

NIH-FDA IIG

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

NEWSLETTER

MARCH 2022

PUBLICATIONS

[NK cells require immune checkpoint receptor LILRB4/gp49B to control neurotropic Zika virus infections in mice](#)

Lee HN, Manangeeswaran M, Lewkowicz AP, Engel K, Chowdhury M, Garige M, Eckhaus MA, Sourbier C, Ireland DD, Verthelyi D

JCI Insight. 2022 Feb 08

DOI: 10.1172/jci.insight.151420, PMID: 35132958, PMCID: PMC8855830

This study demonstrates that LILRB4/gp49B plays an important role in NK cell-mediated control of neurotropic viral infections

[Characterization of the therapeutic effect of antibodies targeting the Ebola glycoprotein using a novel BSL2-compliant rVSVΔG-EBOV-GP infection model](#)

Lee HN, McWilliams IL, Lewkowicz AP, Engel K, Ireland DDC, Kelley-Baker L, Thacker S, Piccardo P, Manangeeswaran M, Verthelyi D

Emerg Microbes Infect. 2021 Dec; 10(1) 2076-2089

DOI: 10.1080/22221751.2021.1997075, PMID: 34674613, PMCID: PMC8583756

This study shows that neonatal VSV-EBOV infection system can be used to facilitate assessment of therapeutics targeting EBOV-GP in the BSL2 conditions.

[Analyzing the Role of Gut Microbiota on the Onset of Autoimmune Diseases Using TNF^{ΔARE} Murine Model](#)

Edwards V, Smith DL, Meylan F, Tiffany L, Poncet S, Wu WW, Phue JN, Santana-Quintero L, Clouse KA, Gabay O

Microorganisms. 2021 Dec 30; 10(1)

DOI: 10.3390/microorganisms10010073, PMID: 35056521, PMCID: PMC8779571

We demonstrate that the gut microbiome landscape changes during the onset of Rheumatoid Arthritis (RA) and Inflammatory Bowel diseases (IBD) and that inflammation mechanism might be driven or mediated by some bacteria, identified in our

publication. Further involvement in mucosal immunity cross-talk studies are underway.

[The interactions between autoinflammation and type 2 immunity: from mechanistic studies to epidemiologic associations](#)

Sylvester M, Son A, Schwartz DM

Front Immunol. 2022 Feb 24; 13 818039

DOI: 10.3389/fimmu.2022.818039, PMID: 35281022, PMCID: PMC8907424

We review the concepts of autoinflammation and type 2 immunity, and the mechanisms by which autoinflammatory and type 2 immune responses can modulate each other. We also discuss the epidemiology of type 2 immunity and clinical allergy in several monogenic and complex autoinflammatory diseases.

[A GMR-based assay for quantification of the human response to influenza](#)

Ravi N, Chang SE, Franco LM, Nagamani SCS, Khatri P, Utz PJ, Wang SX

Biosens Bioelectron. 2022 Feb 17; 205 114086

DOI: 10.1016/j.bios.2022.114086, PMID: 35192997

PMID: 35193447 DOI: 10.1080/14760584.2022.2045198,

We demonstrate the possibility of using a specific type of biosensor, called a giant magnetoresistor (GMR), to measure gene expression in human samples. We used this to measure genes that change in response to influenza infection, but in principle this type of biosensor could be used to quantify the expression of human genes in any other context.

Continued>>

Improved osteoblast function on titanium implant surfaces coated with nanocomposite Apatite-Wollastonite-Chitosan- an experimental in-vitro study

Mukherjee S, Sharma S, Soni V, Joshi A, Gaikwad A, Bellare J, Kode J

J Mater Sci Mater Med. 2022 Feb 21; 33(3) 25

DOI: 10.1007/s10856-022-06651-w, PMID: 35190908, PMCID: PMC8860945

The present study underscores that optimal inorganic-organic phase nanocomposite crack-free coating created on Ti by simple, cost-effective electrophoretic deposition technique may have osteoconductive potential and may have wide application in the field of implantology..

