

The cover features a collage of colorful, stylized biological cells and structures in shades of purple, blue, green, and pink. The text is centered over this background.

NIH-FDA IIG NEWSLETTER

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PUBLICATIONS

[Aberrant type 1 immunity drives susceptibility to mucosal fungal infections.](#)

Break TJ, Oikonomou V, Dutzan N, Desai JV, Swidergall M, Freiwald T, Chauss D, Harrison OJ, Alejo J, Williams DW, Pittaluga S, Lee CR, Bouladoux N, Swamydas M, Hoffman KW, Greenwell-Wild T, Bruno VM, Rosen LB, Lwin W, Renteria A, Pontejo SM, Shannon JP, Myles IA, Olbrich P, Ferré EMN, Schmitt M, Martin D; Genomics and Computational Biology Core, Barber DL, Solis NV, Notarangelo LD, Serreze DV, Matsumoto M, Hickman HD, Murphy PM, Anderson MS, Lim JK, Holland SM, Filler SG, Afzali B, Belkaid Y, Moutsopoulos NM, Lionakis MS. *Science*. 2021 Jan 15;371(6526): eaay5731. doi: 10.1126/science.aay5731. PMID: 33446526

This work showed that in certain settings, enhanced type 1 immunity rather than defective type 17 responses can promote mucosal fungal infection susceptibility. It identifies aberrant T cell-dependent, type 1 mucosal inflammation as a critical tissue-specific pathogenic mechanism that promotes mucosal fungal infection susceptibility in mice and humans with AIRE deficiency.

[Murine model of colonization with fungal pathogen *Candida auris* to explore skin tropism, host risk factors and therapeutic strategies.](#)

Huang X, Hurabielle C, Drummond RA, Bouladoux N, Desai JV, Sim CK, Belkaid Y, Lionakis MS, Segre JA. *Cell Host Microbe*. 2021 Feb 10;29(2):210-221.e6. doi: 10.1016/j.chom.2020.12.002. PMID: 33385336

Candida auris is an emerging multidrug-resistant human fungal pathogen that colonized the human skin leading to hospital transmissions and infection outbreaks. This work developed a translational murine skin topical exposure model for *C. auris* and showed long-term residence within the skin tissue, differential capacity for skin colonization by different *C. auris* clades, dependence on IL-17 receptor signaling for protection from long-term skin colonization, and effective decolonizing strategies.

[An AIREless Breath: Pneumonitis Caused by Impaired Central Immune Tolerance.](#) Ferré EMN, Lionakis MS. *Front Immunol*. 2021 Jan 27; 11:609253. doi: 10.3389/fimmu.2020.609253. PMID: 33584685

This mini-review summarizes the cellular and molecular basis of the autoimmune attack in the AIRE-deficient lung and discusses the relevance and broader applicability of these findings to other interstitial lung diseases seen in secondary AIRE deficiency states such as thymoma and RAG deficiency or in common polygenic autoimmune disorders such as idiopathic Sjögren's syndrome.

[Glucocorticoid-induced eosinopenia results from CXCR4-dependent bone marrow migration](#)

So Gun Hong, Noriko Sato, Fanny Legrand, Manasi Gadkari, Michelle Makiya, Kindra Stokes, Katherine N Howe, Shiqin Judy Yu, Nathaniel Seth Linde, Randall R Clevenger, Timothy Hunt, Zonghui Hu, Peter L Choyke, Cynthia E Dunbar, Amy D Klion, Luis M Franco. Blood 2020 Dec 3;136(23):2667-2678. doi: 10.1182/blood.2020005161.

Glucocorticoids are first-line agents in the treatment of eosinophilic disorders and they induce rapid clearance of eosinophils from the circulation by a previously unknown mechanism. We performed live cell tracking in a rhesus macaque model and found that glucocorticoids induce bone marrow migration of eosinophils, an effect that depends on induction of expression of the glucocorticoid-responsive chemokine receptor CXCR4.

[CD225 Proteins: A Family Portrait of Fusion Regulators.](#)

Coomer CA, Rahman K, **Compton AA**. Trends Genet. 2021 Jan 29:S0168-9525(21)00005-6. doi: 10.1016/j.tig.2021.01.004. Online ahead of print. PMID: 33518406

The CD225 superfamily regulates vesicular membrane fusion events essential to neurotransmission, immunity, development, and metabolism. This article highlights the shared features that drive the function of CD225 proteins such as interferon-inducible transmembrane proteins 3 (IFITM3) and proline-rich transmembrane protein 2 (PRRT2) and is intended to catalyze efforts towards characterizing the lesser-known family members.

