



THE AMERICAN
ASSOCIATION OF
IMMUNOLOGISTS

AAI NEWSLETTER

DECEMBER 2021

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Meet 2021–2022 AAI leadership and volunteers, page 8

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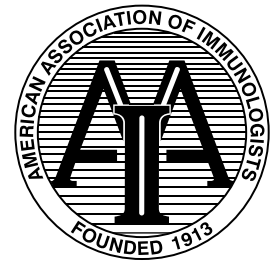
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AAI Council Welcomes Avery August, Joan Goverman

On July 1 of this year, the AAI Council welcomed two new Council members, Councilor Avery August and Secretary-Treasurer Joan Goverman, following their successful candidacies in the 2021 AAI election. Dr. August is serving a four-year term, after which he will be eligible for election to successive one-year terms as AAI Vice President, President, and Past President. Dr. Goverman is serving a three-year term, after which she will be eligible to run for election to a second term.

The election of August and Goverman is of particular significance historically. With his election to the AAI Council, August became the first underrepresented minority scientist to serve as a member of the AAI leadership since the founding of AAI in 1913. Similarly, Goverman's election as Secretary-Treasurer marks only the second-ever election of a woman to that office. (The first was the election of Goverman's predecessor, Edith Lord.)



Avery August, Ph.D. (AAI '99), is a Howard Hughes Medical Institute (HHMI) Professor and professor of immunology in the Department of Microbiology and Immunology at the Cornell University College of Veterinary Medicine. He also serves as vice provost for academic affairs at Cornell University and leads a

group of three advisors to the university president on diversity and equity.

August's research has contributed to understanding the regulation of immune responses by intracellular signaling events. His laboratory examines the signaling pathways regulated by the Tec family of tyrosine kinases that regulate T helper cell differentiation and function, including Th17, and Foxp3⁺ and Foxp3⁻ Type 1 regulatory T cells, as well as the development of CD8⁺ T cell memory. A particular interest is the role of these cells in lung inflammatory diseases, including allergic asthma. His group also studies the role of Tec family kinases in regulating innate memory T cells in the early and adaptive response to infection, and mast cell activation and function during allergic responses. His laboratory has also studied the role of eosinophils during the development of allergic asthma.

"As a member of the AAI for more than 23 years, I have been impressed with, and deeply appreciate, the leadership of the association," wrote August in his 2021 candidate statement. "The AAI has been at the forefront of advocating for increased funding, not just for specific diseases, but for research aimed at advancing our understanding of the fundamental process of immunology, which the AAI recognized very early has an

See Avery August, next page



Joan Goverman, Ph.D., DFAAI (AAI '95), is a professor in the Department of Immunology at the University of Washington, (UW). She served as immunology department chair from 2010 to 2021 and serves as co-PI of the university's NIH-funded Immunology T32 Training Program.

Her research focuses on autoreactive lymphocytes that induce and perpetuate multiple sclerosis. Her laboratory primarily uses murine models to study tolerance mechanisms that typically protect myelin proteins from immune attack, how these tolerance mechanisms are overcome, and how inappropriately activated T cells ultimately drive disease progression. This research includes studying how CD4⁺ T cells, CD8⁺ T cells, and B cells interact with each other, how different microenvironments within the central nervous system (CNS) affect the localization of lesions, and cell trafficking within the CNS. She has described that antigen presentation by dendritic cells and B cells can lead to autoimmunity, and that different T cell subsets drive different aspects of MS disease manifestation. Her research aims to identify potential therapeutic targets to prevent the generation of and damage caused by autoreactive immune cells in CNS autoimmune disease.

By virtue of her election as AAI Secretary-Treasurer, Goverman also chairs the AAI Finance Committee, of which she served as a member from 2019 to 2021. In her 2021 ballot statement, Goverman stated: "As a member of the Finance Committee, it is clear to me that the AAI is incredibly well run and extremely sound financially. This requires strong leadership in balancing competing priorities, anticipating diverse outcomes of financial decisions, and leveraging limited funds for maximal impact. [As a department chair at my institution,] I have been

See Joan Goverman, next page

Avery August (continued)



Dr. August (at far left) pictured with members of his lab
Credit: Cornell Media Relations

impact on many fields. This advocacy has helped foster robust funding for immunology research by the NIH and other agencies. The prominent role of AAI, including its leadership in the COVID-19 vaccine discussion, has been without peer.”

“My early exposure and sense of revelation surrounding the principles of diversity embodied by the adaptive immune system also underpin my interest in serving on the Council. The past year has revealed to many that science continues to be an exclusionary space. I believe that in addition to its leadership in supporting its members and advocating for immunology, The AAI can lead in becoming a more inclusive space for all immunologists—reflective of the fact that the strength of the immune system is literally its diversity! We have an opportunity to cultivate and claim the next generation of immunologists who will be our future. But they will join us only to the extent that we show them that they belong. This will demonstrate that, in addition to joining the field that The AAI has played a huge role in fostering—a field that leads in developing and adapting new cutting-edge tools, where the excitement of vaccine development is palpable, where the promise of cancer immunotherapies such as checkpoint inhibitors and CAR T cells (all of which owe their genesis to the fundamental research being done by immunologists) is still being realized, and a field continuing to reveal how inflammation underpins many chronic diseases—future immunologists will also be joining the most inclusive scientific society.”

An AAI member since 1999, August’s service prior to his election to Council included participation as a member of the AAI Committee on Public Affairs and Publications Committee and appointments as a section editor, associate editor, and ad hoc reviewer for *The Journal of Immunology (The JI)*. He was selected as an AAI Careers in Immunology Fellowship recipient in 2015 and as presenter of the AAI Minority Affairs Committee Guest Lecture (now AAI Vanguard Lecture) at the 2007 AAI annual meeting. For multiple years, August has also

See *Avery August*, next page

Joan Goverman (continued)



Dr. Goverman (third from left) gathered with members of her lab

gratified (and humbled) to see our department’s research and training activities flourish despite shrinking revenues from the state and a very competitive funding climate. It would be a privilege to serve The AAI as Secretary-Treasurer, and thereby help to ensure not only fiscal stability but also resources for new, innovative mechanisms for supporting our work as immunologists in the years ahead.”

Goverman was honored earlier this year as a member of the 2021 class of Distinguished Fellows of AAI. The honor recognizes active, long-term members for distinguished careers and outstanding scientific contributions as well as their service to AAI and the immunology community.

In addition to her service on the Finance Committee, Goverman is a past member of the Committee on Public Affairs, has served as a section editor, associate editor, and ad hoc reviewer for *The JI*, and participated as a member of the AAI Advanced Course in Immunology faculty. She has also served at AAI annual meetings as a major symposium speaker, abstract programming chair, and keynote speaker for the annual Careers in Science Lecture and Roundtables sponsored by the Education Committee and the Committee on the Status of Women.

Goverman has served on numerous NIH study sections and special emphasis panels and is currently the chair of the NIH Clinical Neuroimmunology and Brain Tumors study section. She is also an NIH MERIT Award recipient. She serves on scientific advisory panels on behalf of the Nancy Davis Foundation, Americas Committee for Treatment and Research in Multiple Sclerosis, and the National Multiple Sclerosis Society Research Priority Advisory Council.

Previously, she has served on review panels on behalf of the Max Planck Institute for Neurobiology (Germany), National Multiple Sclerosis Society, Medical Research Council (United Kingdom), Hertie Foundation (Germany), Israel Science Foundation, Multiple Sclerosis Society of Canada, and Wellcome Trust. She has also served on the Council of the Midwinter Conference of Immunologists.

See *Joan Goverman*, next page

Avery August (continued)

served on the AAI Advanced Course in Immunology faculty and as a table leader at the AAI Minority Affairs Committee Careers Roundtable at AAI annual meetings. His AAI awards also include the AAI Laboratory Travel Grant and AAI Minority Scientist Travel Award.

August has served on multiple National Institutes of Health (NIH) study sections, as a member of the National Institute of Allergy and Infectious Diseases Board of Scientific Counselors and the National Institute on Aging Board of Scientific Counselors, and on review panels for the NIH Director's Biomedical Research Workforce Innovation Award and NIH New Innovator Awards.

He has also held additional national and international review panel appointments including for the National Academies Research Associateship Program; American Association for Cancer Research-Historically Black Colleges and Universities Faculty Scholar Award; German Research Foundation; Michael Smith Foundation for Health Research, Canada; U.S.-Israeli Binational Science Foundation, Israel; Wellcome Trust, United Kingdom; and Austrian Science Foundation. He also served on the Prime Minister's Council of Science Advisors, Government of Belize; the Association for Assessment and Accreditation of Laboratory Animal Care International; and the New York Blood Center Board of Trustees.

August's current and past editorial board appointments include service on behalf of *American Journal of Respiratory Cell and Molecular Biology*; *Annual Review of Immunology*; *Frontiers in Immunology*; *Inflammation & Allergy-Drug Targets*; *The International Journal of Biochemistry and Cell Biology*; *mBio*; *Molecular Biology of the Cell*; and *Scientific Reports*.

August's additional career honors include the Distinguished Alumnus Award, Weill Cornell Graduate School of Medical Sciences; Ruth Kirschstein Diversity in Science Award, American Society for Biochemistry and Molecular Biology; E.E. Just Lecture Award, American Society for Cell Biology; Asthma and Allergy Foundation of America Investigator Grant Award; American Heart Association Scientist Development Award; Leukemia Research Foundation Investigator Award; Johnson & Johnson Focused Giving Program Award; and Scholar in Basic Sciences Award, American Society for Histocompatibility and Immunogenetics.

August's national leadership in championing diversity in biomedical research training and career development has included service as chair since 2015 of the Annual Biomedical Research Conference for Minority Students (ABRCMS) Steering Committee and participation as a National Research Mentoring Network Grants Writing Program coach. Included among his institutional

See Avery August, next page

Joan Goverman (continued)

Goverman's current and past editorial board and ad hoc reviewer appointments include service on behalf of *Brain Pathology*, *Cellular & Molecular Life Sciences*, *Cellular Immunology*, *Current Immunology Reviews*, *Immunity*, *Journal of Clinical Investigation*, *Journal of Experimental Medicine*, *Journal of Laboratory Animal Sciences*, *Journal of Neurological Science*, *The Lancet*, *Nature*, *Nature Immunology*, *Nature Medicine*, *Science*, and *Science Immunology*.

Her additional career honors and appointments include the Harry Weaver Neuroscience Junior Faculty Award; Leukemia Society of America Special Fellow; Anna Fuller Cancer Fund Postdoctoral Fellowship; Tumor Immunology Postdoctoral Traineeship; Giannini Postdoctoral Fellowship; NIH National Research Service Award Predoctoral Traineeship; University of California Regents Fellowship; and Melvin M. Snider Prize in Chemistry, Brandeis University.

Prior to completing her appointment as immunology department chair in 2021, Goverman helped mobilize and formalize diversity, equity, and inclusion (DEI) efforts, culminating in creation of the department's DEI Committee in 2019. Focused on student and postdoc recruitment, retention, and experience, the initiative triggered enhanced outreach at minority-focused conferences; publication of a directory highlighting and celebrating department diversity; creation of affinity groups for trainees across basic science programs; reinvigorating outreach and educational activities for middle, high school, and undergraduate students in underrepresented groups; organizing DEI-focused training and anti-racism discussion sessions for department faculty, staff, and trainees; and undertaking development of a DEI roadmap to outline department goals and actions to support the building of a diverse, equitable, and inclusive community into the future.

Goverman has authored more than 75 journal articles and other scientific publications. She has overseen the training of numerous graduate students and postdoctoral fellows and actively mentored trainees in support of their career development, including by championing the interests and advancement of women pursuing careers in STEM fields.

Goverman received a B.S. in chemistry from Brandeis University and her Ph.D. in biological chemistry from the University of California, Los Angeles. A postdoctoral fellowship at UCLA was followed by additional training at the California Institute of Technology.

Goverman was appointed an assistant professor in the Department of Molecular Biotechnology at UW in 1992 and joined the Department of Immunology in 1994. She became an associate professor in 2000, a full professor in 2005, and served as Department of Immunology acting chair in 2009 prior to her appointment as chair in 2010.

Avery August *(continued)*

appointments to promote diversity, equity, and inclusion are: founding co-director (and current senior advisor), Cornell Center for Health Equity; principle investigator (PI), Cornell University Broadening Experiences in Scientific Training (BEST) program grant; co-PI (ongoing), Cornell Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program grant; co-PI (ongoing), Cornell's Sloan Foundation-funded University Centers of Exemplary Mentoring program grant; PI (ongoing), Cornell Initiative for Maximizing Student Development; co-PI, Cornell's NIH-funded ImmunoEngineering T32 Training Program; and PI and director, Alcorn State University – Penn State University Bridges to Doctorate Program.

A native of Belize, August received a B.S. in medical technology from California State University at Los Angeles

and his Ph.D. in immunology from the Weill Graduate School of Medical Sciences of Cornell University. He later served as a postdoctoral fellow at The Rockefeller University with the late Hidesaburo Hanafusa.

August joined the faculty of the Pennsylvania State University in 1999 as an assistant professor, later holding appointments as distinguished professor of immunology in the Department of Veterinary and Biomedical Sciences and director of the Center for Molecular Immunology and Infectious Disease. August joined the Cornell faculty in 2010 as a professor of immunology and chair of the Department of Microbiology and Immunology and has served as vice provost since 2018.

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AAI Leadership and Volunteers

AAI is pleased to recognize those individuals who are serving the organization as leaders and volunteers in 2021–2022.

2021–2022 AAI Council

AAI is led by a volunteer Council composed of eight scientists elected by voting AAI members. Forward-looking in their determination to answer the significant questions facing scientists, Council members are charged to speak on behalf of the AAI membership and act in the best interests of AAI. These leaders of AAI are recognized experts in their specific fields and experienced administrators.