Boosting NAD+ blunts TLR4-induced type I IFN in control and systemic lupus erythematosus monocytes

Wu J, Singh K, Lin A, Meadows AM, Wu K, Shing V, Bley M, Hassanzadeh S, Huffstutler RD, Schmidt MS, Blanco LP, Tian R, Brenner C, Pirooznia M, Kaplan MJ, Sack MN

J Clin Invest. 2022 Mar 01; 132(5)

DOI: 10.1172/JCI139828, PMID: 35025762, PMCID: PMC8884917

This study reveals a novel NAD+ dependent, immunomodulatory mechanism to blunt type 1 interferon signaling in healthy control and systemic lupus erythematosus (SLE) patient monocytes. The mechanism uncovered is mediated via increased production of the purine metabolite inosine, which in turn blunts autophagy which together limit TLR4-induced interferon alpha production.

CD26 expression on donor harvest as a risk predictive biomarker for developing graft-versus-host disease post-allogeneic hematopoietic stem cell transplantation: A ten-year follow-up study

Punatar S, Kandekar S, Khattry N, Gokarn A, Prabhash K, Bakshi A, Rane P, Mathew L, Chiplunkar S, Kode J

Cancer Biomark. 2022; 33(1) 17-28

DOI: 10.3233/CBM-210137, PMID: 34334382

Allogeneic hematopoietic stem cell transplantation (ASCT) is the preferred treatment option for patients with several hematologic disorders and immunodeficiency syndromes. Graft-versus-host disease (GVHD) is an immune mediated post-transplant complication which has a major impact on long-term transplant outcomes. Current efforts are focused on identification of new markers that serve as potential predictors of GVHD and other post-transplant clinical outcomes. Our findings suggest a role of CD26 expression on human donor harvest as a potential predictor of acute GVHD. This association warrants further exploration.

Graft-Versus-Solid-Tumor Effect: From Hematopoietic Stem Cell Transplantation to Adoptive Cell Therapies

Barisic S, Childs RW

Stem Cells. 2022 Mar 23

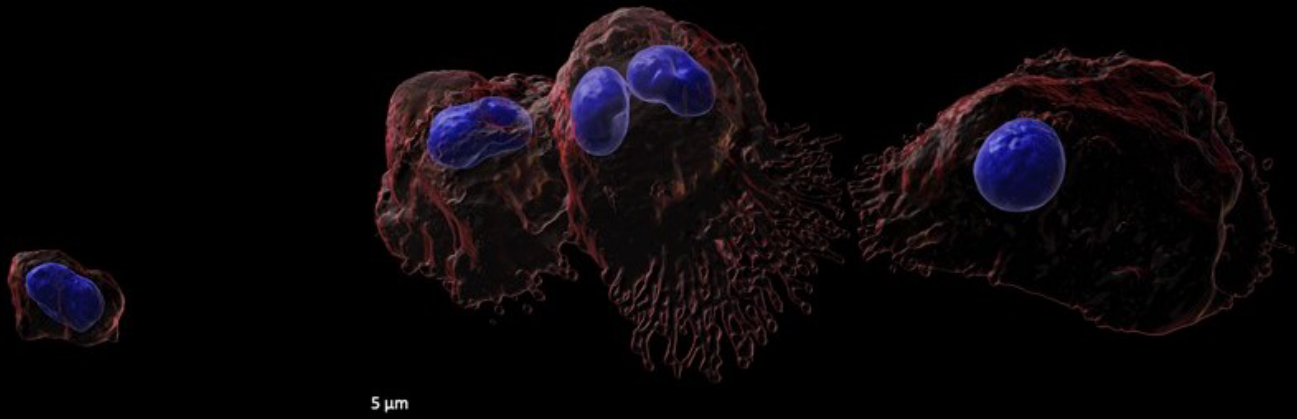
DOI: 10.1093/stmcls/sxac021, PMID: 35325242

In this article, we review the results of clinical trials of allogeneic HSCT in solid tumors. We focus on lessons learned from correlative studies of these trials that hold the potential for the creation of tumor-specific immunotherapies with greater efficacy and safety for the treatment of malignancies.

Is this why we call them growth factors?

Untreated

GM-CSF-treated



Primary human monocytes cultured for seven days in the presence or absence of GM-CSF.

This image shows the dramatic change in size and membrane morphology that occurs when these cells transition from monocytes to a macrophage-like state in the presence of GM-CSF.

