NIH-FDA IIG

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

NEWSLETTER

MAY 2024

PUBLICATIONS

The Immune Landscape of Pheochromocytoma and Paraganglioma: Current Advances and Perspectives

Uher O, Vanova K, Taieb D, Calsina B, Robledo M, Clifton-Bligh R, Pacak K
Endocr Rev. 2024 Feb 20:bnae005.
doi: 10.1210/endrev/bnae005. PMID: 38377172

The review article discusses the immune escape mechanisms of PPGL tumors, their classification based on immune signatures, and emerging immunotherapeutic strategies. The reviewA highlights the importance of converting "cold" tumors into "hot"A tumors to improve responses to immunotherapy and outlines potential future treatments combining immunotherapyA with otherA modalities.A

Regulation of T helper cell differentiation by the interplay between histone modification and chromatin interaction

Liu S, Cao Y, Cui K, Ren G, Zhao T, Wang X, Wei D, Chen Z, Gurram RK, Liu C, Wu C, Zhu J, Zhao K.
Immunity. 2024 May 14;57(5):987-1004.e5.
doi: 10.1016/j.immuni.2024.03.018. PMID: 38614090

Liu et al. found that the H3K4me1 landscape established byA MLL4 in naïve CD4+ T cells is critical for rewiring chromatin interaction network orchestrated by GATA3 during Th2 differentiation. CTCF binding site HSS3 restrains LCR-Il4 promoterA interaction and IL-4 expression.A

Sex-biased immunogenicity of a mucosal subunit vaccine against SARS-CoV-2 in mice

Li J, Hsu KS, Howe SE, Hoang T, Xia Z, Berzofsky JA, Sui YS.
Frontiers in Immunology. 2024 May 20
doi: 10.3389/fimmu.2024.1386243

This shows that a mucosalA vaccine against SARS-CoV-2 shows a clear sex-bias in both antibody and T cell responses as well as in protection, with consistently greater response in female mice. This may be related to a greater myeloid cell response in males that could be immunosuppressive.A

Aberrant CD8+T cells drive reproductive dysfunction in female mice with elevated IFN- levels

Bafor EE, Erwin-Cohen RA, Martin T, Baker C, Kimmel AE, Duverger O, Fenimore JM, Ramba M, Spindel T, Hess MM, Sanford M, Lazarevic V, Benayoun BA, Young HA, Valencia JC
Front Immunol. 2024 Apr 18:15:1368572.
doi: 10.3389/fimmu.2024.1368572. PMID: 38698852

Our findings reveal that chronic IFN- elevation increases recirculating effector memory CD8+T cells in the murine ovaryA and uterus triggered which drive reproductive dysfunction and infertility.

Prevalence of anti-lymphocyte IgM autoantibodies driving complement activation in COVID-19 patients

Pérez-Díez A, Liu X, Calderon S, Bennett A, Lisco A, Kellog A, Galindo F, Memoli MJ, Rocco JM, Epling BP, Laidlaw E, Sneller MC, Manion M, Wortmann GW, Poon R, Kumar P, Sereti I
Front Immunol 2024 Apr 17:15:1352330.
doi: 10.3389/fimmu.2024.1352330. PMID: 38694513

Around 20% of hospitalized COVID-19 patients have IgM anti-lymphocyte antibodies during disease and early convalescence periods, while approximately 60% of the patients displayA complement (C3b and C1q) deposition on their lymphocytes. During acute disease the percentage of CD4 T cells with C3b is inversely correlated with CD4 T cell numbers.A

State of pneumococcal vaccine immunity

Akkoyunlu M.
Hum Vaccin Immunther. 2024 Dec 31;20(1)2336358.
doi: 10.1080/21645515.2024.2336358. PMID: 38567485

This review discusses the current state of host immunity against the pneumococcal vaccines in use and under development.

Sustained antigen delivery improves germinal center reaction and increases antibody responses in neonatal mice

Lotspeich-Cole L, Parvathaneni S, Lee RC, and Akkoyunlu M.
NPJ Vaccines. 2024 May 25;9(1):92.
doi: 10.1038/s41541-023-00764-1. PMID: 38796539

This study shows that neonatal mouse antibody responses to a pneumococcal conjugate vaccine can be improved if the vaccine is divided into multiple doses and administered sequentially instead of a traditional bolus dose. The antibody improvement is accompanied by enhanced germinal center reaction.