The Council consists of four officers, a President, Vice-President, Secretary-Treasurer, and Past President, and four additional Councilors. In addition, the Council has four *ex officio* non-voting members, the Chairs of the Publications and Program Committees, the Editor-in-Chief of *The Journal of Immunology*, and the Chief Executive Officer of the association.

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2021–2022 AAI Committees and Chairs

The 12 standing committees of The AAI, along with ad hoc committees, help fulfill the AAI mission of advancing research in immunology and related disciplines, fostering the interchange of ideas and information among investigators, and promoting public understanding of immunology and its importance to human health.

AAI committees are served by appointed members and, in the case of five—Awards, Finance, Nominating*, Program, and Publications—by a combination of elected and appointed members. Duties of each committee are those specifically authorized under the bylaws, established by other rules of AAI, and assigned by action of the AAI Council. In advance of the Council's spring and fall meetings, each committee chair is obligated to report on the committee's ongoing, planned, and proposed future activities.

Collectively, AAI committee members work together to:

- promote immunology research and advance the efforts of those who carry it out
- contribute to the professional development of AAI member scientists and trainees
- safeguard and responsibly allocate the resources of AAI
- advocate for the immunological community on public policy issues that affect the conduct and funding of research, and
- educate the public and lawmakers about the importance of supporting immunological discovery and its groundbreaking contributions to confronting and countering disease.

*The Nominating Committee is composed entirely of elected members.

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Dr. Francis Collins to Step Down from His Role as NIH Director

AAI President Gary Koretzky issues statement of appreciation



Francis Collins

NIH recently announced that Francis Collins, M.D., Ph.D., will end his more than 12-year tenure as NIH director in late December. Dr. Collins first assumed the role of NIH director in August 2009 after being appointed by President Barack Obama and confirmed by the U.S. Senate. He was then retained as director by both Presidents Donald Trump and Joe Biden, a reflection of the significant bipartisan respect and support Collins has enjoyed over the years. After stepping down as director, Collins plans to continue his research at his laboratory at the NIH National Human Genome Research Institute.



Gary Koretzky

AAI President Gary Koretzky, M.D., Ph.D. (AAI '92), issued

a statement on behalf of AAI, thanking Collins for his “12 years of exemplary leadership as NIH director” and “wish[ing] him the very best as he begins the next chapter of his career” (see <https://bit.ly/3mezODj>).

STAT reports that Collins' replacement is likely to be selected by the White House before the end of the year. If a new NIH director is not nominated and confirmed by the Senate by then, President Biden will likely appoint an acting director to lead the agency until a permanent director is confirmed.

Senate Releases Draft Funding Bills

Government currently operating under a continuing resolution

The Senate Appropriations Committee unveiled all 12 of its draft annual appropriations bills for fiscal year (FY) 2022 in October, including the Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS) appropriations bill that funds NIH. These draft bills are not expected to be considered by the relevant committees and instead will likely serve as the starting

point for negotiations with the House on final FY 2022 spending bills. The draft Senate Labor-HHS funding bill includes a \$5 billion funding increase for NIH, with \$2.6 billion allocated to the regular NIH budget and \$2.4 billion allocated to the Advanced Research Projects Agency for Health (ARPA-H), the new agency proposed by President Biden in his FY 2022 budget request. (For more, see “ARPA-H: Common Themes from the NIH/OSTP Stakeholder Listening Sessions” on page 18).

As reported in the last edition of the *AAI Newsletter*, the House of Representatives approved a seven-bill spending package in late July that includes the Labor-HHS bill. This House bill includes an even more generous \$6.5 billion funding increase for NIH, with \$3.5 billion devoted to the regular NIH budget and \$3 billion set aside to create ARPA-H. Taken together, the Senate and House Labor-HHS bills demonstrate that NIH funding remains a major congressional priority and that the agency could see a significant funding increase when a final Labor-HHS appropriations bill is enacted.

With none of the appropriations bills signed into law by October 1, 2021 (the beginning of the new fiscal year), Congress and the White House had to work together to enact a continuing resolution (CR), which funds government agencies and programs at approximately last year's level through December 3. Although a CR is an important tool to continue government funding, it comes with its downsides. For example, NIH Institutes and Centers typically set conservative paylines until they have more clarity on how much funding they will receive in a final appropriations law. In addition, NIH generally funds non-competing research grant awards at approximately 90 percent of the previously committed level when a CR is in effect.

AAI Participates in Virtual Rally for Medical Research Capitol Hill Day

AAI was pleased to participate once again in the annual Rally for Medical Research Capitol Hill Day (Rally Hill Day), which was held this year on September 23. Rally Hill Day brings together a wide range of stakeholders, from academia to patient advocates to the pharmaceutical and biotechnology industries, for the common goal of advocating for increased funding for NIH. AAI has supported Rally Hill Day, both financially and through the participation of members and staff, since its inception in 2013.



The Utah/Idaho group, including Schumacher (at top left) and Jensen (at bottom left) met with Senator James Risch (R-ID) and members of his staff.



Dr. Joshua Obar



Dr. Tullia Bruno



Dr. Lauren Ehrlich

For the second year in a row, all meetings with Members of Congress and their staffs were conducted virtually, some by video and some by phone. This enabled broad participation from across the country, with more than 400 participants from 46 states and the District of Columbia, who met collectively with more than 280 congressional offices. AAI was officially represented by seven individuals: AAI Committee on Public Affairs (CPA) Chair Peter E. Jensen, M.D. (AAI '87); CPA members Tullia C. Bruno, Ph.D. (AAI '17), Lauren I. Ehrlich, Ph.D. (AAI '02), and Joshua J. Obar, Ph.D. (AAI '05); former AAI CPA member Ling Cao, M.D., Ph.D. (AAI '08); AAI Director of Public Policy and Government Affairs Lauren G. Gross, J.D.; and AAI Manager of Science Policy and Legislative Affairs Jake Schumacher.

Participants this year delivered three primary messages for federal lawmakers, the first being a well-deserved thank you to Members of Congress for their support of NIH, which has led to robust funding increases

for six consecutive years. Attendees also stressed the importance of continuing that momentum by asking Congress to provide NIH with a budget increase of at least \$3.5 billion for its regular operations for FY 2022 (excluding any funding that might be provided to launch ARPA-H). Finally, participants asked for congressional



The Maine group, including Cao (at top left) met with Senior Policy Advisor Megan DesCamps and Legislative Correspondent Evan Schweikert from the Office of Senator Angus King (I-ME).

support of an AAI-endorsed bill, the Research Investment to Spark the Economy Act, which would authorize \$10 billion in supplemental funding for NIH specifically to help trainees and scientists whose research was interrupted by the pandemic.

Administration Announces \$65 Billion Pandemic Preparedness Plan

The White House recently released its plan for transforming the nation's pandemic preparedness infrastructure to better prepare for and respond to future pandemics and other biological threats. The 10-year, \$65.3 billion plan, entitled "American Pandemic Preparedness: Transforming our Capabilities," lays out goals under 5 pillars:

I. Transforming our Medical Defenses, including dramatically improving and expanding our arsenal of vaccines, therapeutics, and diagnostics.

II. Ensuring Situational Awareness about infectious-disease threats, for both early warning and real-time monitoring.

III. Strengthening Public Health Systems, both in the U.S. and internationally to be able to respond to emergencies, with a particular focus on reducing inequities and protecting the most vulnerable communities.

IV. Building Core Capabilities, including personal protective equipment, stockpiles and supply chains, biosafety and biosecurity, and regulatory improvement.

V. Managing the Mission, with seriousness of purpose, commitment, and accountability akin to the Apollo mission, which brought our astronauts to the moon decades ago.”

This plan is the result of President Biden’s request at the very start of his term for an in-depth review of U.S. pandemic response capabilities, taking into account lessons learned from the COVID-19 pandemic and the reasonable likelihood that another pandemic, potentially even more serious and deadly, could occur in the near future. The plan lays out optimistic yet reasonable goals that would allow a rapid and efficient response to any pandemic or biological threat, even if vastly different from COVID-19. The administration is currently in discussions with congressional leaders to include \$15 billion in the reconciliation bill to initially fund this plan, with the rest of the decade-long plan to be funded through future appropriations.

President Biden Announces PCAST Members

On September 22, President Biden announced the members of the President’s Council of Advisors on Science and Technology (PCAST) (see <https://bit.ly/3Gju07G>). Comprised of experts and leaders in areas ranging from agriculture to neuroscience to cybersecurity, PCAST serves as a body of external advisors who make policy recommendations to the President and the White House on matters of science, technology, and innovation. This year’s roster is described as the “most diverse PCAST in U.S. history”: women comprise half and people of color and immigrants comprise more than one-third of PCAST. Additionally, for the first time since its inception, not just one but two of the three co-chair positions are filled by women.

PCAST held its first meeting on September 28–29, 2021, on “Strengthening U.S. Science and Technology Global Leadership for the 21st Century” and “The State of U.S. Preparedness & Public Health as Revealed by the Pandemic.” Their second meeting on October 18–19,

2021, focused on “Climate Change, Energy, and the Environment.” All meeting agendas, speaker biographies, presentations, and written public comments can be found at <https://whitehouse.gov/pcast/meetings>.

ARPA-H: Common Themes from the NIH/OSTP Stakeholder Listening Sessions

NIH and the White House Office of Science and Technology Policy (OSTP) held a series of listening sessions over the summer to solicit feedback from stakeholders on the proposed ARPA-H. There were 15 sessions in total, with some via invitation only and others open to the public. Each session was organized around particular biomedical science topics to hear collectively from interested stakeholder and community groups.

ARPA-H would support high-risk, high-reward research that aims to advance human health through bold innovation and acceleration of research breakthroughs. The listening sessions sought to garner input regarding current areas of opportunity as well as some of the barriers to accelerating biomedical research breakthroughs. More than 5,100 stakeholders, including representatives of almost 250 organizations across academia, industry, patient advocacy, philanthropy, and other sectors, provided feedback and comments through the sessions. From them, the following common themes around two main areas emerged:

“Scientific Portfolio

- Ensure the programs ARPA-H develops complement NIH’s existing research portfolio, as well as other biomedical research funders, and does not duplicate it.
- Elevate the importance and criticality of addressing health inequities and promoting health equity across all aspects of ARPA-H – from the people it hires to the programs it develops.
- Advance technologies and platforms that are broadly applicable across the spectrum of biomedical and health research and avoid focusing on disease-specific programs.
- Accelerate data accessibility, integration, interoperability, sharing, standards, and tools, and leverage artificial intelligence (AI) in creative ways.
- Focus on de-risking commercialization and translation to push products closer to market in areas with high unmet need and that are not well-supported by industry to bring new therapeutic and diagnostic options to patients rapidly.

Process

- Integrate the community, patients, and their providers early in the program development process to ensure the end-users’ perspectives are considered in program design and implementation.

- Promote and prioritize multi-disciplinary collaboration and partnerships – from drawing in scientists from other disciplines (e.g., physics, economics, sociology) to working with industry, academia, non-profits, and others.”

NIH and OSTP held an additional listening session on October 20, 2021, to give stakeholders a further opportunity to learn more about the ARPA-H proposal and provide feedback on some of the themes that emerged during the earlier sessions. A recording and summary will be available on <https://nih.gov/arpa-h/events>.

NIH Expands Support for Childcare Costs for Ruth L. Kirschstein National Research Service Award (NRSA) Recipients

In an effort to support more “family-friendly work environments for the NIH-supported workforce,”

NIH announced in March that it will allow full-time NRSA fellows (F award recipients) to request support for childcare costs. In September, NIH expanded the eligibility for childcare cost coverage to full-time NRSA-supported trainees (T award recipients) starting in FY 2022 (see <https://bit.ly/3bf8dv8>).

Under the new policies, NRSA fellows and trainees are eligible to receive \$2,500 per budget period to defray childcare costs provided by licensed childcare providers. If both parents are supported by NRSA, each parent is eligible to receive \$2,500 per budget period. Coverage for childcare costs is permitted for dependent children up to age 13 (disabled children up to 18) but is not available for elder or non-child dependent care. NRSA fellows and trainees may request childcare costs for all remaining years of project funding based on dependent age eligibility.



AAI Establishes COVID-19 Resources and Information Web Page

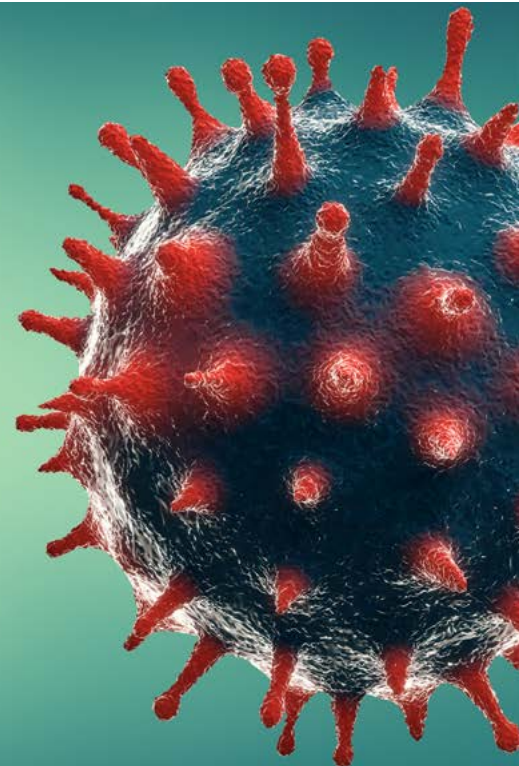
In response to the global coronavirus pandemic, AAI has established a *COVID-19 Resources and Information* page on its website to assist the immunology community in accessing essential pandemic resources, including articles and other information of interest to scientists and the public.