[Observation and Quantification of Eosinophil Motility.](#)

Barretto KT, Mosher DF, Jarjour NN, Curran CS, Esnault S, Johansson MW. Methods Mol Biol. 2021;2241:139-148.

This methods chapter describes protocols to identify changes in human blood eosinophil cell shape, pattern of movement, and state of granules in response to combinations of mediators and adhesive proteins found in extracellular matrix.

[Infection trains the host for microbiota-enhanced resistance to pathogens](#)

Apollo Stacy, Vinicius Andrade-Oliveira, John A McCulloch, Benedikt Hild, Ji Hoon Oh, P Juliana Perez-Chaparro, Choon K Sim, Ai Ing Lim, Verena M Link, Michel Enamorado, Giorgio Trinchieri, Julia A Segre, Barbara Rehermann, Yasmine Belkaid. Cell. 2021 Feb 4;184(3):615-627.e17. doi: 10.1016/j.cell.2020.12.011. Epub 2021 Jan 15.

This work revealed a process by which the host, prompted by prior infection, can deploy the amino acid taurine as a nutrient to nourish and train the microbiota, thereby promoting its resistance to subsequent infection.

AWARDS

CONGRATULATIONS to Dr. Anthony Fauci and Dr. Steven Rosenberg, winners of the 2021 Dan David prize.



Dr. Steven Rosenberg pioneered the first effective immunotherapies for patients with advanced cancer.

Chief, Surgery Branch at the National Cancer Institute in Bethesda, Maryland and Professor of Surgery at the Uniformed Services University of Health Sciences and at the George Washington University School of Medicine and Health Sciences in Washington, D.C., Dr. Rosenberg is also Foreign Adjunct Professor in Cell Therapy, Department of Laboratory Medicine at the Karolinska Institutet in Stockholm, Sweden.

His basic and clinical studies of interleukin-2 directly resulted in the approval of this immunotherapy by the US Food and Drug Administration for the treatment of patients with metastatic melanoma and renal cancer, many of whom remain disease-free over 25 years after treatment.

His studies of cell transfer immunotherapy that resulted in durable complete remissions in patients with metastatic melanoma were the first to directly demonstrate the effective role of T lymphocytes in human cancer immunotherapy. He pioneered the development of gene therapy and was the first to successfully insert foreign genes into humans. He was the first to demonstrate the effectiveness of genetically engineered CAR-T cells to mediate the regression of B-cell malignancies in humans, a treatment now approved by the FDA for widespread use.

In his more recent work, Dr. Rosenberg established new approaches for the application of immunotherapy to patients with a variety of common solid epithelial cancers by targeting the unique mutations present in the patient's cancer.

Dr. Rosenberg is a member of the Institute of Medicine of the National Academy of Sciences. He has published over 1100 papers in the peer-reviewed literature. His h-index of 185 continues to make him one of the highest cited clinician/scientists in the world.



Anthony S. Fauci, M.D. is director of the National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health, where he oversees an extensive research portfolio focused on infectious and immune-mediated diseases.

As the long-time chief of the NIAID Laboratory of Immunoregulation, Dr. Fauci has made many seminal contributions in basic and clinical research and is one of the world's most-cited biomedical scientists. He was one of the principal architects of the President's Emergency Plan for AIDS Relief (PEPFAR), a program that has saved millions of lives throughout the developing world.

Trained as a physician and immunologist, Dr. Fauci joined NIAID and subsequently became, and has remained its Director for the past 36 years. In this capacity, he designed PEPFAR (the President's Emergency Plan for AIDS Relief) under President George Bush, which has brought remarkable relief throughout the most devastated parts of the world, especially Africa. As the most renowned U.S. infectious disease expert, he has demonstrated leadership in responding to outbreaks of SARS, MERS, Ebola, and now Covid-19.

Today, Dr. Fauci is the most influential public health leader in the U.S. and is widely respected throughout the world for his efforts against the coronavirus. As NIAID director he has led research efforts on the development of diagnostics, therapeutics and vaccines for Covid-19. He is the voice of reason for randomized, controlled trials for evaluating antiviral drugs and other therapeutics. These efforts have led to useful therapeutics that have markedly reduced death rates for hospitalized Covid-19 patients.