Chaperone mediated MHC-I peptide exchange in antigen presentation

Jiang J, Natarajan K, Margulies DH
IUCrJ. 2024 May 1;11(Pt 3):287-298.
doi: 10.1107/S2052252524002768. PMID: 38656309

This paper reviews structural and mechanistic studies of the MHC-I chaperones TAPBPR and tapasin in their role in antigen presentation.

Developmental conversion of thymocyte-attracting cells into self-antigen-displaying cells in embryonic thymus medulla epithelium

Ohigashi I, White AJ, Yang MT, Fujimori S, Tanaka Y, Jacques A, Kiyonari H, Matsushita Y, Turan S, Kelly MC, Anderson G, Takahama Y
Elife. 2024 Mar 11:12:RP92552.
doi: 10.7554/eLife.92552. PMID: 38466627

This study demonstrates that embryonic medullary thymic epithelial cells (mTECs) that express the chemokine CCL21 carry a developmental potential to give rise to self-antigen-displaying mTECs, including Aire-expressing mTECs. The results reveal that the sequential conversion of thymocyte-attracting subset into self-antigen-displaying subset serves to assemble functional diversity in the thymus medulla epitheliums.

Functionally diverse thymic medullary epithelial cells interplay to direct central tolerance

Ushio A, Matsuda-Lennikov M, Kalle-Youngoue F, Shimizu A, Abdelmaksoud A, Kelly MC, Ishimaru N, Takahama Y
Cell Rep. 2024 Apr 23;43(4):114072.
doi: 10.1016/j.celrep.2024.114072. PMID: 38581680

This study reports that CCL21-expressing medullary thymic epithelial cells (mTECs) and Aire-expressing mTECs non-redundantly cooperate to direct self-tolerance to prevent autoimmune pathology, by optimizing the deletion of self-reactive T cells and the generation of regulatory T cells. The study also detects cooperation for self-tolerance between Aire and Fezf2, the latter of which unexpectedly regulates thymic tuft cells.

BTK drives neutrophil activation for sterilizing antifungal immunity

Desai JV, Zarakas MA, Wishart AL, Roschewski M, Aufiero MA, Donkó Á, Wigerblad G, Shlezinger N, Plate M, James MR, Lim JK, Uzel G, Bergerson JR, Fuss I, Cramer RA, Franco LM, Clark ES, Khan WN, Yamanaka D, Chamilos G, El-Benna J, Kaplan MJ, Staudt LM, Leto TL, Holland SM, Wilson WH, Hohl TM, Lionakis MS.
J Clin Invest. 2024 May 2:e176142.
doi: 10.1172/JCI176142. PMID: 38696257

BTK is known for its role in BCR signaling and BTK inhibitors have transformed the therapy of lymphoid malignancies but have caused opportunistic fungal infections via unknown mechanisms. This study shows that BTK drives neutrophil antifungal activity via p40phox and RAC2 activation and that GMCSF can mitigate the neutrophil defects caused by BTK inhibition.

Soluble immune checkpoints: implications for cancer prognosis and response to immune checkpoint therapy and conventional therapies

Pitts SC, Schlom J, Donahue RN
J. Exp Clin. Cancer Res. 2024 May 31;43(1):155.
doi: 10.1186/s13046-024-03074-z. PMID: 38822401

Immune checkpoint inhibitors (ICI) have revolutionized cancer immunotherapy. This review discusses current literature on the production, function, and expression of nine soluble immune checkpoints in patients with solid tumors and explores their role as biomarkers of response to ICI as well as to conventional therapies in cancer patients.