Resources and information that can be found include:

- Links to WHO and CDC web sites
- AAI response to the crisis
- AAI members making news
- NIH alerts, clinical trials, and initiatives
- selected references and studies
- a global COVID-19 daily tracker
- and more

Visit the *COVID-19 Resources and Information* web page at www.aai.org/COVID-19-Resources.

AAI members are invited to submit stories of their research and other efforts related to COVID-19 for inclusion on this page. Please send your stories to bcoulter@aai.org. Inclusion will be at the discretion of AAI.



Baltimore Receives Lasker Award Honors

David Baltimore, Ph.D., DFAAI (AAI '84), has been named the recipient of the Lasker–Koshland Award for Special Achievement in Medical Science, reflecting his contributions as one of the premier biomedical scientists of the last five decades. The award cites the breadth of his discoveries in virology, immunology, and cancer; his visionary academic leadership at multiple institutions; his mentoring of trainees who have become prominent scientists in their fields; and his career-long statesmanship working at the interface of policy and biological research as an advocate for science and for ethical conduct.



Dr. Baltimore is president emeritus and a distinguished professor of biology in the Division of Biology and Biological Engineering at the California Institute of Technology. He is a recipient of the Nobel Prize in Physiology or Medicine, a distinction he shares with Renato Dulbecco and Howard Temin “for their discoveries concerning the

interaction of tumor viruses and the genetic material of the cell.” His research has focused on how the immune system develops and functions, and how immunity can be engineered by gene transfer to fight pathogens and cancer. His laboratory’s basic research focuses on how the transcription factor nuclear factor kappa light chain enhancer of activated B cells (NFκB) and microRNAs control gene expression. His group’s translational research studies how T cells, dendritic cells, and muscle cells can be adapted to express or produce appropriate T cell receptors, antigens, or antibodies to fight cancer and viruses, respectively.

Baltimore was named in 2019 to the inaugural class of Distinguished Fellows of AAI, who are active, long-term members recognized for distinguished careers and outstanding scientific contributions as well as their service to AAI and the immunology community. Baltimore’s additional AAI honors include the 2009 Excellence in Mentoring Award, the 1990 Behring-Heidelberg Award, and selection as a 1990 AAI Distinguished Lecturer. He is also a past special symposium and major symposium speaker at AAI annual meetings and has served as an ad hoc reviewer for *The Journal of Immunology* (*The JI*).

Barton and Mucida Named HHMI Investigators

Gregory M. Barton, Ph.D. (AAI '09), and Daniel Mucida, Ph.D. (AAI '15), have been named Howard Hughes Medical Institute (HHMI) investigators, who are selected for the rigor and innovation that characterizes their biomedical research and their potential to make transformative discoveries over time. Each of this year’s 33 new investigators will receive roughly \$9 million over a seven-year term, which is renewable pending a successful scientific review.



Dr. Barton is a professor in the Department of Molecular and Cell Biology at the University of California, Berkeley. His research focuses on how Toll-like receptors (TLRs) discriminate between self and non-self. His laboratory studies how intracellular TLR trafficking affects their function, host–microbe interactions, and how innate immunity affects adaptive immunity.

Barton was the 2010 recipient of the AAI-BD Biosciences Investigator Award. He has served on the AAI Awards, Program, and ad hoc Fellowship Committees and as a major symposium speaker and abstract programming chair at AAI annual meetings. He has also served on the AAI Introductory Course faculty and as an associate editor and ad hoc reviewer for *The JI*.



Dr. Mucida is a professor in the Department of Immunology, Virology, and Microbiology at the Rockefeller University. His research focuses on three main areas of immune responses that occur in the intestine. His laboratory studies how inflammation versus tolerance are mediated by gut lymphocytes, including intraepithelial

lymphocytes (IELs). An additional research focus studies how gut neuronal cells and the immune system interact and how these interactions shape the local immune response. His group also studies how the introduction of innocuous antigens via the intestinal lumen results in a dampening of the immune response, a response known as oral tolerance.

Mucida has served as a major symposium speaker at the AAI annual meeting and as an ad hoc reviewer for *The JI*.

Bensinger, Byndloss, Chu, and Leifer are HHMI Gilliam Fellowship Program Mentors

Steven J. Bensinger, D.V.M., Ph.D. (AAI '06), Mariana X. Byndloss, D.V.M., Ph.D. (AAI '18), Hiutung Chu, Ph.D. (AAI '21), and Cynthia A. Leifer, Ph.D. (AAI '07), are among this year's doctoral adviser-graduate student tandems selected to receive HHMI Gilliam Fellowships for Advanced Study, which foster the development of scientific leaders committed to advancing diversity and inclusion in the sciences. Gilliam Fellowships support promising graduate students from groups that are underrepresented in science while bolstering the efforts of their thesis advisors to build inclusive training environments.



Dr. Bensinger is a professor in the Department of Microbiology, Immunology and Molecular Genetics at the University of California, Los Angeles. His laboratory researches the impact of lipid metabolism on inflammation and immunity, specifically the proliferation, differentiation, effector function, and survival of immune cells. His research has helped to link lipid metabolism to intracellular signaling networks of inflammation and regulation, with implications for autoimmunity, carcinogenesis, metabolic disorders, and infection.

Bensinger has served as a major symposium speaker at the AAI annual meeting and an associate editor for *The JI*. He is also a past recipient of the AAI Early Faculty Travel Award.

Bensinger's graduate student advisee and Gilliam Fellowship co-recipient is Kelly Kennewick, a Ph.D. student in UCLA's Molecular Biology Interdepartmental Doctoral Program. Her work focuses on investigating the crosstalk between lipid metabolism and T cell immunity.



Dr. Byndloss is an assistant professor in the Department of Pathology, Microbiology, and Immunology at Vanderbilt University Medical Center. Her research focuses on the links between gut microbiota, host metabolism, and non-communicable chronic inflammatory diseases, such as inflammatory bowel

disease, obesity, and colorectal cancer. Main projects in her laboratory include studying microbiota dysregulation as a result of intestinal inflammation, and inflammation-induced epithelial metabolism resulting in gut dysbiosis.

Byndloss's graduate student advisee and Gilliam Fellowship co-recipient is Nicolas Shealy, a Ph.D. candidate in Vanderbilt's Microbe-Host Interactions Graduate Program. He studies the metabolic interactions of pathogenic Enterobacteriaceae and the gut microbiota, with a focus on the production and utilization of short chain fatty acids and amino acids.



Dr. Chu is an associate professor in the Department of Pathology at the University of California, San Diego (UCSD). Her research focuses on the symbiotic relationships between commensal microbiota and their host. Her laboratory studies commensal bacteria-specific mucosal tolerance, how the host immune system recognizes

commensal bacteria, and how and if inflammation affects this tolerogenic state.

Chu's graduate student advisee and Gilliam Fellowship co-recipient is Marvic Carrillo-Terrazas, a Ph.D. student in UCSD's Biomedical Sciences Graduate Program. Her work focuses on understanding how the intestinal environment drives bacterial strain variation and shapes immunomodulatory function.



Dr. Leifer is a professor in the Department of Microbiology and Immunology at the Cornell University College of Veterinary Medicine. Her research focuses on innate immune recognition of infection, inflammation, and damage via TLRs. Her laboratory studies how TLR signaling is regulated, including intracellular

regulatory mechanisms, and how extracellular signals affect intracellular, and then broader immune responses. Her work has implications in immune responses to vaccines, infection and inflammation, and biomaterials.

Leifer serves as chair of the ad hoc AAI Grant Review for Immunologists Program (GRIP) Committee and is a past associate editor and ad hoc reviewer for *The JI*. She has received multiple AAI awards, including the Careers in Immunology Fellowship, Laboratory Grant, and Junior Faculty Travel Award.

Leifer's graduate student advisee and Gilliam Fellowship co-recipient is Karla García-Martínez, a doctoral candidate in Cornell's Biomedical and Biology Sciences Graduate Program. Her work focuses on how TLRs are regulated and how they relay signals to give rise to protective immune responses.

Crotty Achieves “World Expert” Status for Vaccine Research

Shane Crotty, Ph.D. (AAI '04), has earned the ranking of “World Expert” in vaccine research as determined by Expertscape’s PubMed-based algorithms, which place him in the top 0.1 percent of scholars publishing information about vaccines over the past 10 years.



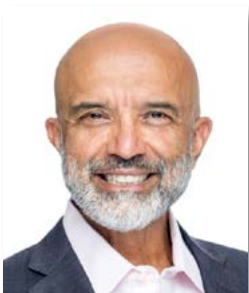
Dr. Crotty is a professor in the Center for Infectious Disease and Vaccine Research at the La Jolla Institute for Immunology (LJI). There, he is a member of the LJI Coronavirus Task Force, which studies the immune responses to SARS-CoV-2. More broadly, his laboratory studies immune responses to vaccines. Crotty’s

research has described T follicular helper cells as integral to generating antibodies, which also has implications for cancer, autoimmunity, and allergies. Currently, in addition to his SARS-CoV-2 research, his laboratory is researching vaccines for human immunodeficiency virus, influenza, and strep throat.

Crotty was the 2012 recipient of the AAI-BD Biosciences Investigator Award and is also a past recipient of the Pfizer-Showell Award presented by AAI. He currently serves on the AAI Nominating Committee, is a past member of the Program Committee, and has served as an associate editor and ad hoc reviewer for *The JI*.

Dixit is Vilcek Prize Honoree

Vishva M. Dixit, M.D. (AAI '16), has been honored with the Vilcek Prize in Biomedical Science for his groundbreaking discoveries on the molecular events required for apoptosis and pro-inflammatory signaling. The Vilcek Foundation Prizes celebrate the intellectual and cultural contributions of foreign-born scientists and artists to the fabric of life in the United States. Dixit is among the world’s most-cited scientists whose work has elucidated molecular mechanisms of inflammation and shaped scientific understanding of biology and human health.



Dr. Dixit is vice president of early discovery research and physiological chemistry at Genentech. As a faculty member in the Department of Pathology at the University of Michigan, Dixit launched his investigations on the mechanism of action of tumor necrosis factor in apoptosis. He showed that caspase was a key

component of the death-receptor-induced apoptotic pathway and elucidated other critical elements in this process. He has continued his investigations of cell death and inflammation at Genentech with a focus on the development of therapeutics. Recent work by his laboratory has examined the role of ubiquitin hydrolases in these pathways and characterized adaptor proteins that activate pro-inflammatory caspases. His research has enhanced our understanding of inflammation and cell death in both normal development and disease.

Dixit has participated as a major symposium chair and speaker at AAI annual meetings and served as an ad hoc reviewer for *The JI*.

Fitzgerald, Kaplan Elected to National Academy of Medicine

Katherine A. Fitzgerald, Ph.D. (AAI '06), and **Mariana J. Kaplan, M.D. (AAI '02)**, are among scientists recently honored with election to the National Academy of Medicine (NAM) in recognition of their outstanding professional achievement and commitment to service in helping advance the medical sciences, health care, and public health. Dr. Fitzgerald’s NAM election citation specifically recognizes her pioneering work on innate immune receptors, signaling pathways, and regulation of inflammatory gene expression. Dr. Kaplan’s citation recognizes her seminal contributions to advancing understanding of the pathogenic role of the innate immune system in systemic autoimmune diseases, atherosclerosis, and immune-mediated vasculopathies.



Dr. Fitzgerald is a professor of medicine and the Worcester Foundation in Biomedical Sciences Chair at the University of Massachusetts Chan Medical School, where she also serves as vice chair for research in the Department of Medicine and director of the Program in Innate Immunity. The overarching theme

of her research is to understand the molecular mechanisms that control inflammation in response to a variety of self and pathogenic antigens. Fitzgerald’s laboratory researches how nucleic acids and their intracellular localization drive inflammation in response to the presence of a pathogen or autoimmune disease. She also studies the biology, triggers, and regulation of inflammasomes that drive inflammation by activating caspase-1, resulting in the secretion of interleukin-1 and interleukin-18, and rapid cell death (pyroptosis). Her group also focuses on long non-coding RNAs and how they control immune cell function. Lastly, her group studies the role of innate immune pathways in response to malaria infection.

Fitzgerald was the 2014 recipient of the AAI–BD Biosciences Investigator Award. She served multiple terms as elected chair of the AAI Nominating Committee and is a past associate editor and section editor for *The JI*. She has also participated as a major symposium chair and speaker and abstract programming chair at AAI annual meetings and as a faculty member for the AAI Advanced Course in Immunology.



Dr. Kaplan is chief of the Systemic Autoimmunity Branch at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), where she also serves as NIAMS deputy scientific director. Kaplan's research revolves around understanding the innate and adaptive immune responses

that break immune tolerance and drive autoimmune disease, clinical phenotypes, vascular damage, and organ

damage resulting from systemic lupus erythematosus (SLE). Her laboratory studies the role of neutrophils and neutrophil extracellular traps in autoimmune disease pathogenesis. The research group also studies how vascular damage in SLE is driven by type I interferons and how immune cell metabolism changes in autoimmune diseases. Lastly, her group works to identify novel biomarkers and potential therapeutic targets to prevent cardiovascular damage and regulate pathogenic autoimmune responses in SLE and other systemic rheumatic diseases.

Kaplan is a past member of the AAI Membership Committee and has served as an associate and section editor for *The JI*. She has also participated as a major symposium chair and speaker at the AAI annual meeting, as a faculty member for the AAI Advanced Course in Immunology, and as a lab host and mentor for the AAI High School Teachers Summer Research Program in Immunology.

