure of my lab but I am planning to be in Emeritus status. As such, you will continue to get emails from me :-) as I will be able to retain my NIH privileges. I will admit that I never developed major outside interests (we all know that research is not a 9-5, 5 days/week job) and while I do enjoy traveling, this will prove to be difficult for a number of reasons. I will stay involved with the International Cytokine and Interferon Society and continue to help with the society newsletter that I have edited since 1989.

What advice would you like to give to the NIH/FDA immunologist community?

One bit of advice that I would like to offer is that if you have an idea that you think will make the NIH/FDA better, pursue it and make it happen. If you make sure that your lab is surrounded by windows and not mirrors, you can make your lab and the broader NIH/FDA communities even better.

Continued>>

Bench-to-Bedside in Action

Translating immunology to transform clinical care

Harnessing fundamental knowledge to advance our understanding of disease and develop novel treatment strategies is a major mission of the NIH. Each month we highlight interesting clinical trials taking place at the NIH Clinical Center that are doing just that.

Exploring the Effect of NAD Boosing on Immunometabolism and Immunity in Systemic Lupus Erythematosus. PI's: Michael N. Sack, M.D, Ph.D and Mariana J. Kaplan M.D, NHLBI and NIAMS. NIH Clinical Center.

Background: Systemic lupus erythematosus (SLE) occurs predominantly in women and is driven, in part, by type I interferon dysregulation and neutrophil hyper-responsiveness. Neutrophils in females have reduced mitochondrial bioenergetic capacity which affects immunometabolism. Nicotinamide adenine dinucleotide (NAD)+ boosting with nicotinamide riboside (NR) blunts type 1 IFN activation in-vivo in monocytes of healthy subjects and ex-vivo in SLE subjects. Whether the effects of NR on innate immune cell metabolic remodeling and/or to alterations in mitochondrial bioenergetics and/or fidelity orchestrates the anti-inflamatory role of NAD-boosting in SLE remain uncharacterized.

Hypothesis: NAD+ boosting by NR supplementation will modulate metabolic pathways in lupus and blunt type 1 interferon signaling. Moreover, as type 1 interferon drives endothelial dysfunction, linked to increased cardiovascular risk, the effect of NR on endothelial function will be examined.

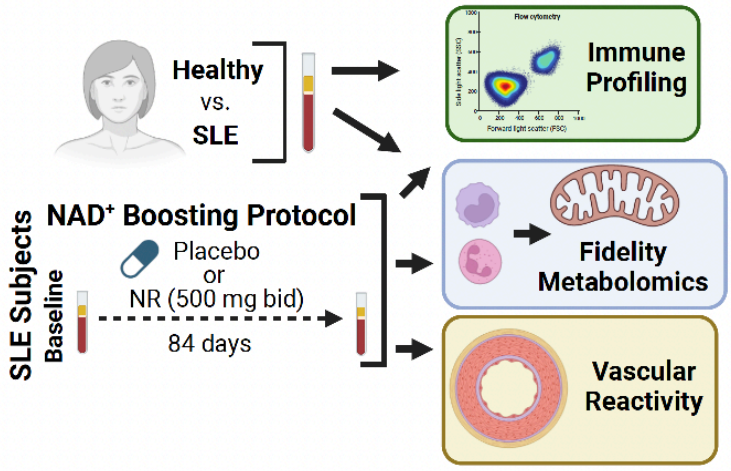


Fig 1. Overview of NAD-boosting protocol in SLE.

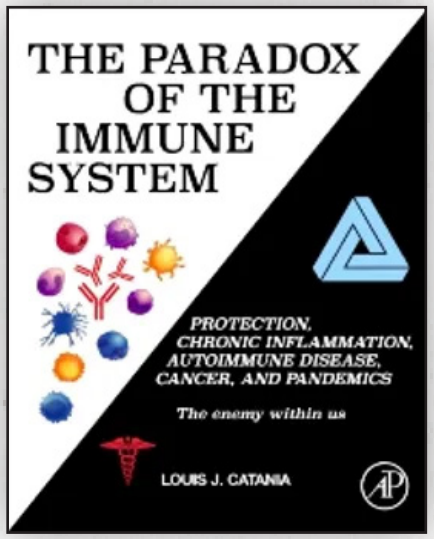
Study Design: This is a double-blind placebo controlled study in female SLE subjects. Additionally, the SLE subjects will be compared to a control cohort for baseline comparisons of immunometabolism and mitochondrial biology. Following baseline assessment, SLE subjects will either take placebo or NR (500 mg twice daily for 12 weeks). The primary end point will be to assess the effect of NR vs. placebo on blunting type I IFN signaling by measuring monocyte IL-1b secretion compared to baseline. Exploratory enpoints include analysis in control vs SLE subjects to compare mitochondrial function and immunometabolism using 13-C-labelled metabolites for dynamic metabolomics. In the SLE placebo vs. NR study, comparative metabolomic assessments will occur and given the role of inflammation on endothelial dysfunction, vascular reactivity will be compared in the SLE intervention groups at baseline and following 12 weeks of placebo or NR supplementation.

What we hope to learn: Further characterize the immunometabolic and mitochondrial distinctions between SLE and healthy controls. Evaluate whether NAD boosting administration in-vivo will blunt immune responsiveness, improve mitochondrial fidelity and function and improve vascular function in SLE.

Continued>>

CALL FOR CONTRIBUTORS

Adapted from a comprehensive textbook ***The Paradox of the Immune System***, a free website created by the author Dr. Louis Catania and his assistant Carol Brady, www.immuneparadox.com, is designed as an educational tool about immunology for the lay public and for scientists who are not immunologists. The goal is to reach interested laypersons and health professionals wishing to review basic immunology and its current applications in healthcare.



https://www.immuneparadox.com/

Based on the feedback, the creators would like to call for contributors to expand the site, starting with new blogs about "**The Aging Immune System**" and "**Mucosal Immunity**". The first blog would be for the lay public, with the second version being for the scientific community. One can compare the "layperson style" to the "science version" in a selected blog to appreciate expected readership levels.

If you are interested in being part of this initiative and creating either of these blogs, please contact Dr. Howard Young at younghow@mail.nih.gov. Please note that this educational initiative has no current financial sponsors so no compensation will be offered, but authorship will be properly credited. Later, the blogs will also be converted into podcasts.

Again this is an initiative to support a website that provides education about immunology. There is no cost to use the site and neither Dr. Catania or Dr. Young have any financial interest in this effort. Everything about the website has been done on a volunteer basis.

Continued>>

Immunology Interest Group
SEMINAR SERIES

Upcoming seminars

October 2023

October 4, 2023
Han-Yu Shih (NEI)
Host: John O'Shea

October 11, 2023
Ben Afzali (NIDDK)
Host: Michail Lionakis

October 18, 2023
Tim Sparwasser (Mainz)
Host: Christian Mayer

October 25 2023
Thierry Gauthier (NIDCR)
Host: Wanjun Chen and Valentina Ottaviani

November 2023

November 1, 2023
Joseph A. Bellanti (GtU)
Host: Amy Zhang

November 8, 2023
Jun Huh (Harvard)
Host: Hyun Park

November 29, 2023
Judith Agudo (Dana Farber)
Host: Li Yang

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 presentation.

Continued>>

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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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