In addition to traditional vaccine methods, he and his team recognized the value of novel vaccine approaches, such as mRNA vaccines, and quickly moved them into clinical development. Several of these vaccines have gained approval and are now being widely distributed to inoculate millions of people worldwide against the coronavirus.

Dr. Fauci is scientist, humanist, communicator, and has been the trusted advisor of seven U.S. Presidents in meeting infectious disease threats. He has received many honors, including the Presidential Medal of Freedom, the National Science Medal, and 45 honorary degrees.

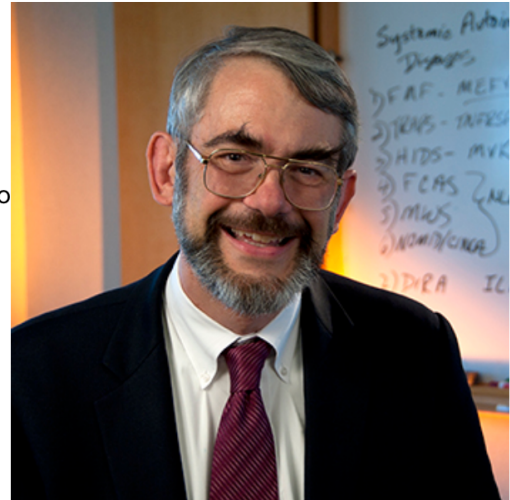
And congratulations to Dr. Dan Kastner, winner of The Crafoord Prize in Polyarthritis, 2021, awarded by the Royal Swedish Academy of Sciences.

https://www.crafoordprize.se/press_release/the-crafoord-prize-in-polyarthritis-2021

Dan Kastner, USA, has described an entirely new group of rare autoinflammatory diseases. His discoveries have brought new knowledge and led to the development of effective treatments. The Royal Swedish Academy of Sciences is awarding him this year's Crafoord Prize in Polyarthritis, worth six million Swedish kronor (approx. USD 700,000).

Daniel (Dan) L. Kastner, receives this year's Prize in Polyarthritis "for establishing the concept of autoinflammatory diseases". He has identified the mechanisms responsible for familial Mediterranean fever, TRAPS and other diagnoses within this group. They are genetic diseases that are unusual in most of the world, but may have a higher incidence in some areas. One or two of every thousand people in the eastern Mediterranean have familial Mediterranean fever, while TRAPS was initially discovered among families in Ireland and Scotland.

Even just 20 years ago, researchers could not explain why those afflicted had recurring fevers, abdominal pain, joint inflammation, troublesome rashes and muscle aches. Dan Kastner started by studying patients with familial Mediterranean fever, and discovered that it was caused by a mutation in a single gene. He then identified the cause of TRAPS and established the concept of autoinflammatory diseases.



Dan Kastner, National Human Genome Research Institute. Photo: NHGRI.

In autoimmune diseases and autoinflammatory diseases, the body's tissues are attacked by the immune system. However, in autoinflammatory disease the problem is within the immune system itself. Recently, research has broadened the understanding of rare (monogenic) and more common (polygenic) autoinflammatory diseases such as Crohn's disease and gout.

"Dan Kastner is often called the father of autoinflammatory diseases, a title that he thoroughly deserves. His discoveries have taught us a great deal about the immune system and its functions, contributing to effective treatments that reduce the symptoms of diseases from which patients previously suffered enormously, sometimes leading to premature death," says Olle Kämpe, chair of the Prize Committee.

Dan Kastner is currently working on Behçet's disease, which is often found along the old Silk Road and is caused by inflammation in the blood vessels. He is delighted to receive this award.

"The phone call from the Academy took me totally by surprise, and I must confess to having been almost speechless when I was told the wonderful news. I can't begin to express how much of an honour it is to be the recipient of this year's Crafoord Prize. I owe so much to my patients, to my colleagues in the clinic and in the laboratory, and of course to my family, all of whom did so much to make this possible," says Dan Kastner.

NEW APPOINTMENTS, PROMOTIONS

Moving on up: On March 1st, **Dr. Lydia Roberts** will move from her current position as a research fellow to a Staff Scientist position in the Bosio laboratory at Rocky Mountain Labs. Congratulations, Lydia!