The Journal of Immunology

Topical Reviews Collections



The *Journal of Immunology* Topical Reviews collection provides an authoritative, up-to-date overview of critical areas in immunology. These reviews focus on rapidly developing topics and provide an indication of future directions.

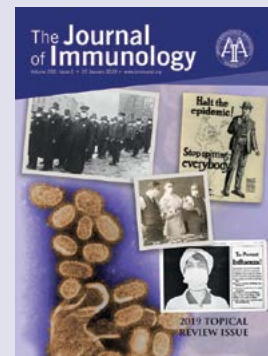
2021: Stromal Immunology: Frameworks for Development and Response



2020: Neuroimmunology: To Sense and Protect



2019: Immunity to Influenza: Closing in on a Moving Target





Thomas A. Waldmann, M.D. (AAI '71)

September 21, 1930 – September 25, 2021

AAI extends condolences to the family, friends, and colleagues of Thomas A. Waldmann, M.D., AAI '71, a renowned immunologist at the National Institutes of Health (NIH) for more than six decades, who died on September 25.

Dr. Waldmann was a distinguished investigator and chief emeritus of the Lymphoid Malignancies Branch of the National Cancer Institute, NIH. He served as chief of the branch from 1971 (when it was known as the Metabolism Branch) until 2019.

Among his numerous career honors, Waldmann was the 2007 recipient of the AAI-Dana Foundation Award for Human Immunology (known today as the AAI-Steinman Award for Human Immunology Research) and presented the corresponding award lecture at the 2007 AAI annual meeting. He served as a past AAI representative to the International Union of Immunological Societies Nomenclature Committee and as an associate editor and editorial board member for The Journal of Immunology.

The following remembrance was authored by Waldmann's NIH and AAI-member colleagues Warren J. Leonard, M.D. (AAI '86), NIH Distinguished Investigator, chief of the Laboratory of Molecular Immunology, and director of the Immunology Center, National Heart, Lung, and Blood Institute; and Jay A. Berzofsky, M.D., Ph.D. (AAI '77), chief of the Vaccine Branch, Center for Cancer Research, National Cancer Institute. AAI gratefully acknowledges the submission.

Thomas Alexander Waldmann (1930–2021)

Thomas Alexander Waldmann, or “Tom” to his friends, was born in New York City on September 21, 1930, and died on September 25, 2021, just four days after his 91st birthday.

Within his remarkable 65-year-long active career at NIH, he saw the identification, cloning, and characterization of a huge range of major immunological cell surface and secreted molecules, and in several critical instances contributed to these advances, as well as to the development of immunotherapeutic approaches that could not have been dreamed of when he started at NIH in 1956. Tom’s scientific career evolved as did the field of immunology, and he was a scholar of great depth whose knowledge spanned the field and who helped to open new areas of immunological research. Tom’s major drive was to translate his basic discoveries to clinical cures for disease, and his own work was truly from bench to bedside and bedside to bench, serving as a role model for three generations of physician-scientists.

Tom attended the University of Chicago as an undergraduate and then graduated from Harvard Medical School in 1955.

After an internship at the Massachusetts General Hospital, he arrived at NIH in 1956 as a clinical associate, working under Nat Berlin in the Metabolism Branch, National Cancer Institute. He had many opportunities to leave over the years for positions at major universities, but Tom never left and became branch chief in 1971, a position he held until 2019. Tom worked actively until just before his passing, combining basic science with the unique translational opportunities provided by the NIH Clinical Center. He was incredibly prolific, publishing more than 870 articles, including many landmark papers.

Tom’s initial research related to erythropoiesis, but he soon developed an interest in the metabolism of secreted proteins, including albumin and immunoglobulins, determining the plasma half-life of human immunoglobulin *in vivo* for the first time. Those studies linked his research to immunology, a field to which he was attracted based on the power of the then-recent polio vaccine and the idea of modulating the immune response to control a range of diseases.

His interest in immunoglobulin metabolism led him, with Warren Strober and R. Michael Blaese, to immunodeficiencies such as hypogammaglobulinemia and protein-losing enteropathies, of which one was named after Tom. Over time, he focused on adult T cell leukemia (ATL), a profound disease that is caused by the human retrovirus, HTLV-I, and which is associated with defective immune function; indeed, with Samuel Broder, Tom showed that ATL cells were a monoclonal population of suppressor T cells.

In an effort to develop an antibody to CD4⁺ T cell activation markers, Takashi Uchiyama and Sam Broder in Tom's laboratory developed monoclonal anti-Tac antibody, which turned out to be the first antibody to the human IL-2 receptor α chain. Tom took full advantage of this serendipity, characterizing normal activated lymphocytes as well as ATL cells, which express an overabundance of "Tac antigen," thereby making them susceptible to anti-Tac. The antibody also facilitated the cloning of cDNAs encoding IL-2R α by one of us (WJL) and Warner Greene, with Tom. Tom also developed anti-Tac into a humanized therapeutic antibody, Daclizumab, which he used to cure a subset of ATL patients, and this antibody was FDA-approved for the treatment of multiple sclerosis. Tom additionally collaborated with Ira Pastan to generate toxin-armed Daclizumab.

Moreover, Tom's laboratory co-discovered IL-15—in his case as a molecule derived from an HTLV-I-transformed T cell line that he demonstrated shared with IL-2 the signaling components of the receptor (IL-2R β and the common γ chain) but that dramatically differs in its main actions. With Sigrid Dubois and Yutaka Tagaya in his lab, he demonstrated that IL-15 is presented primarily in *trans* by IL-15R α on dendritic cells to the IL-2R β and common γ chains on T and NK cells, whereas IL-2 signals in *cis*, with IL-2R α as well as the IL-2R β and the common γ chain together forming the high-affinity IL-2 receptor complex. Moreover, IL-15 was required for NK cell development and promoted CD8⁺ memory T cells, but unlike IL-2, did not promote activation-induced cell death or induce the generation of T regulatory cells. Tom orchestrated the development of cGMP-grade IL-15 and performed the first in-human trials with IL-15 in the quest to develop its therapeutic potential for cancer.

Tom achieved scientific "greatness" and delivered more than 100 named lectures, was elected to the National Academy

of Medicine, the National Academy of Sciences, and the American Academy of Arts and Sciences, and received many awards and honors, including the 2007 AAI-Dana Foundation Award for Human Immunology (known today as the AAI-Ralph Steinman Award for Human Immunology Research).

However, Tom was also an individual for whom family invariably came first, always reserving time for his wife Kathy, his three children, Richard, Robert, and Carol, and their spouses and children. He was a dear friend to many as well as a cherished mentor who trained future leaders in immunology. He was also an award-winning photographer who served as president of the NIH Camera Club and mentor to many aspiring photographers as well as immunologists.

Tom left a massive imprint on immunology and the many immunologists he mentored. With his passing, our field has lost one of its giants; he will be missed by many as a colleague, friend, mentor, and extraordinary physician-scientist.

* * * * *

The Waldmann family invites donations in Dr. Waldmann's memory to the International Medical Corps: www.internationalmedicalcorps.org/waldmann.

In addition to the small service and burial held in October, a more formal celebration of Dr. Waldmann's life is planned for a future date.

For additional Waldmann tributes, see also:

- Pumphrey Funeral Home: www.pumphreyfuneralhome.com/obituaries/Dr-Thomas-Alexander-Waldmann?obId=22538215
- NIH Intramural Research Program Blog: <https://irp.nih.gov/blog/post/2021/10/nih-mourns-the-passing-of-thomas-a-waldmann>
- National Cancer Institute Center for Cancer Research In Memoriam: <https://ccr.cancer.gov/news/article/in-memoriam-thomas-a-waldmann-md-1930-2021>

To view Waldmann's 2015 interview as part of the AAI Oral History Project, visit www.aai.org/About/History/AAI-Awardees/ThomasAWaldmann.



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Christine A. Biron, Ph.D., DFAAI (AAI '84)

d. 10/16/2021 (age 70)

AAI extends condolences to the family, friends, and colleagues of Christine A. Biron, Ph.D., DFAAI (AAI '84), a devoted and active AAI member of 37 years who died unexpectedly on October 16.

Dr. Biron was the Esther Elizabeth Brintzenhoff Professor of Medical Science at Brown University, where she had also served as director of the Pathobiology Graduate Program and later as chair of the Department of Molecular Microbiology and Immunology.

Biron was elected in 2021 as a Distinguished Fellow of AAI, one of the highest honors bestowed by AAI. This honor recognizes active, long-term members for distinguished careers and outstanding scientific contributions as well as their service to AAI and the immunology community.

Biron was a past member and chair of the AAI Awards Committee and also served on the Finance, Nominating, and Program Committees. In 2015, she was selected as an AAI Distinguished Lecturer. She also participated at AAI annual meetings as a major symposium chair and speaker as well as serving as an abstract programming chair. Additionally, she was a past section editor and associate editor for The Journal of Immunology and served as a faculty member for the AAI Advanced Course in Immunology.

The following remembrance was authored by Biron colleagues Jordan S. Orange, M.D., Ph.D. (AAI '04), professor and chair, Columbia University Medical Center; Marion T. Kasaian, Ph.D. (AAI '90), scientist, Pfizer Research; and Helen C. Su, M.D., Ph.D., senior investigator, NIAID, NIH. AAI gratefully acknowledges their submission.

On October 16th, we lost a trailblazer in immunology, a strong advocate for women in science and career development, a committed and caring colleague and teacher, and a dear friend, Dr. Christine Anne Biron. There is much to be said about her career and life, but some key themes must be stated right away. Christine was a scientist because she was curious, loved discovery-based research, and took joy in her work. She believed in pursuing the truth with robustness and rigor and taking on questions that mattered even when they seemed impossible to solve. She never retreated from an approach or experiment because it was too difficult or too intensive and often wondered whether those might be the best questions to pursue. Some of the experiments she performed herself were inspiring and have greatly influenced the field. Also, Christine was generous with her time and efforts on behalf of others. She was eager to give feedback on and help improve an idea, giving her very best energies and thoughts and almost always asking key and even transformative questions about hypotheses.

Christine was born and raised in Bellingham, MA, the oldest of five siblings. Her father was the town moderator and her mother a strong matriarch, and they instilled in her the values of industry, integrity, and responsibility. After receiving her undergraduate degree in biochemistry at the University of Massachusetts (UMass) Amherst, she obtained her Ph.D. in microbiology and immunology at the University of North Carolina (UNC) Chapel Hill.

In her Ph.D. work with Joseph Pagano, she examined cytotoxic T lymphocyte (CTL) and natural killer (NK) cell responses against Epstein Barr virus (EBV), exploring the role of interferon in their activation and blastogenesis. She challenged the idea that NK cells were end stage, incapable of further expansion. In a postdoctoral fellowship with Raymond Welsh in the laboratory of Michael Oldstone at Scripps, and continuing at the UMass Medical School in Worcester, MA, Christine took on the challenging initiative to purify cells after experimental viral infection of mice according to size using centrifugal elutriation. In some extremely difficult experiments published in 1982 and thereafter, she was able to demonstrate that the large blasting cells observed early after viral infection were the ones possessing the NK cell activities.

In launching her own independent research program at UMass, Christine went on to show that blast NK cells were induced in response to interferons elicited during viral infection. These pioneering studies confirmed the proliferative capacity of NK cells, while elucidating cytokine regulation of NK cell antiviral and immunopathogenic responses. These interactions were further delineated in a 1999 *Annual Review of Immunology* treatise entitled “NK cells in antiviral defense: function and regulation by innate cytokines” (<https://pubmed.ncbi.nlm.nih.gov/10358757/>), which has been cited well over 1,500 times.

While mostly focused upon murine experimental immunology, Christine ventured into human immunology through the extensive characterization of an NK cell deficient adolescent patient, who experienced successive waves of severe infections with herpes-group viruses. This landmark study, for which Christine performed most of the NK cell characterization and profiling herself, was published in the *New England Journal of Medicine* in 1989 (<https://pubmed.ncbi.nlm.nih.gov/2543925/>) and has been cited approximately 1,000 times. In an era in which innate mechanisms were considered secondary to the adaptive responses, this report clearly demonstrated the profound importance of NK cells in herpesviral defense in humans. This theme of phenotypic and functional characterization associated with immune deficiency has carried forward to this day and has been validated through the existence of many similar phenotypes and associated Mendelian genotypes.

In 1987, Christine moved to Brown University as assistant professor of medical science. She would remain dedicated to building the immunology program at Brown and to investigating cytokine control of antiviral responses for the rest of her career. One aspect that set Christine apart was her willingness to confront the complexities and intricacies of *in vivo* models. There is a role for reductive research and simplification, but she understood that what happens inside an animal is nuanced, with antiviral responses regulated in both time and space, greatly influencing the ultimate outcome. From the initial observation that lymphocytic choriomeningitis virus (LCMV) is cleared by CD8⁺ CTL, while murine cytomegalovirus (MCMV) is also controlled by NK cells, Christine identified waves of innate and adaptive cellular responses orchestrated by cytokines. In MCMV infection, dendritic cells (DCs) release an early wave of interleukin-12 (IL-12), activating NK cells to produce interferon (IFN)- γ . In an elegant example of cross-regulation, subsequent plasmacytoid DC (pDC)-induced IFN- α/β feeds back to limit this IL-12 secretion and, along with IL-2, potentiates NK cell expansion. In LCMV infection, however, an early wave of IFN- α/β activates NK expansion, but prevents IL-12 induction, limiting IFN- γ production. Subsequent T cell activation and generation of transforming growth factor (TGF)- β reduces NK proliferation, driving the shift from innate to adaptive immunity. Spatial trafficking of NK cells from bone marrow to secondary compartments underlies these dynamics, localizing the NK cells to receive cellular activation signals and to propagate the response.