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The Role of Interferon-gamma in Autoimmune Polyendocrine Syndrome Type 1

Oikonomou V, Smith G, Constantine GM, Schmitt MM, Ferré EMN, Alejo JC, Riley D, Kumar D, Dos Santos Dias L, Pechacek J, Hadjiyannis Y, Webb T, Seifert BA, Ghosh R, Walkiewicz M, Martin D, Besnard M, Snarr BD, Deljookorani S, Lee CR, DiMaggio T, Barber P, Rosen LB, Cheng A, Rastegar A, de Jesus AA, Stoddard J, Kuehn HS, Break TJ, Kong HH, Castelo-Soccio L, Colton B, Warner BM, Kleiner DE, Quezado MM, Davis JL, Fennelly KP, Olivier KN, Rosenzweig SD, Suffredini AF, Anderson MS, Swidergall M, Guillonneau C, Notarangelo LD, Goldbach-Mansky R, Neth O, Monserrat-Garcia MT, Valverde-Fernandez J, Lucena JM, Gomez-Gila AL, Garcia Rojas A, Seppänen MRJ, Lohi J, Hero M, Laakso S, Klemetti P, Lundberg V, Ekwall O, Olbrich P, Winer KK, Afzali B, Moutsopoulos NM, Holland SM, Heller T, Pittaluga S, Lionakis MS.
N Engl J Med. 2024 May 30;390(20):1873-1884.
doi: 10.1056/NEJMoa2312665. PMID: 38810185

In this study, interferon-gamma was found to play a centralA role in driving the multiorgan autoimmune injury ofAIRE deficiency. This finding was confirmed in studies in animals and resulted in a trial of the JAK1/2 inhibitor, ruxolitinib, in APECED patients who exhibited dramatic responses. These data support APECED as an "interferon-gammopathy" that can be targeted therapeutically

Ebola virus-induced eye sequelae: a murine model for evaluating glycoprotein-targeting therapeutics

Lee HN, Xu B, Lewkowicz AP, Engel K, Kelley-Baker L, McWilliams IL, Ireland DDC, Kielczewski JL, Li J, Fariss RN, Campos MM, Baum A, Kyratsous C, Pascal K, Chan CC, Caspi RR, Manangeeswaran M, Verthelyi D.
EBioMedicine. 2024 May 31;104:105170.
doi: 10.1016/j.ebiom.2024.105170. PMID: 38823088

Anti-EBOV-GP antibodies can improve survival among Ebola virus disease patients, but improved therapeutics are needed to reduce life altering sequelae. Our animal model offers a newA platform to examine the acute and long-term effect of the virus in the eye and the relative impact of therapeutic candidates targeting EBOV-GP.A

Functional genomics identifies N-acetyllactosamine extension of complex N-glycans as a mechanism to evade lysis by natural killer cells

Zhuang X, Woods J, Ji Y, Scheich S, Mo F, Rajagopalan S, Coulibaly ZA, Voss M, Urlaub H, Staudt LM, Pan KT, Long EO.
Cell Rep. 2024 Apr 23;43(4):114105.
doi: 10.1016/j.celrep.2024.114105. PMID: 38619967

A genome-wide screen identified one of the strongest contributors to lysis of target cells by NK cells as signal peptide protease-like 3, which cleaves and releases transmembrane glycosyl-transferases in the Golgi apparatus. Absence of SPPL3 causes elongation of complex N-glycans, which masks ligands of NK activation receptors and impairs rituximab binding to CD20.A

Antigenic Characterization of Novel Human Norovirus GII.4 Variants San Francisco 2017 and Hong Kong 2019

Tohma K, Landivar M, Ford-Siltz LA, Pilewski KA, Kendra JA, Niendorf S, Parra GI.
Emerg Infect Dis. 2024 May;30(5):1026-1029.
doi: 10.3201/eid3005.231694. PMID: 38666659; PMCID: PMC11060466.

Two new norovirus GII.4 variants were recently reported circulating globally (2017- 2022). In this study, we demonstrated that these two newAvariants are antigenically distinct from previously circulating variants, suggesting that they have the potential to become predominant noroviruses.A

Analysis of Archival Sera from Norovirus-Infected Individuals Demonstrates that Cross-Blocking of Emerging Viruses is Genotype-Specific

Pilewski KA, Ford-Siltz LA, Tohma K, Kendra JA, Landivar M, Parra GI.
J Infect Dis. 2024 Feb 21:jiae085.
doi: 10.1093/infdis/jiae085. Epub ahead of print. PMID: 38382087.