Image Credit:

Robert Kwiat
IRTA postbac
Franco Lab – NIAMS/NIH

Davide Randazzo, PhD
Light Imaging Core - NIAMS

Bench-to-Bedside in Action

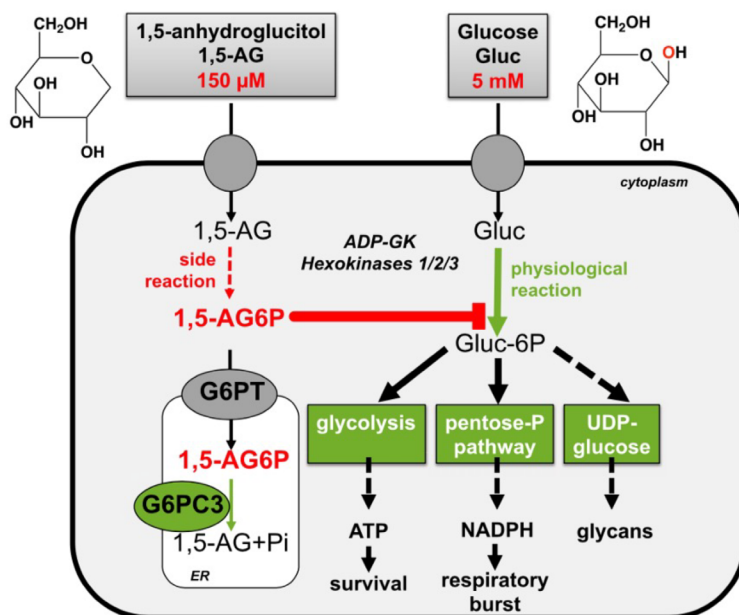
Harnessing immunology and translating to transform care

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.

A Phase 1 Study of Empagliflozin as a Treatment for Severe Congenital Neutropenia Due to G6PC3 Deficiency

PI: David H. McDermott, MD (LMI, NIAID)

Severe congenital neutropenia (SCN) is a rare primary immunodeficiency caused by a variety of genetic defects that result in the blood absolute neutrophil count being chronically below 500 cells/microliter. SCN is a prominent feature of 2 metabolic disorders: SCN4 and glycogen storage disease 1b caused by biallelic mutations in the glucose-6-phosphatase 3 (G6PC3) and glucose-6-phosphate translocase (G6PT) enzymes respectively. Both of these metabolic disorders cause intracellular accumulation of a toxic metabolite termed 1,5-anhydroglucitol-6-phosphate (1,5-AG-6P) that interferes with glucose metabolism (Figure). The precursor molecule (1,5-AG) is at high concentrations in the serum as it is absorbed from many foods, is not metabolized, and is slowly excreted in the urine due to reabsorption with glucose. Neutrophils are highly dependent on glycolysis for their functions: movement to the sites of infection, phagocytosis, reactive oxygen species generation, and bacterial killing and therefore SCN4 results in frequent serious infections and inflammatory bowel disease. In some cases, it is also associated with pulmonary hypertension. Preclinical mouse studies and a small human pilot study in G6PT deficiency have shown benefits to using empagliflozin to increase urinary glucose and 1,5-AG excretion. Our pilot human study seeks to extend these findings to G6PC3 deficiency related neutropenia and explore whether other phenotypes like pulmonary hypertension might also respond. Empagliflozin (Jardiance) is an oral, FDA approved medication for type 2 diabetes and heart failure.



Veiga-da-Cunha, et al., *PNAS* 2018

Learn more at: <https://clinicaltrials.gov/ct2/show/NCT05078879>

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SPOTLIGHT

Dr. Shih is an investigator in the National Eye Institute and leads the Neuro-Immune Regulome Unit.

To learn more about her work visit:

<https://www.nei.nih.gov/research/research-labs-and-branches/we-are-nei-intramural/han-yu-shih>

Tell us about your science.