The signaling downstream of cytokine regulation, and how this facilitates response to and protection from immunopathology, subsequently emerged as a major focus for Christine. Building on the observation that IL-12/ signal transducer and activator of transcription (STAT)4 is critical for NK cell IFN- γ expression, whereas IFN- α/β /STAT1 drives NK cytotoxicity but negatively

regulates IFN- γ , Christine investigated the dynamics of STAT expression in infection. Her 2002 landmark publication in *Science* (<https://pubmed.ncbi.nlm.nih.gov/12242445/>) demonstrated that STATs were fundamental in both inducing and regulating the antiviral interferon response. These groundbreaking observations gave rise to many related works and avenues, encapsulated nicely in a 2006 perspective published in *Science* entitled “Type I interferons and the virus-host relationship: a lesson in détente” (<https://pubmed.ncbi.nlm.nih.gov/16690858/>). Her body of work is truly central to immunology’s understanding of the coordination of antiviral and innate cytokine regulation and response.

A unifying characteristic of Christine’s papers is their rigor and humility. She never overstated her findings and felt that robust works would speak for themselves and stand the test of time. She taught her trainees that the ideal was to be able to make the same point in six different ways and that one could never be careful enough. One colleague, speaking for many, stated that her work was to be noticed and always believed. Naturally, to achieve this ideal required long hours and tenacity, habits which she modeled and imparted to others along with an enthusiasm for experimental discovery.

Christine’s infectious love of science inspired students, trainees, and colleagues throughout her career, including 12 postdoctoral fellows, three M.D./Ph.D. students, and six graduate students. She was known at Brown for her lively advanced seminar courses, which also drew undergraduates, many of whom were inspired to pursue scientific careers. For much of her teaching career, she dedicated herself to ensuring that the medical students would thoroughly understand immunology in preparation for their future careers as physicians. Christine had an intense focus on those who worked in her laboratory. She cared about people and invested the energy to get to know them, finding ways to bring science to them in a meaningful way and inspire them to (as she would say) “get hooked by science.” That is what happened to so many of us, thanks to her special talents, kindness, brilliance, and attention. Mentoring others was incredibly important to Christine, and she maintained lifelong connections with several of her former trainees. She was especially supportive and encouraging of junior colleagues, including women faculty who were faced with barriers in their career advancement.

Christine’s inquisitive nature and scientific curiosity were apparent even as a graduate student at UNC, when she was teased for being the one who was always first to ask questions at meetings, courses, or lectures. Throughout her career, she continued to be generous with her time and offered perspectives and suggestions that influenced the thinking and direction of her colleagues. She served on various editorial boards, was a member and Distinguished Fellow of AAI, was a member of the American Society for

Virology, and was an elected fellow of both the American Association for the Advancement of Science and the American Academy of Microbiology. Additionally, she had the distinction of serving on the Board of Scientific Counselors for both the National Institute of Allergy and Infectious Diseases and the National Cancer Institute.

Outside of her work, Christine was the quintessential New Englander who enjoyed spending time with her close-knit family, often at her cottage on Cape Cod, where she would also invite friends and close colleagues. She was an amateur photographer and had a beautiful soprano voice. Her distinctive laughter was emblematic of her enthusiastic personality. She was also an intensely private and courageous person of faith who accomplished much

despite having an increasingly debilitating autoimmune disease. To honor her, in 2020 an annual endowed lectureship was established in her name at Brown University. We are grateful to have known her; she will be sorely missed.

The inaugural Dr. Christine Biron Molecular Microbiology and Immunology Lectureship at Brown University was held on October 28, 2021. Donations in Christine's memory may be made at <http://brown.edu/go/Biron>.

* * * * *

See also the obituary published by the family in the Providence Journal: <https://www.providencejournal.com/obituaries/f0060481>

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AAI Participates in Virtual European Congress of Immunology 2021

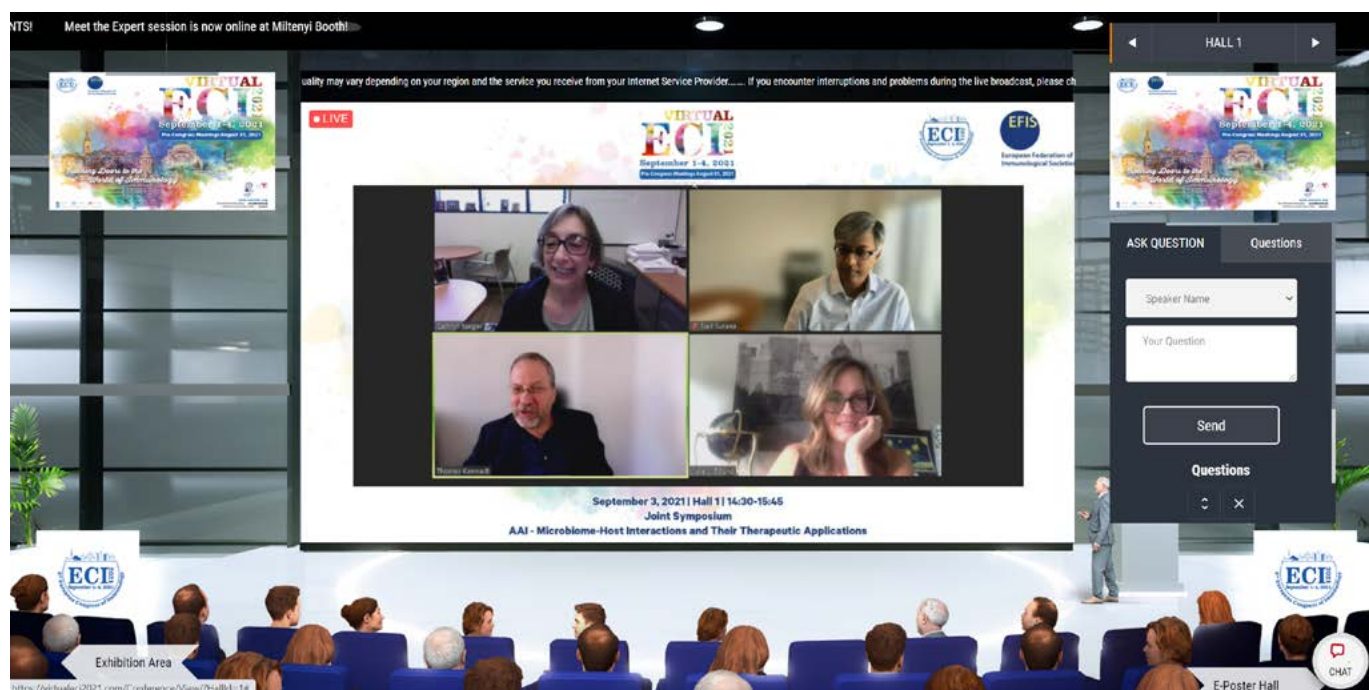
The 6th European Congress of Immunology (ECI) took place virtually September 1–4, 2021. AAI members were among the many attendees enjoying the conference.

AAI co-sponsored a well-attended symposium at the ECI with the European Federation of Immunological Societies (EFIS). The session, “Microbiome–Host Interactions and Their Therapeutic Applications,” was chaired by Cathryn Nagler, Ph.D., DFAAI (AAI ’90), Bunning Food Allergy Professor, University of Chicago, and Thomas Kamradt, M.D. (AAI ’01), professor, University Hospital Jena, Germany. Nagler opened the session with a talk about regulation of allergic responses to food by intestinal bacteria. June L. Round, Ph.D. (AAI ’12), professor, University of Utah, then presented on the role of microbe-immune interactions in obesity. Neil Surana, M.D., Ph.D. (AAI ’16), associate professor, Duke University, closed the session, speaking on regulation of inflammatory diseases by the microbiota.

AAI was pleased to sponsor registration grants to support 21 talented scientists in attending Virtual ECI 2021:

- Adeleye Oluwatosin Adeshakin, Ph.D. (AAI ’18), research scientist, University of Chinese Academy of Sciences, China

- Rizwan Ahmed, Ph.D. (AAI ’16), postdoctoral fellow, Johns Hopkins School of Medicine
- Yanina Helga Arana, Ph.D. (AAI ’21), associate professor, Universidad San Martin de Porres, Peru
- Rami Bechara, Ph.D., Pharm.D. (AAI ’18), postdoctoral fellow, University of Pittsburgh
- Pavani Beesetty, Ph.D. (AAI ’21), postdoctoral fellow, University Health Network, Canada
- Zerick T. Dunbar (AAI ’19), graduate student, Meharry Medical College
- Taru S. Dutt, Ph.D. (AAI ’19), postdoctoral fellow, Colorado State University
- Jhon Ralph De La Peña Enterina (AAI ’19), graduate student, University of Alberta, Canada
- Vibha Jha, Ph.D. (AAI ’21), research associate, University of Colorado
- Mirela Kuka, Ph.D. (AAI ’20), assistant professor, Università Vita-Salute San Raffaele, Italy
- Thomas Andreas Liechti, Ph.D. (AAI ’21), postdoctoral fellow, Vaccine Research Center, NIAID, NIH



AAI-EFIS Joint Symposium speakers (clockwise from top left) Cathryn Nagler, Neil Surana, and June Round answer attendee questions moderated by session co-chair Thomas Kamradt.



AAI virtual exhibit booth at Virtual ECI 2021

- Xinxin Liu, M.D. (AAI '21), graduate student, Huazhong University of Science and Technology, China
- E. Ashley Moseman, Ph.D. (AAI '18), assistant professor, Duke University School of Medicine
- Angélica Olmo-Fontánez (AAI '21), graduate student, University of Texas Health Science Center at San Antonio
- Julie K. Olson, Ph.D. (AAI '06), associate professor, University of Minnesota
- Thomas Riffelmacher, Ph.D. (AAI '19), postdoctoral fellow, La Jolla Institute for Immunology
- Jordan Rixon (AAI '19), graduate student, University of California, Davis
- Dakota Rogers (AAI '21), graduate student, McGill University, Canada
- Crystal C. Walline, Ph.D. (AAI '17), assistant professor, University of North Carolina at Pembroke
- Yingying Wei, Ph.D. (AAI '19), graduate student, Tongji Hospital of Tongji Medical College, HUST, China
- Weihao Zheng, Ph.D. (AAI '21), postdoctoral fellow, University of California, San Francisco

AAI also joined fellow societies in hosting a virtual booth in the ECI exhibit hall. The AAI booth was part of an “Immunology Village” that included booths from EFIS, the International Union of Immunological Societies, German Society for Immunology, Austrian Society of Allergology and Immunology, British Society for Immunology, Turkish Society of Immunology, and more.

The 7th ECI will be held in Dublin, Ireland, in 2024.



Cathryn Nagler presents a talk on food allergies during the AAI-EFIS Joint Symposium at Virtual ECI 2021.

AAI Education Committee Highlight: Teaching Tools

In 2016, the AAI Education Committee initiated a new session focused on improving immunology education: the Immunology Teaching Interest Group (ITIG). The ITIG is an informal group comprised of past speakers and attendees of the ITIG sessions, including current immunology educators spanning a range of institutions and levels. It serves as a resource for novel teaching tools and practices that can be implemented in courses to enhance immunology education. The session has grown from an audience of 20 in 2016 to more than 100 participants in 2019 (the last time the session was held in person due to the cancellation of IMMUNOLOGY2020™). Because of the great interest in this topic, the AAI Newsletter features “Teaching Tools” articles highlighting ITIG presentations.

Employing Self-Paced, Feedback-Infused Learning to Facilitate Mastery of Basic and Clinical Immunology



Natalie C. Steinel, Ph.D. (AAI '19)
Assistant Professor
University of Massachusetts Lowell,
Lowell, MA



Michael Lee, Ph.D.
Associate Professor
Dell Medical School, University of
Texas at Austin, Austin, TX

For medical students, integration of basic immunology concepts with relatable clinical cases/diseases helps students understand the “why” behind clinical phenomena. An effective way to achieve this conceptual coherence is by designing learning activities that not only emphasize the causal aspects of the disease, but also test knowledge and provide feedback.¹ Providing timely feedback on assessments can lead to greater rates of knowledge acquisition, especially when the feedback appropriately accounts for the difficulty level of each question.² Learning activities that both integrate content and reinforce learning in this manner can also make the experience more engaging and the knowledge retention more durable, particularly if prior knowledge (i.e. from pre-reading or prior lectures) is reactivated.³

To promote conceptual coherence for first-year medical students, we designed self-learning modules (SLMs), which present clinical scenarios interspersed with assessments linked to relevant basic immunology learning objectives. For example, the topic of antibody effector functions and cross-reactivity is presented in the context of acute rheumatic fever, CD8⁺ T cell function in the context of chronic and acute viral infections, or immune checkpoints in the context of cancer immunotherapies. These SLMs were developed for Foundations of Disease

(FOD), a required 6-week transdisciplinary flipped course covering immunology, medical microbiology, microbial pharmacology, and infectious disease at the Dell Medical School, University of Texas at Austin.⁴ In FOD, SLMs were completed by small groups (five to seven students), with faculty facilitators present to assist as needed.

SLM cases can be delivered on paper, but purpose-built digital platforms such as kuraCloud or Smart Sparrow allow for the inclusion of A/V media (for example, a video of a clinical procedure or patient presentation) and a diverse array of assessment types beyond simple multiple-choice questions (for example, image annotation, matching, completing a table, graphing). SLMs can also be created and delivered using learning management systems like Canvas or Blackboard; however, available question types may be more limited. A major advantage of using digital platforms to present SLMs is the integration of immediate feedback for each assessment item, creating a mechanism for students to correct their mental model of a concept in real time. Students can reattempt missed questions and correct their responses, helping to reinforce critical concepts. Furthermore, with some digital platforms, adaptive algorithms can be used to tailor content to the abilities of the student(s), providing advanced content or remediation as needed.