To better understand how re-exposure shapes humoral immunityA to future norovirus strains, we profiled the antibody responses following two community gastroenteritis outbreaks linked to noroviruses in 1971. Our data show that, while broad cross-reactive responses can be detected in specific individuals, infection generates narrow immunity directed towards the infecting genotype. Finally, we developed a novel assay to demonstrate the epitope-specificity and discrete compartments of the neutralizing response.A

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IIG Translational Immunology Symposium

Environmental Triggers to Advanced Therapeutics

Honoring Jay A. Berzofsky, M.D., Ph.D.'s half-century of scientific impact

Website and abstract submission site to open shortly

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2024 NIH-FDA IIG

Summer Scholars in Residence

Seminar Series

June 24 (Mon), 12:00pm (EST)

Lis Antonelli
(René Rachou Institute, Brazil)

June 25 (Tue), 3:30pm (EST)

Seth Masters
(Houdson Institute, Australia)

July 19 (Fri), 1:30pm (EST)

Judi Allen
(University of Manchester, UK)

July 31 (Wed), 2:30pm (EST)

Eui-Cheol Shin
(KAIST, Korea)

*Aug 7 (Wed), 10:30am (MST), 12:30 (EST)

Emily Speranza
(Lerner Research Institute, US)

Aug 28 (Wed), 10:00am (EST)

Doreen Cantrell
(University of Dundee, UK)

Location
Bethesda, Bldg 4 / Rm 433

(* Aug 7; at Rocky Mountain Lab / Zoom for remote)

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Newly elected members National Academy of Sciences (NAS)

The National Academy of Sciences is a private, nonprofit institution that was established under a congressional charter signed by President Abraham Lincoln in 1863. It recognizes achievement in science by election to membership, and—with the National Academy of Engineering and the National Academy of Medicine—provides science, engineering, and health policy advice to the federal government and other organizations.

List of 2024 newly elected NAS members at NIH. **The IIG members are listed in bold text.** Congratulations to all inductees:

Kunkel, Thomas A.; distinguished investigator and chief, Laboratory of Structural Biology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, N.C.

Kwon-Chung, Kyung (June) J.; distinguished investigator and chief, Molecular Microbiology Section, Laboratory of Clinical Immunology and Microbiology, National Institutes of Health, Bethesda, MD.

Rosenberg, Steven A.; chief, Surgery Branch; and senior investigator and head, Tumor Immunology Section, Center for Cancer Research, National Cancer Institute, Bethesda, MD.

Trinchieri, Giorgio; chief, Laboratory of Integrative Cancer Immunology, distinguished investigator, and head, Cancer Immunology Section, Center for Cancer Research, National Institutes of Health, Bethesda, MD.

Wolin, Sandra L.; chief, RNA Biology Laboratory, senior investigator, and head, National Cancer Institute RNA Biology Initiative, National Cancer Institute, National Institutes of Health, Frederick, MD.

https://www.nasonline.org/news-and-multimedia/news/2024-nas-election.htmlA

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Immunology Interest Group SPOTLIGHT

Dr. Fei Mo is a principal investigator in Tumor Vaccine & Biotechnology Branch, Division of Cell Therapy 2, Office of Therapeutic Products, Center for Biologics Evaluation and Research, FDA.

Tell us about your science.

My lab focuses on understanding the challenges associated with the effectiveness of immune cell and gene therapy products, such as CAR-T cells. We aim to identify the factors contributing to the cytotoxicity and self-renewal capacity of these therapeutic immune cells and develop novel `strategies to control their functionality within the tumor microenvironment. Additionally, we are exploring alternative methods to improve the quality of allogeneic immune cell products.

Fei Mo, Ph.D.

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

During the last two years of my undergraduate study, the discovery of Yamanaka factors sparked my curiosity about the potential changes iPSC technology could bring. I was trained as a cell biologist in graduate school and then wondered how my knowledge could be applied. The promise of PD-1 inhibitors and CAR-T therapy in cancer treatment during the final years of my graduate studies motivated me to pursue a postdoctoral fellowship in cancer immunology. I feel fortunate to live in an era where basic research is translating into clinical advances that save lives.

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

I continuously draw inspiration from many great people around me, including family members, friends, mentors, colleagues, and fellows. Their immense support has been crucial in enabling me to initiate my independent research.

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

I anticipate significant advancements in cell and gene therapies. The concept of using cells as "living drugs" to provide durable responses for diseases prone to relapse, such as cancers and autoimmune diseases, is attractive. Additionally, the field of aging and aging-related diseases requires extensive interdisciplinary research efforts. I am optimistic that AI and machine learning techniques will uncover new insights in these areas.