My laboratory applies multidisciplinary genomic approaches to study cytokine regulation in immune cells that contribute to inflammation in diseases of the eye and brain. By integrating cutting-edge techniques and computational approaches including single cell RNA-seq, ATAC-seq, ChIP-seq, and Hi-C, we have identified lineage-specific and stimulus-induced regulomes in tissue-resident innate and adaptive lymphocytes. An uncontrolled immune response has been linked to many neurological disorders, including glaucoma, uveitis, multiple sclerosis, Alzheimer's disease, Parkinson's disease, age-related macular degeneration and post-traumatic inflammation. Understanding the basic pathophysiology of cytokine production in these contexts – for example, their cellular source and regulation – represents a promising path for drug target discovery.

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

Having a father who teaches physics in high school, I've always been fascinated with fundamental scientific concepts from math to biology. At college, I asked myself, "what can I do to follow my passion for science and also help patients at the same time"? The answer I got was "being a scientist." As soon as I started translational research, I realized immunology is involved in almost all kinds of disorders, including autoimmune and infectious diseases as well as cardiovascular and neurological diseases. I am interested in understanding how my favorite biological materials – DNAs – contribute to immunoregulation in homeostasis and in a variety of diseases.

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

I was fortunate to have great mentors who helped me navigate my career path during pre- and post-doc training. My postdoc mentor, Dr. John O'Shea, himself is a role model for a successful scientist with great knowledge, creativity, and kindness. He always saw the bright side of the results even though they are negative and often challenged us to think about the same question from different angles. In his lab, I learned how to conduct research independently and be collaborative at the same time. His training paved the way for me to become a PI.

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

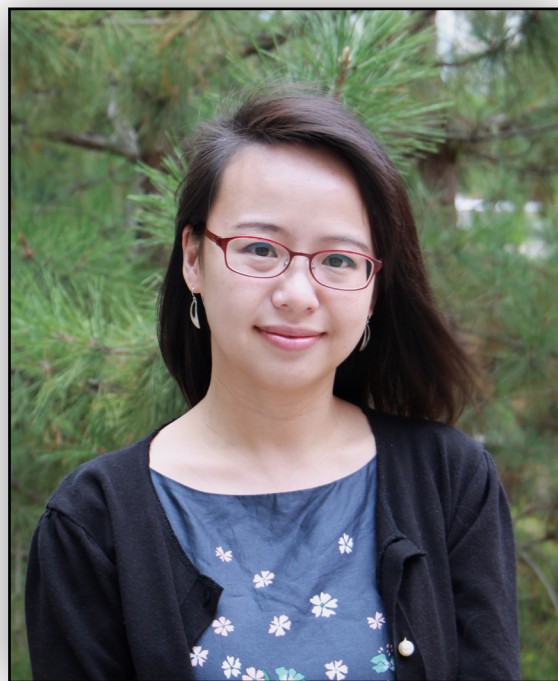
Recently, the role of neuroinflammation has been increasingly appreciated in neurological diseases and aging. Together with advances in single cell and CRISPR biology, I envision many molecular mechanisms that control neuroinflammation to be unveiled, which will allow us to identify novel target-specific therapies.

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

One of the reasons that made me stay at NIH is how collaborative and interactive the NIH-FDA Immunology community is. I have been a member of IIG since 2013 when I joined NIH. The IIG mailing list for reagents/protocols is so helpful and the weekly seminars provide new insights in immunology. In addition the annual workshops are always eye-opening. Overall, I enjoy working with local collaborators and having discussions with top immunologists within the IIG.

How do you spend your free time?

I am a fan of travel and delicious food. When the weather permits, I enjoy hiking, trailing and kayaking with my family. I also like to do yoga and aerobic dance. These activities make me relaxed.



Han-Yu Shih, Ph.D.

Immunology Interest Group SEMINAR SERIES

April 2022



April 6, 2022

Susan Kaech

Metabolic regulation of T cells in infection and cancer



April 13, 2022

Alessandro Sette

Adaptive responses to SARS CoV2 and its variants in natural infection and vaccination



April 20, 2022

Graham Anderson

Thymus generation and regeneration



April 27, 2022

Richard Flavell

Mechanisms of pathogenesis revealed by a humanized model of COVID-19

May 2022



May 4, 2022

Florent Ginhoux

Myeloid cell heterogeneity

May 18, 2022

TBD



May 25, 2022

Garry Nolan

Cancer rearranges the rules in tissue building blocks. A new class of targets for therapy?

Missed a seminar?

Catch up on all your 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.

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that join the lab:

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