Student evaluations indicated that SLMs were well received because the student group could set the pace of learning, as opposed to traditional cases presented by an instructor who set the pace for the entire class. Students appreciated immediate guidance if they had questions and said they benefited from the support of faculty facilitators. One issue raised by our medical students was whether SLMs could be moved to pre-class work rather than in class. The “portable” nature of these digital activities means they could easily be converted to an out-of-class/homework activity. It’s unclear if this shift would impact knowledge attainment, but it would certainly rob students of in-class faculty support and the opportunity for valuable teamwork/socialization skill building.

These exercises are an effective mechanism to promote conceptual coherence, not only for medical students, but for immunology students at all levels. The SLM design has also been successfully adapted for undergraduate and graduate immunology students, with cases centering on published articles instead of clinical scenarios.

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PLAN AHEAD FOR **IMMUNOLOGY2022™**

INFORMATION TO HELP YOU PLAN YOUR ATTENDANCE AT IMMUNOLOGY2022™

Mark your calendar—the AAI annual meeting is back as an in-person, onsite event! IMMUNOLOGY2022™ will be held May 6–10 in Portland, Oregon. The 105th AAI annual meeting will feature incredible science in this beautiful Pacific Northwest city.



Plan Ahead for IMMUNOLOGY2022™

Website

For the most up-to-date information, please visit www.immunology2022.org to explore the scientific program, abstract submission and abstract-driven sessions, career advancement sessions and events, travel awards, social events, registration, discounted hotel accommodations, visiting Portland, and more. You can also download, print, email, and share the *IMMUNOLOGY2022™ Call for Abstracts*.

Dates and Location

IMMUNOLOGY2022™ will be held May 6–10, 2022, at the Oregon Convention Center in Portland. Temperatures in May average 66 degrees for highs and 44 for lows, offering visitors beautiful spring days to stroll through the city's many gardens.

For information on sights to see, things to do, and places to dine, visit www.travelportland.com.

Other important dates:

December 6, 2021

Registration Opens

December 20, 2021

Abstract Submission (*opened November 2*) Closes
Travel Award and Grant Applications Due

March 29, 2022

Early Registration Discount Ends

April 3–14, 2022

Discounted Hotel Rates End (*date varies by hotel*)

Scientific Program

The President's Address by AAI President Gary A. Koretzky, M.D., Ph.D. (AAI '92), officially starts the meeting on Friday evening, May 6. Dr. Koretzky's talk is entitled "Immunology: Building on the Past to Meet the Moment." The 2022 AAI Lifetime Achievement Award will be presented during this event.

On Day 4 of the meeting (Monday), Koretzky will chair the President's Symposium, "From Fundamental Investigation to Revolutions in Health Care: Stories of Immunological Discovery." This session will feature leaders in the field, including Arthur Weiss, M.D., Ph.D., DFAAI (AAI '81), Carl H. June, M.D., DFAAI (AAI '87), M. Virginia Pascual, M.D. (AAI '09), and Raphaela T. Goldbach-Mansky, M.D., M.H.S. (AAI '16). The 2022 AAI Excellence in Mentoring Award will also be presented during this event.

Each full day of the meeting concludes with a Distinguished Lecture presented by one of three outstanding scientists: Robert D. Schreiber, Ph.D., DFAAI (AAI '76), Katherine A. Fitzgerald, Ph.D. (AAI '06), and Yasmine Belkaid, Ph.D. (AAI '13). Eight Major Symposia, each featuring five to six speakers, will address topics of immediate interest. Sessions organized by NIH institutes/centers, guest societies from around the

world representing multiple subdisciplines, and many AAI committees will present intriguing research. This dynamic lineup of exciting science and more can be viewed at www.immunology2022.org.

Abstracts

The most interactive part of any scientific meeting is the presentation of unpublished data in the form of abstracts. Select abstracts will be presented in podium presentations (Block Symposia), and all abstracts will be featured in Poster Sessions in the Exhibit Hall. *Poster Sessions will be scheduled daily during dedicated time, unopposed by any other sessions.*

Abstract submission opened on November 2, 2021, and will close December 20, 2021. To submit an abstract, visit www.immunology2022.org/abstracts.

Abstract topic categories include:

- Antigen Processing and Presentation
- Basic Autoimmunity
- Cellular Adhesion, Migration, and Inflammation
- Cytokines and Chemokines and their Receptors
- Hematopoiesis and Immune System Development
- Immediate Hypersensitivity, Asthma, and Allergic Responses
- Immune Mechanisms of Human Disease
- Immune Response Regulation: Cellular Mechanisms
- Immune Response Regulation: Molecular Mechanisms
- Immunology Education
- Innate Immune Responses and Host Defense: Cellular Mechanisms
- Innate Immune Responses and Host Defense: Molecular Mechanisms
- Lymphocyte Differentiation and Peripheral Maintenance
- Microbial, Parasitic, and Fungal Immunology
- Mucosal and Regional Immunology
- Technological Innovations in Immunology
- Therapeutic Approaches to Autoimmunity
- Transplantation Immunology
- Tumor Immunology
- Vaccines and Immunotherapy
- Veterinary and Comparative Immunology
- Viral Immunology

Career Development

In addition to the latest scientific advances in the field, IMMUNOLOGY2022™ will offer professional development sessions for scientists at every career stage. Two perennially popular sessions are the *Careers in Science Lecture and Roundtables* (sponsored by the AAI Education Committee and the Committee on the Status of Women) and the *Careers Roundtables and Speed Networking Session* (sponsored by the AAI Minority Affairs Committee). These interactive sessions feature experienced scientists ready to answer your career questions and lead discussions on many career-oriented

topics. These are ticketed events; you will be able to purchase tickets during the online registration process.

The AAI Education Committee will sponsor two popular sessions: *Careers in Biotech*, a panel discussion with networking afterward, and the *Immunology Teaching Interest Group*, which will focus on strategies to improve the teaching of immunology.

Other sessions and resources include:

- *How to Convert Your CV into a Résumé*
- *Chalking Up Success: The All-Important Chalk Talk and Preparing for a Faculty Interview*
- *Interviewing for a Job*
- *How to Have a Successful Postdoctoral Experience*
- *NIH Grants Workshop*
- Jobs Board (for employers and job hunters)

Travel Awards

Travel award and grant applications opened November 2, 2021, and will close December 20, 2021. The following awards assist successful applicants with travel support to attend the meeting:

- Lefrançois-BioLegend Award
- Chambers-Thermo Fisher Scientific Award
- Lustgarten-Thermo Fisher Scientific Award
- Pfizer-Showell Travel Award
- AAI Undergraduate Faculty Travel Grant
- AAI Early Career Faculty Travel Grant
- AAI Laboratory Travel Grant
- AAI Trainee Abstract Award
- AAI Trainee Poster Award
- AAI-Thermo Fisher Trainee Achievement Award
- AAI Minority Scientist Travel Award

You can learn about the details of each of these awards by visiting www.immunology2022.org/awards.

Registration and Housing

Registration opened December 6, 2021. To register now, and access the early bird rates, go to www.immunology2022.org/register.

Make your hotel reservations now to take advantage of specially discounted hotel rates for meeting attendees. Rooms are booked on a first-come, first-served basis. To get the best price and selection, reserve your room early: www.immunology2022.org/meeting-hotels/.

Exhibit Hall

The Exhibit Hall at IMMUNOLOGY2022™ will bring attendees and exhibitors together for three days of exhibit displays,

poster presentations, networking opportunities, and Exhibitor Workshops hosted by exhibiting companies.

Attendees can assess products, services, and technologies designed to support and advance their research. It is estimated that over 150 companies will exhibit.

Attendees participating in the “**Passport to Prizes Raffle**” will be entered to win American Express gift cards.

Social Events

Social events at the AAI annual meetings are always the ideal occasion to reunite with old friends and meet new colleagues. Immediately following the **President’s Address on Friday, May 6**, attendees will gather for the opening night **Welcome Back Reception**, which will feature a lineup of Portland’s world-famous food trucks just outside the Convention Center, featuring cuisines for every taste. Reunite with friends, make new acquaintances, and plan your week. One complimentary drink ticket is included in your registration. Delicious and different! *Registered attendees only. Attendees of this event must be 21 years of age or older.*

On Monday, May 9, the IMMUNOLOGY2022™ Gala will be held at the Portland Art Museum (www.portlandartmuseum.org), which features outstanding exhibits ranging from modern trends to historic art periods. Take part in interactive exhibits, view films, or gaze at classic pieces. The museum shop will also be open. Uniquely, the Portland Art Museum recognizes and honors the Indigenous communities—past, present, and future—of the region on whose ancestral lands it stands. Attendees will have access to the full museum. Food and drinks will be available, and as is the Gala’s tradition, you will have the opportunity to express yourself on the Grand Ballroom dance floor! Tickets will be available for purchase during the registration process. *Attendees of this event must be 21 years of age or older.*

COVID-19 Policy

Immunizations

For the health and safety of meeting participants, all registrants and staff will be required to provide proof of being fully vaccinated against SARS-CoV2 (COVID-19). This proof will be requested after you have registered for the meeting.

Masks

Mask and social distancing requirements will comply with the requirements of the Oregon Convention Center, the city of Portland, Multnomah County, and the state of Oregon.

More information regarding safety precautions will be available on the IMMUNOLOGY2022™ website at www.immunology2022.org/register/.

BACTERIA EATERS: The “Twort-d’Hérelle Phenomenon”

Electron micrograph of bacteriophages attached to bacterium
Graham Beards

Two decades after diphtheria antitoxin became a clinical success at the end of the 19th century, greatly reducing death from the disease, especially among young children, a new phenomenon with claims of vast therapeutic potential against bacterial infections burst onto the scene. The “Twort-d’Hérelle Phenomenon,” also known as “transmissible lysis of bacteria,” was named after its two co-discoverers: Frederick William Twort and Félix Hubert d’Hérelle. We know it now as bacteriophage.

The Discoveries of Bacteriophage

In 1915 Twort, a British physician and microbiologist, published a paper in the *Lancet* describing a “glassy and transparent” transformation on agar plates where bacteria would not grow even when subcultured. He was able to take samples from the glassy area of the colony and replicate results over multiple generations of micrococcus, demonstrating that the agent was transmissible. These



Frederick Twort, c. 1914
Obituary Notices of Fellows of the Royal Society

samples remained lethal to bacterial cultures even after passing through a fine porcelain filter that would trap bacteria. Further, Twort concluded that the substance required bacteria for growth.¹ He postulated that the micrococcus itself might be secreting an enzyme able to pass through a filter that both caused lysis and stimulated further enzyme production, and that this transmission

“might almost be considered as an acute infectious disease of micrococci.”² Before Twort could conduct further experiments, however, the First World War interrupted his career. As the paper was about to go to press, he joined the Royal Army Medical Corps and was shipped out to Greece. Following the war, Twort moved “on to other work.”³

In 1917, independent of Twort’s research, d’Hérelle, a French-Canadian microbiologist researching enteric bacteria of dysentery patients at the Pasteur Institute, published a short paper in *Comptes rendus de l’Académie des Sciences* describing the lysing of bacteria over multiple propagations.⁴ He named this “invisible microbe that is antagonistic to the dysentery bacillus” the bacteriophage (a bacteria-eater, from the Greek *phagein* meaning “to devour”). D’Hérelle concluded his paper with a few observations: that the bacteriophage is a “microbe of immunity;” it has specificity; and there is a real potential to treat bacterial infections with phage therapy.⁵

D’Hérelle would publish a few more short bacteriophage papers in *Comptes rendus* before publishing his first book *Le Bactériophage: son rôle dans l’immunité* (*The Bacteriophage: Its Role in Immunity*) in 1921. It was this book, and the English translation by Yale University bacteriologist and immunologist George H. Smith (AAI 1918), published by Williams and Wilkins in 1922, that popularized bacteriophage therapy.⁶

The Dominant Theories of Immunity

To understand d’Hérelle’s use of the word “immunity” in his first paper and in the title of his book, it would help to first consider the competing theories of immunity at the time and how the bacteriophage aligned or conflicted with them.