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

The great science and the dedicated scientists.

How do you spend your free time?

I enjoy traveling to witness natural wonders. I also like gardening and reading.

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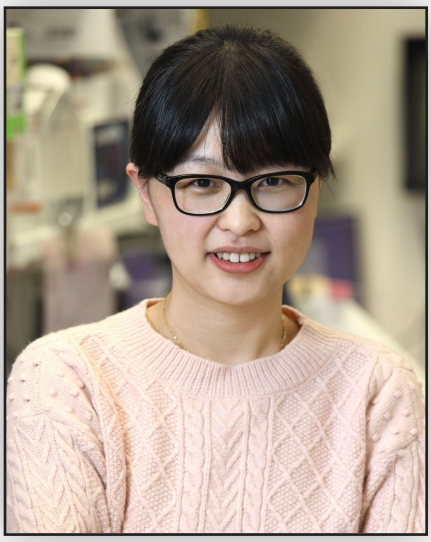
Immunology Interest Group SPOTLIGHT

Dr. Lichun Ma is a Stadtman Tenure-Track Investigator in the Cancer Data Science Laboratory, National Cancer Institute (NCI), NIH. To learn more about her work, visit: https://irp.nih.gov/pi/lichun-ma


Lichun Ma, Ph.D.

Tell us about your science.

My lab centers on understanding tumor heterogeneity in the context of tumor initiation and evolution in liver cancer by using spatial single-cell approaches. Tumor heterogeneity is the observation that cancer cells can show distinct differences from patient to patient, from primary to secondary tumors, or even between cells within the same tumor. This phenomenon is a major barrier to effective cancer interventions. A better understanding of tumor heterogeneity is critical for improving cancer treatment. Using cutting-edge technology in spatial single-cell omics assays, my research program develops novel systems biology approaches to understand tumor heterogeneity in liver cancer. Specifically, we delve into the intricate interplay among cells to decipher how cell-cell communications or cellular neighborhoods shape tumor heterogeneity and plasticity.

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

I never thought of myself as a researcher in cancer biology. My background is in Electronic Engineering. This trajectory went along with me to my PhD study, where I embarked on a project focusing on computational modeling of EGFR mutation-induced drug resistance in lung cancer. As I delved deeper into this research, I found myself fascinated with cancer-related problems. I was further attracted by the intricate interplay between tumor cells and the immune system, and the ability of tumors to evade immune surveillance.

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

I was fortunate to receive my postdoctoral training at the National Cancer Institute under the supervision of Dr. Xin Wei Wang. In his lab, I had the invaluable opportunity to start a journey into the intricate realm of tumor heterogeneity by leveraging state-of-the-art single-cell approaches. This transformative experience has significantly enriched my knowledge in cancer biology and empowered me to carve out my own niche in spatial tumor biology.

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

In my opinion, AI has the potential to transform biomedical research.

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

The NIH-FDA Immunology community provides a great platform for individuals to connect, collaborate, and exchange ideas. In addition, the community's seminars, featuring leading experts in the field, serve as invaluable learning opportunities.

How do you spend your free time?

I do enjoy badminton and hiking when I have free time. However, as a single mom, my priorities have shifted, and now I devote nearly all my moments after work to my wonderful 10-month-old baby, accompanying her and witnessing every single milestone she achieves during her growth.

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Bench-to-Bedside in Action

Translating immunology to transform clinical care

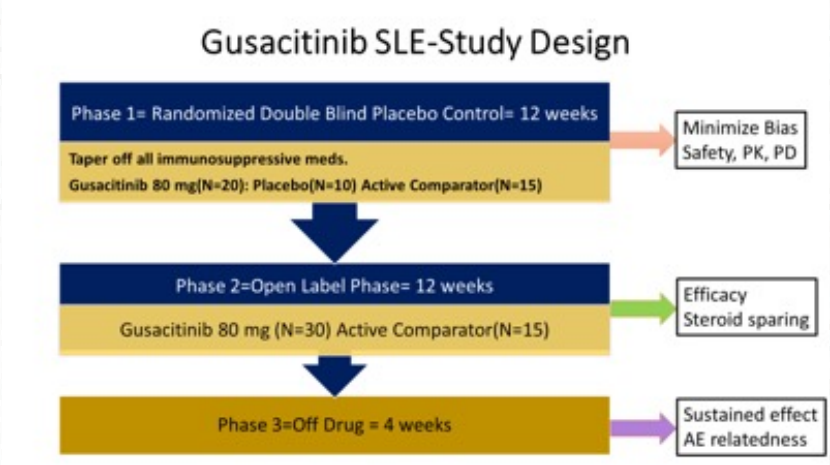
Harnessing fundamental knowledge to advance our understanding of disease and develop novel treatment strategies is a major mission of the NIH. Each month we highlight interesting clinical trials taking place at the NIH Clinical Center that are doing just that.

Phase 1b Study to Evaluate Gusacitinib (a dual JAK/SYK inhibitor) in Systemic Lupus Erythematosus. PI: Sarfaraz A. Hasni MD. – National Institute of Arthritis and Muscoloskeletal and Skin Diseases

Background: The current treatment of patients with the autoimmune disease systemic lupus eythematosus (SLE) include a variety of immunosuppressive medications in combination with corticosteroids. This treatment must be continued lifelong, carries risk of significant toxicities and is effective in a subset of patients. Furthermore, premature cardiovascular disease has become one of the most important causes of morbidity and mortality in patients with SLE and it is not explained by the Framingham risk equation. To this date, no drug used in lupus appears to significantly decrease cardiovascular risk. Therefore, identifying a drug that has both immunomodulatory and vasculoprotective effects would fill an important unmet need in this disease. Many inflammatory cytokines implicated in SLE pathogenesis, including type I and II interferons (IFNs), signal through JAK-STAT pathway. Our recently completed study using tofacitinib revealed a significant decrease in the type I IFN gene signature, levels of low-density granulocytes and circulating NETs as well improved HDL profile and arterial stiffness. SYK inhibition will target abnormally activated B cells and T cells in SLE.

Hypothesis: We hypothesize that the dual inhibition of JAK and SYK in SLE will target the aberrant cytokine signaling most importantly type I IFN as well as abnormally functioning immune cells promoting autoimmunity.

Study Design:



What we hope to learn: This is first study of dual JAK/SYK inhibitor in human SLE. Our objective is to understand the effects of dual JAK and SYK inhibition on Interferon gene signatures, serum cytokine levels, neutrophil NET formation, and immune cells phenotype. We are also interested in modulation of cardiometabolic risk variables such as lipid profile, vascular stiffness, and endothelial dysfunction by investigating Gusacitinib in SLE.

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Immunology Interest Group
SEMINAR SERIES

Upcoming seminars

June 2024

June 5, 2024
Ivan Zanoni (Harvard)
Host: Michail Lionakis

June 26, 2024
Caroline Sokol (Harvard)
Host: Ron Germain

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.

Note: Dr. Helen Su (NIAID) presented the IIG Seminar on February 14, 2024 in place of Dr. Thirumala-Devi Kanneganti (St. Jude).

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Join the IIG Steering Committee!

We are seeking nominations of dedicated, energetic members of the immunology community to serve on the Immunology Interest Group (IIG) Steering Committee. The IIG Steering Committee is a group of enthusiastic individuals responsible for organizing the weekly IIG seminar series, the annual Immunology Workshop, and the IIG newsletter. Only through your willingness to volunteer can the IIG remain a vibrant and beneficial organization.

We are seeking nominations for immunologists in the following four categories:

- Tenured PI (2 year term; 3 positions available)
- Tenure Track Investigator / Assistant Clinical Investigator (2 year term; 3 positions available)
- Staff Scientist / Staff Clinician (2 year term; 3 positions available)
- Postdoctoral Fellow / Graduate Student (1 year term; 4 positions available)

*Note: Trainee members must be available from September 2024-September 2025.

To foster an open and inclusive environment, the IIG steering committee would like to solicit nominations from all sectors (including all institutes/locations within the FDA and NIH) and demographics within the IIG community. Allowing diverse voices and perspectives will help strengthen the IIG's goals and directions.

Please feel free to nominate yourself or others.

To submit nominations, please visit:
https://forms.office.com/g/vQsXzD7ZiK

For multiple nominations please select the option 'submit another response' after submitting your nomination.