Félix d’Hérelle
Smithsonian Institution Archives

In the late 19th and early 20th centuries, the term immunity was frequently used to describe resistance to “natural” infections, whereas immunity acquired through vaccination was considered something different. And for researchers at the time, “it was not at all clear that ‘natural’ immunity and ‘acquired’ immunity were mechanistically related.”⁷ Further, there were two divergent

theories attempting to explain natural immunity: cellular, associated with Élie Metchnikoff; and humoral, associated with Paul Ehrlich.⁸

Metchnikoff observed that when starfish larvae were punctured with a splinter, cells moved toward the injury and began to engulf foreign bodies. This led him to hypothesize that organisms had specialized cells that were able to defend against intruders. These cells that could identify, engulf, and kill foreign microorganisms were soon named “phagocytes.” In subsequent studies, Metchnikoff was able to observe that phagocytes have specificity as to which foreign organisms they attacked.⁹

Ehrlich’s research about immunity was focused on how animals could acquire immunity against a disease through prior infection or vaccination—vaccines for smallpox and rabies were the only effective ones for humans at the time. It was known that human blood in *in vitro* experiments could agglutinate bacteria as well as a variety of “toxins,” like the one produced by diphtheria. To make sense of what was occurring *in vivo*, Ehrlich

hypothesized, using chemistry terminology, that there were substances (perhaps proteins) in the blood that could act on a specific bacteria or toxin resulting in either “agglutination” (bacteria or other microscopic objects) or “flocculation” (toxins and soluble other substances). He later expanded this theory, once again using chemistry terminology, to try to describe the specificity of the agglutination and flocculation reactions. His addendum that the blood substances were composed of “core” and “side-chains” found some adherents, but subsequent research proved that the complexity of immune cells and substances could not be analogized easily to chemistry concepts.¹⁰

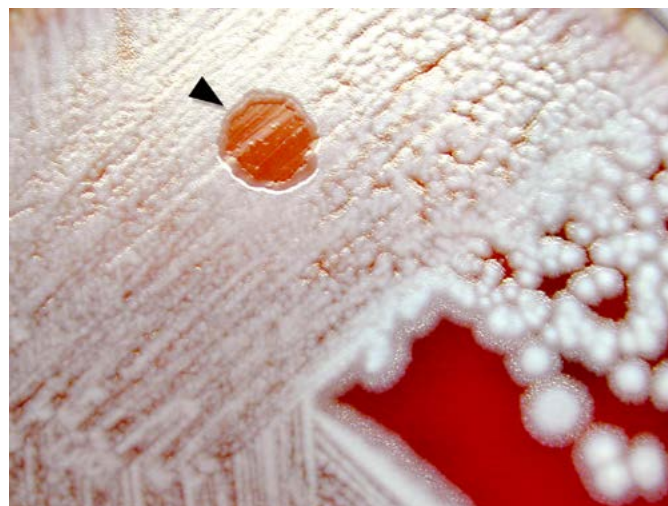
For their theories on the immune system, Metchnikoff and Ehrlich shared the Nobel Prize in Physiology or Medicine in 1908 “in recognition of their work on immunity.” Though both had adherents, in the late 19th century Ehrlich’s humoral theory was put into clinical practice by Émile Roux and Emil von Behring, who created the first successful diphtheria antitoxins and pushed the limits of serum therapy, which was a method to passively immunize humans and animals against specific diseases.¹¹ (See “Hero Horses in the Fight Against Disease,” *AAI Newsletter* October 2021, for more information.) The clinical success of the diphtheria antitoxin raised the stature of Ehrlich’s theory as well as the potential for successfully curing, or even providing acquired immunity, against other bacterial infections.

Bacteriophage Theory

D’Hérelle, however, found that neither the humoral nor cellular theory of immunity fit his experimental observations using bacteriophages as a curative treatment. In experiments

with chickens and humans, d’Hérelle provided results that showed bacteriophage therapy (also called bacteriophagy) could be successful in cases where the specific bacteria were known and the corresponding bacteriophage was provided to the subject. As a result, he proposed a new theory for immunity based on the bacteriophage.

According to historian of science William Summers, d’Hérelle understood “that in natural immunity (as opposed to the ‘artificial’ situation of experimentally induced infections), man and animals resisted and eventually recovered from disease



Petri dish showing where phage suspension has lysed bacteria culture
CDC



Élie Metchnikoff, 1913
Gallica Digital Library

because of the appearance of phages which destroyed the infecting bacteria.”¹² The evidence d’Hérelle used to support this understanding came from a dysentery study where patients recovering from their infection after the administration of a bacteriophage suspension specific to the bacterium responsible for their infection showed a remarkable increase of the titer of phage in their stool.

A two-phase mechanism for immunity by bacteriophage was described in more detail by d’Hérelle in *The Bacteriophage*. After the specific bacterium responsible for the infection was identified, a bacteriophage specific to that bacterium was put into a suspension, which was then administered to the patient. The first phase, “exogenous immunity,” lasted 24 to 48 hours and was marked by the presence of “bacteriophage protobes virulent to the pathogenic bacterium.” The second phase, “endogenous immunity,” could last up to 14 months and was a response to a “stimulus being provided by the products of bacterial dissolution as contained in the bacteriophage suspension.” During an epidemic, the exogenous phase is maintained because the near constant reinfections maintain the bacteriophages.¹³

For d’Hérelle, the bacteriophage, not a cellular or humoral response, was responsible for immunity, and by 1926 he was certain that bacteriophagy could be used to successfully treat bacillary dysentery, staphylococcus infections, and, potentially, bubonic plague.

Jules Bordet



Jules Bordet, nd.
National Library of Medicine

A major problem for this theory was presented by Jules Bordet (AAI 1960). In the interim between d’Hérelle’s first bacteriophage article and the publication of *The Bacteriophage*, Bordet was awarded the 1919 Nobel Prize in Physiology or Medicine “for his discoveries relating to immunity.” The director of the Pasteur Institute in Brussels, Bordet had spent decades researching

and describing the lysis process in vitro and in vivo. These included the discovery of complement, the development of complement fixation tests, the identification of the bacterium that causes whooping cough, and advances in understanding the bacteriolytic and hemolytic effects in vivo.

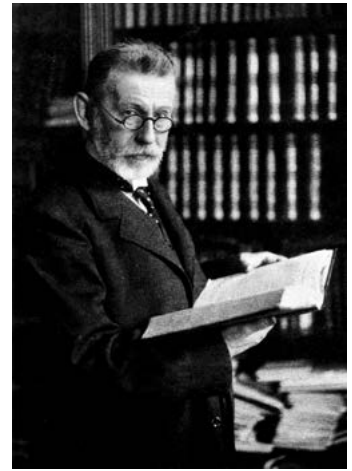
Lacking sufficient magnification to see the bacteriophage, researchers could only understand it by observing its effects, fueling intense debate about what exactly the bacteriophage was—a lysing enzyme (Bordet) or a “microbe of immunity,” perhaps a virus (d’Hérelle)—and how it fit into the competing theories of immunity. As strange as it may seem today, Bordet’s concept of the bacteriophage as a “self-perpetuating lytic enzyme” fit neatly into the humoral theory and serum therapy and carried the prestige of a recent Nobel laureate.¹⁴ It would remain the dominant theory until advances in electron microscope magnification in the late 1930s.

Proliferation of Bacteriophage

The controversy surrounding the bacteriophage did not prevent the proliferation of corresponding research and clinical therapies. The success of diphtheria antitoxin provided a lesson in combatting bacterial disease with a humoral-based serum therapy. The hope was that the new phenomenon would pave the way for additional serum therapies for other bacterial infections in humans and animals.

While the vast majority of the early research with bacteriophages occurred in Europe (most notably in Paris, Brussels, and London), American researchers began publishing on the topic by the early 1920s, even prior to the translation of *The Bacteriophage*.

The first American institution to take bacteriophage seriously as a research topic was the Department of Bacteriology at the University of Michigan, chaired by Frederick G. Novy (AAI 1920, president 1924–25). Novy, who received his first shipment of bacteriophages from d’Hérelle in 1921, collaborated on this research with younger investigators in his department, including Paul de Kruif (AAI 1921) and Philip Hadley (AAI 1927).¹⁵ Hadley would go on to make significant contributions to bacteriophage research in the 1920s and 1930s. De Kruif left Michigan a year later for a position at the Rockefeller Institute for Medical Research (RIMR). He drew on his experiences with his mentors at both institutions when he collaborated with Sinclair Lewis on the best-selling novel



Paul Ehrlich
National Library of Medicine

HISTORY

Arrowsmith.¹⁶ (See “Paul de Kruif and Microbe Hunters,” *AAI Newsletter* January/February 2019, for more information.)

At RIMR, de Kruif shared a laboratory with André Gratia, a Belgian microbiologist who came to the institute in 1920 to study bacteriophages. Gratia soon published papers on his discovery of a bacteriophage capable of infecting staphylococcus and *E. coli*.¹⁷ Gratia returned to Belgium in 1921 but had left an indelible mark on de Kruif. Gratia's research was mirrored by that of the protagonist Martin Arrowsmith—both were pioneers in phage research and both discovered phages that would lyse staphylococcus.¹⁸

Bacteriophage research would continue at RIMR and get a boost with the arrival of Jacques J. Bronfenbrenner (AAI 1920, president 1942–46) in 1923. Bronfenbrenner began a decades-long study of bacteriophages to explain their physical properties and understand and control their lysis. (Five years later, Bronfenbrenner accepted an appointment as chair of the Department of Bacteriology and Immunology at the Washington University School of Medicine in St. Louis and continued his phage research.)

1920s and AAI

Already widely investigated in Europe by the mid-1920s, bacteriophage research was sprouting up in laboratories beyond Ann Arbor and New York City. A survey of articles published in *The Journal of Immunology (The JI)* in the 1920s reveals phage research programs at Loyola University School of Medicine (Chicago), Baylor University, Yale University School of Medicine, and Stanford University. Compared to similar journals, such as the *Journal of Experimental Medicine*, *The JI* seems to have taken a cautious approach to publishing bacteriophage research, with a mere eight papers published during the decade. Likewise, it was not a topic featured prominently at the American Association of Immunologists (AAI) annual meetings; only two speakers on the subject presented their research: Emil Weiss (AAI 1928), “The Bacteriophage Anti-bacteriophage Reaction,” in 1927; and D. M. Cowie and Henry G. Poncher, “Observations on the Intestinal Bacteriophage in the Specific Infectious Diseases,” in 1928.¹⁹

1930s

The pace of phage research and phage therapy trials continued to accelerate well into the 1930s, but signs of problems with bacteriophage therapies were becoming more evident. Although bacteriophage therapy was “being widely used for many types of bacterial infection,” at the time, there were neither clear guidelines for clinical trials—the familiar control groups and double-blind studies were decades in the future—nor for the standardization of materials and methods.²⁰ Considering the fact that scientists continued to debate whether bacteriophages were enzymes or viruses,²¹ it is understandable that the clinical studies were unable to generate accurate data on dosage, safety, and efficacy.

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Advertisement of bacteriophages
National Library of Medicine

D'Hérelle emphasized that the crucial step in successful bacteriophagy was matching phage strain to the specific bacterial infection. This process, however, was both time consuming and labor intensive for individual clinical cases and exacerbated by the paucity of readily available phage strains. In an attempt to remedy part of this problem, pharmaceutical companies, including Eli Lilly & Co., E. R. Squibb & Sons, and Swan-Myers (a division of Abbott Laboratories), were “manufacturing bacteriophage and offering it to the medical profession.” A *Journal of the American Medical Association (JAMA)* review of the Lilly, Squibb, and Swan-Myers phage preparations demonstrated the lack of standards—including the amount of preservatives or lack thereof, virulence, and mixture of different phage strains—and marked a further move away from d'Hérelle's ideal bacteriophagy.²²

AMA Phage Report

Criticism of the purported successes of bacteriophagy increased in the early 1930s with titles such as “Limitations of Bacteriophage Therapy” appearing in journals.²³ At this time, the American Medical Association (AMA) Council of Pharmacy and Chemistry, founded in 1905 to advocate for clinical experimentation and evaluate the “chemical identity and efficacy of drugs in humans,” began a review of bacteriophagy in scholarly literature.²⁴ The first report was published in 1934, authored by two Yale University professors: immunologist and bacteriologist Stanhope Bayne-Jones (AAI 1917, president 1930–31) and infectious disease specialist Monroe Eaton (AAI 1937).

The report, “Bacteriophage Therapy: Review of the Principles and Results of the Use of Bacteriophage in the Treatment of Infections,” was published across three issues of *JAMA* in December 1934.²⁵ In the report, the demonstrable ability of bacteriophage to lyse bacteria *in vitro* was recognized, but those results did not carry over into *in vivo* studies.

The authors reached the conclusions that “lytic action in the body is inhibited or greatly impeded by blood and other body fluids”; that the “therapeutic action” of the components mixed with the phage before injection needs additional study; that the literature “reveals that the evidence for the therapeutic value of lytic filtrates is for the most part contradictory”; and that “there is no evidence that lysis or killing of bacteria by bacteriophage occurs *in vivo*.”²⁶

Of particular interest is an additional conclusion reached by the authors: to accept that the “facts appear to indicate” bacteriophage is “inanimate, possibly an enzyme,” though they do leave the door open that it could be a virus. Bordet publicly tried to keep that door closed, stating during the prestigious Croonian Lecture in 1930 that the “invisible virus of d’Hérelle does not exist.” It is the bacteria themselves, subjected to the lysis, which reproduce the lytic principle. Bacteriophagy is accordingly a case of autolysis.²⁷ The Bordet theory about the nature of the bacteriophage remained dominant in the American scientific community.²⁸

The conclusions of the report, however, did not stop bacteriophage research and publication of results—better studies might be more successful. Indeed, phage research continued to spread, with new adherents

like F. Macfarlane Burnet (AAI 1961), a young Australian researcher in England who would decades later win the Nobel Prize in Physiology or Medicine for discovering “acquired immunological tolerance.” While his phage research did not spawn breakthroughs in therapy, it did give Burnet insight into specificity, mutation, and resistance.²⁹

1930s and AAI

In the 1930s, *The JI* continued its conservative publication of articles related to bacteriophage research with only seven papers. One of these, however, directly challenged some of the conclusions of the AMA report. In their 1935 article “The Adaptation of a Staphylococcus Bacteriophage to an Artificially Produced Anti-Bacteriophagic Serum,” d’Hérelle and Morris L. Rakietsen, who conducted bacteriophage research together at Yale University, disputed the claim that *in vitro* bacteriophage was uniformly diminished by human serum and showed instead that some strains of bacteriophage were able to maintain lysis successfully in the presence of serum.³⁰

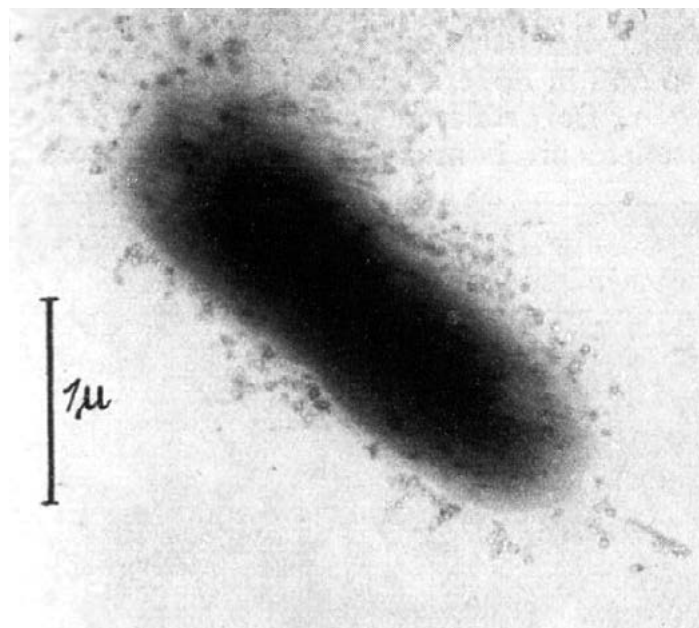
The AAI annual meetings at this time had a dearth of bacteriophage research with only two talks on the topic: Frances C. Frisbee and Ward J. MacNeal, “Therapeutic Application of Bacteriophage in Staphylococcus Bacteremia,” in 1932; and Philip Levine (AAI 1925) and Arthur W. Frisch (AAI 1938), “The Specificity of Multiplication of Bacteriophage,” in 1935.³¹

The Decline of Phage Therapy

The issues of bacteriophagy outlined in the Bayne-Jones and Eaton *JAMA* report were clearly not insurmountable to the dedicated phage researcher, despite failure to demonstrate a successful therapy. What eventually moved the field away from phage research was the advent, expansion, and demonstrable

success of sulfa drugs in the 1930s. Prontosil, patented in 1932, was cheaper and easier to produce and was effective against a wider variety of bacterial infections than bacteriophage therapy. Its success spawned a rush to put new sulfa drugs (and other antimicrobial chemotherapies) on the market.

In 1939, with Europe once again engulfed in a world war, non-war research ground to a halt. The United States would enter the war two years later, and scientific research likewise was quickly refocused to the war effort.



First electron micrograph of a bacteriophage
Naturwissenschaften

In pre-war Germany, the electron microscope was developed and, before the war broke out, achieved sufficient magnification to capture the first images of viruses. When a bacteriophage sample was placed in the microscope in 1939, the picture that developed vindicated d'Hérelle—the bacteriophage was a virus. The image was published in a German scientific journal the following year. Due to the war, however, it would be a few years more before the debate was put to rest.

Bacteriophage therapy research did not end in the 1930s. It continued into the 1940s in the United States and Europe, only to finally be shelved in the archive following the discovery and development of antibiotics. D'Hérelle did continue his research in Ukraine, where, after the war, the Soviet Union had a national program dedicated to phage therapy.³²

Experience with bacteriophages altered the career trajectories of some researchers, including a young Alfred Hershey (AAI 1942) under the mentorship of Bronfenbrenner at Washington University. The lessons learned from studying the bacteriophage helped usher in a new field of biology following the war: molecular biology.

The JI and talks at the annual meetings told a different story for AAI. Evidence points to a conservative approach to bacteriophage research. Whether reflecting the fact that bacteriophages themselves were still not fully understood or that fundamentals of the immunological response to bacterial infections were still in dispute, it seems a cautious approach in the literature and at meetings proved a successful tack for the association and the field.

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- 17 Gratia, 471–2.
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Material Culture of Immunology: “Jeryl Lynn Mumps Virus Cannister”

This series highlights objects in museums connected to the history of immunology. Material culture consists of the physical objects that help us understand cultural and social relations. These artifacts illustrate the role of immunology throughout history.

This unassuming stainless-steel canister played a crucial role in saving millions upon millions of children from the effects of mumps. It was one of five vessels that held the seed stock



Seed stock cannister for Jeryl Lynn Strain
National Museum of American History

for the Jeryl Lynn strain of mumps virus used to produce over three billion doses of vaccine.

The Jeryl Lynn strain was named after the daughter of Maurice Hilleman¹ (AAI 1949), a microbiologist and immunologist who had previously developed a vaccine for Japanese B encephalitis during the Second World War. Hilleman also discovered antigenic shift and drift in influenza and developed a vaccine that help prevent a serious flu pandemic in 1957.

Five-year-old Jeryl Lynn woke her father up at 1:00 a.m. on March 23, 1963, complaining of swelling and pain in her throat. Hilleman quickly diagnosed mumps, then drove to his laboratory at Merck to retrieve cotton swabs and nutrient broth. He took these supplies home, swabbed Jeryl Lynn's throat, and returned the sample to his lab.²

Hilleman attenuated the mumps virus by repeatedly passing it through chicken embryo cells. In 1966, one of the first children to receive a dose of the experimental vaccine was Jeryl Lynn's own sister, Kirsten.

Later, the seed stock for the Jeryl Lynn strain was placed in five 15-liter cannisters for safe storage. By 2015, however, the green neoprene stoppers had started to fail. Merck scientists

had to carefully transfer the seed stock to new containers without contaminating it. Failure could have resulted in a global shortage of mumps vaccine while new seed stock was produced, a process that would have taken up to seven years.³

The transfer was successful, the vaccine supply was uninterrupted, and in 2017, the Hilleman family donated this cannister along with other artifacts from Hilleman's life, including his lab coat and several of his many vaccines, to the Smithsonian.

Over his long career, Hilleman was responsible for developing over 40 vaccines, including eight of the current standard childhood vaccinations. His vaccines continue to save millions of lives every year.⁴

Maurice Hilleman's cannister, lab coat, and vaccines are held in the Division of Medicine and Science at the Smithsonian National Museum of American History.

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Vials of investigational live mumps vaccine (Jeryl Lynn Strain)
National Museum of American History

AAI Grants and Awards 2021

December 20

AAI Travel Awards to IMMUNOLOGY2022™, Portland, OR

- **Prize/Award:** Awards in 11 categories recognizing the promise and bolstering the professional development of investigators of all career stages through support for travel to the AAI annual meeting
- **Eligibility:** AAI members in good standing who meet specific conditions for each award (see program details at link below)
- **Details:** www.aai.org/Awards/Travel
- **Contact:** (301) 634-7178; awards@aai.org

2022

January 20

AAI Public Policy Fellows Program

- **Prize/Award:** Up to 10 year-long fellowships through which participants explore how federal legislative action and agency activities impact the conduct and funding of biomedical research and how AAI works with, and on behalf of, AAI members for the best possible outcome; participants travel to Washington, DC, for a two-day program on Capitol Hill and participate in AAI public affairs activities at the AAI annual meeting
- **Eligibility:** Early career AAI member researchers who are within 15 years of having received their terminal degree and are committed to a career in biomedical research and to learning about and participating in the public policy and legislative activities of AAI
- **Details:** www.aai.org/PPFP
- **Contact:** jschumacher@aai.org

February 15

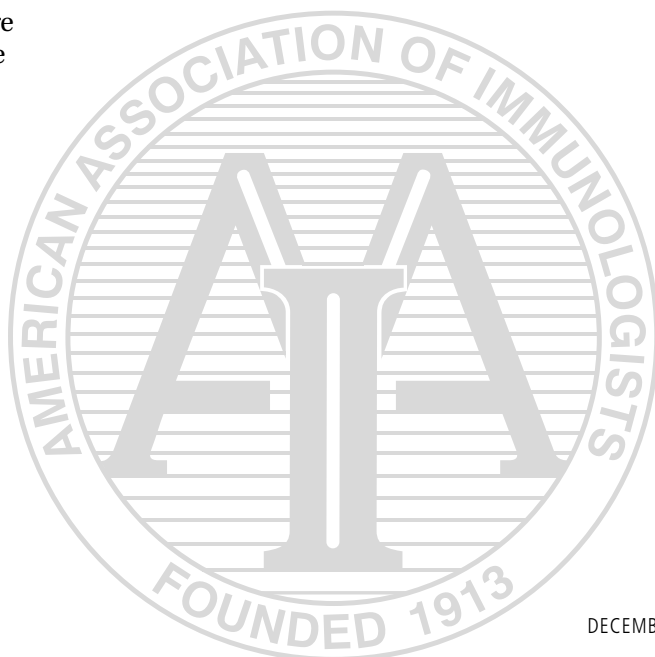
AAI Travel for Techniques Awards

- **Prize/Award:** Multiple awards providing up to \$1,500 each in reimbursement of travel expenses for a visit to another laboratory, specifically to learn a technique beneficial to the award applicant's research
- **Eligibility:** AAI regular and associate member scientists with independent research programs; awarded travel may be that of the applicant, applicant's trainee, or applicant's lab member (traveler must be an AAI member); award selection is based on relevance of the technique to the applicant's program and on financial need
- **Details:** www.aai.org/TravelforTechniques
- **Contact:** (301) 634-7178; awards@aai.org

March 15

AAI Careers in Immunology Fellowships

- **Prize/Award:** Multiple awards in support of the laboratories of AAI member principal investigators (PIs), each providing one year's salary for a graduate student or postdoctoral fellow working in the PI's lab
- **Eligibility:** Any AAI member principal investigator with less than \$350,000 (excluding PI salary) in annual direct costs funding who seeks salary support for an AAI member trainee working in the PI's lab
- **Details:** www.aai.org/CIFP
- **Contact:** fellowships@aai.org



March 15

AAI High School Teachers Summer Research Program in Immunology

- **Prize/Award:** Multiple awards providing high school science teachers with the opportunity to participate in a four- to six-week, hands-on summer research experience in the lab of an AAI member; program provides stipend, assistance from an educational consultant in developing an innovative classroom curriculum to be published by AAI on the program website, support to attend a national professional meeting to present program experiences, and support to attend the three-day AAI Introductory Course in Immunology, Part I, to learn the basic principles of the discipline
- **Eligibility:** High school teachers seeking creative ways to bring the excitement of cutting-edge research and discovery to their classrooms while developing their ability to cultivate the next generation of talented biomedical investigators and enhance public understanding of the critical nexus between basic research and human health
- **Details:** www.aai.org/HSTProgram
- **Contact:** (301) 634-7826; infoaai@aai.org

Non-AAI Grants and Awards

Visit the AAI website at www.aai.org/GrantsAwardsDeadlines for links to non-AAI grant and award program listings and deadlines.

Connect with AAI!

Want to hear the latest from The American Association of Immunologists? You can find AAI and its journals, *The Journal of Immunology* and *ImmunoHorizons*, through your favorite social media channels:



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If you'd like to join the AAI email list, please email infoaai@aai.org.

MEETINGS AND EVENTS

Mark Your Calendar for These Important Dates!

Dear readers, please note that the meetings listed on these pages were still scheduled at press time, but due to the global COVID-19 pandemic, cancellations may occur. Please check an individual meeting's website to confirm that it is still scheduled.

2021

VIRTUAL MEETINGS

December 15

B Cells in Cancer Consortium (BC3)

Free Virtual Seminar Series

Each seminar features three presentations from experts in the field.

<https://bit.ly/3zYlmma>

2022

ON-SITE MEETINGS

January 22–25

60th Midwinter Conference of Immunologists

Asilomar Conference Grounds, Pacific Grove, CA
www.midwconfimmunol.org/

February 19–23

BPS2022, 66th Biophysical Society Annual Meeting

San Francisco, CA
www.biophysics.org/2022meeting

May 6–10

IMMUNOLOGY2022™

AAI Annual Meeting

Oregon Convention Center, Portland, OR
www.immunology2022.org



May 14–17

NK2022, 19th Meeting of the Society for Natural Immunity (SNI)

Hyatt Coconut Point, Bonita Springs, FL
www.nk2022.org/

June 10–13

Autoimmunity 2022: 13th International Congress on Autoimmunity

Athens, Greece

<https://autoimmunity2022.kenes.com/>

September 20–23

Special Joint Meeting:

Cytokines 2022 Hybrid and ILC4 2022

Hilton Waikoloa Village, Big Island, HI

Cytokines 2022 Hybrid: 10th Annual Meeting of the International Cytokine and Interferon Society (ICIS)

<https://hawaii.cytokinesociety.org/>

4th International Conference on Innate Lymphoid Cells (ILC4 2022)

www.ilc2020.org

October 26–29

SLB 2022, the 55th Annual Meeting of the Society for Leukocyte Biology: Leukocytes on the Wave for Translating Medicine

Hilton Waikoloa, Hawai'i

www.leukocytebiology.org/meetings

2023

ON-SITE MEETINGS

May 11–15

IMMUNOLOGY2023™

AAI Annual Meeting

Walter E. Washington Convention Center, Washington, DC

www.aai.org/FutureMeetings



Fall 2023 (Exact Dates TBD)

17th International Workshop on Langerhans Cells and Related Myeloid Cells of the Skin

Jerusalem, Israel

www.lc2021.org

November 27–December 2

IUIS 2023: 18th International Congress of Immunology

Cape Town, South Africa

<https://iuis2023.org/>

2024

ON-SITE MEETINGS

May 3–7

IMMUNOLOGY2024™

AAI Annual Meeting

Phoenix Convention Center, Phoenix, AZ

www.aai.org/FutureMeetings



Coming in the January 15, 2022 issue of

The Journal of Immunology

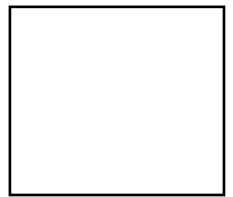
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Future AAI Annual Meetings

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2022



IMMUNOLOGY2022™

May 6 – 10
Portland, Oregon

2023



IMMUNOLOGY2023™

May 11 – 15
Washington, DC

2024



IMMUNOLOGY2024™

May 3 – 7
Phoenix, Arizona