If you cannot access Microsoft Forms, please respond to watanabem@mail.nih.gov with the following information about the nominee(s): name, position (see above), institute, email address, confirmation they will run for election if selected, if previously served on the IIG committee and a brief explanation why you have nominated this individual.

Nominations will close on this Friday, June 14th.

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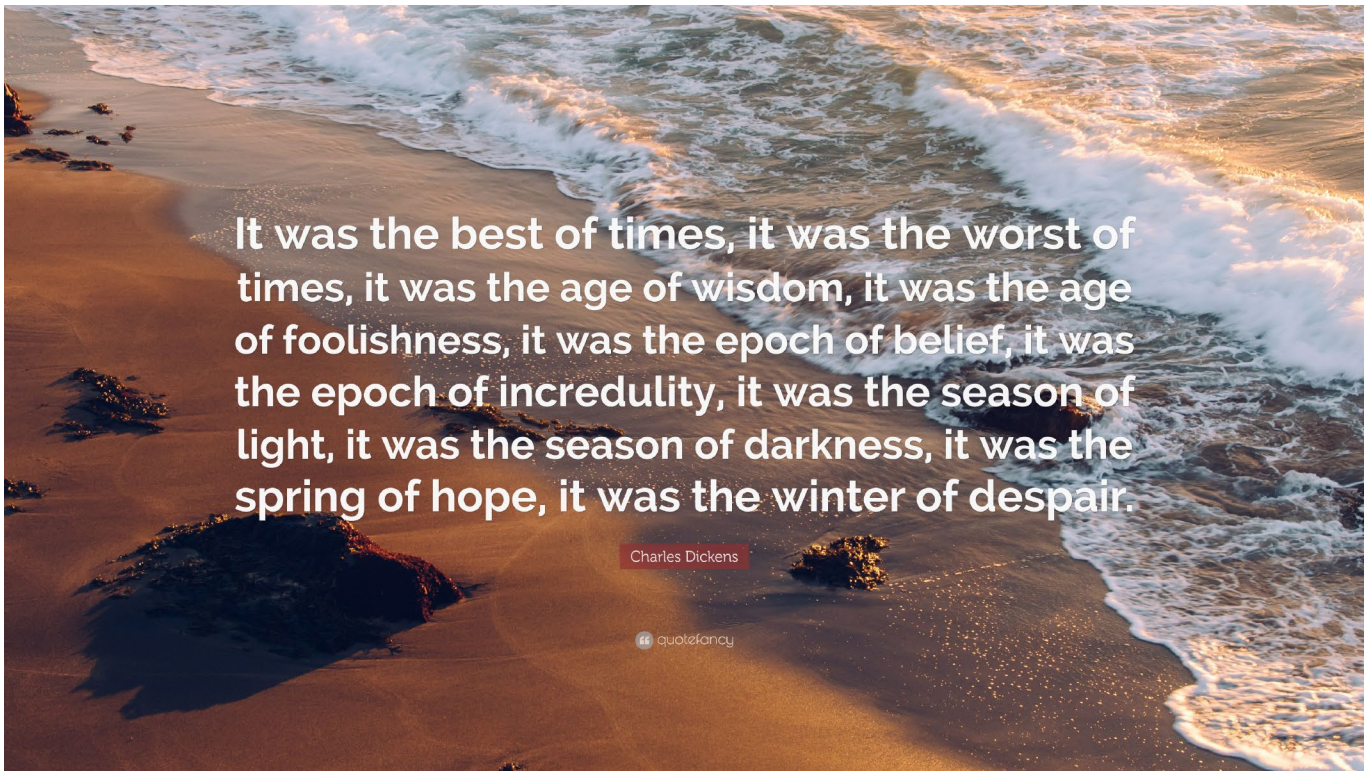
AI and Immunology

Artificial Intelligence is becoming an integral part of scientific research, and immunologists today are facing both opportunities and challenges with the transformative power of AI. The IIG Newsletter wants to hear your voice on the promises and perils of AI in immunological research. We are planning to start a recurring column on the topic of AI and Immunology, with the goal of promoting a comprehensive understanding of AI and brainstorming ways to properly utilize its power to advance immunological science.

Please reach out to our editors if you would like to contribute to the column!



https://quotefancy.com/quote/11877/Charles-Dickens-It-was-the-best-of-times-it-was-the-worst-of-times-it-was-the-age-ofA

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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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