



AAI

The American Association of Immunologists

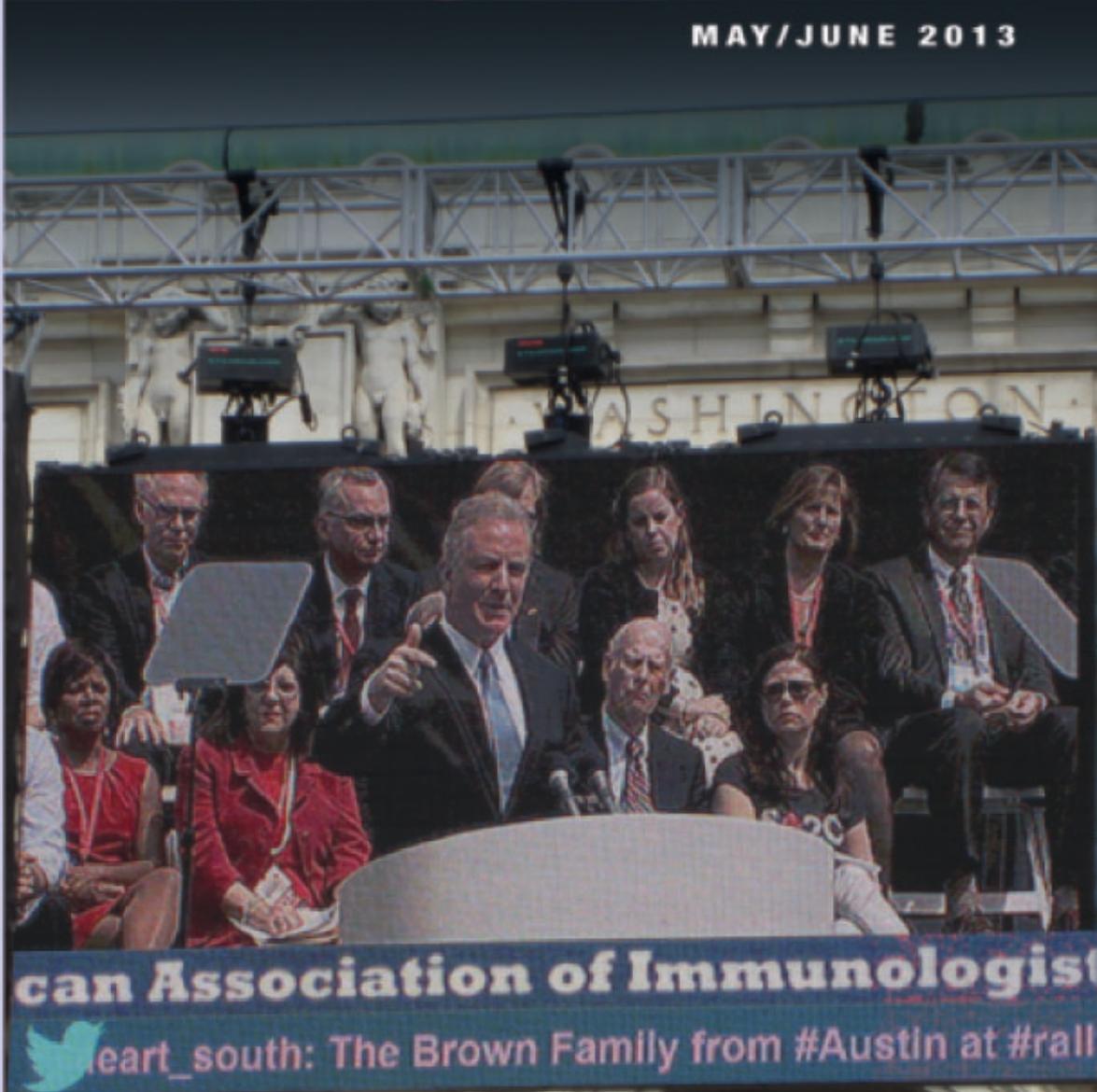
NEWSLETTER

MAY/JUNE 2013

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Cover photo: J. Schumacher



AAI supports AACR “Rally for Medical Research”

Projected on jumbotron at recent Rally for Medical Research in Washington, Rep. Chris Van Hollen (D-MD) addresses attendees. **See page 7**



2013 Introductory Course in Immunology

July 13–18, 2013 • The University of Pennsylvania, Philadelphia, Pennsylvania

Director: Michael P. Cancro, Ph.D., *University of Pennsylvania, Perelman School of Medicine*

Co-Director: Christopher A. Hunter, Ph.D., *University of Pennsylvania School of Veterinary Medicine*

Don't miss the most comprehensive introduction to immunology available!

This intensive two-part course, taught by world-renowned immunologists, provides a comprehensive overview of the basics of immunology. This course is for students new to the discipline or those seeking more information to complement general biology or science training. **Part I (July 13–15)** is a detailed introduction to the basic principles of immunology and is suitable for students with a general biology background. **Part II (July 16–18)** is a clinically oriented lecture series focusing on specialty areas.

Parts I and II may be taken independently at the discretion of the student.

Faculty

Christopher A. Hunter, *University of Pennsylvania School of Veterinary Medicine*

Introduction to the Immune System

Kathleen E. Sullivan, *Children's Hospital of Philadelphia*
Innate Immunity: Introduction to the Cells

J. Oriol Sunyer, *University of Pennsylvania School of Veterinary Medicine*
Complement

Igor E. Brodsky, *University of Pennsylvania School of Veterinary Medicine*
Innate Immunity: Introduction to Pattern Recognition and Intracellular Signaling

Jennifer A. Punt, *Haverford College*
Introduction to Adaptive Immunity

Terri M. Laufer, *University of Pennsylvania, Perelman School of Medicine*
MHC Restriction and Thymic Selection

Laurence C. Eisenlohr, *Jefferson Medical College*
Antigen Processing and Presentation

Edward M. Behrens, *Children's Hospital of Philadelphia*
Dendritic Cells: The Bridge Between Innate and Adaptive Immunity

Jonathan D. Powell, *Johns Hopkins University School of Medicine*
Effector T Cell Differentiation and Response

Michael P. Cancro, *University of Pennsylvania, Perelman School of Medicine*
B Cell Activation and Humoral Immunity

Gary A. Koretzky, *University of Pennsylvania, Perelman School of Medicine*
Signaling in the Immune System

Andrew D. Luster, *Massachusetts General Hospital, Harvard Medical School*
Trafficking of Immune Cells

Ethan M. Shevach, *NIAID, NIH*
T and B Cell Tolerance

Cathryn Nagler, *University of Chicago*
Mucosal Immunology

David Artis, *University of Pennsylvania, Perelman School of Medicine*
Type 2 Immunity and Parasite Infections

Christopher A. Hunter, *University of Pennsylvania School of Veterinary Medicine*
Cytokines

Jonathan S. Maltzman, *University of Pennsylvania, Perelman School of Medicine*
Solid Organ Transplantation

Robert H. Vonderheide, *University of Pennsylvania, Perelman School of Medicine*
Tumor Immunology

Sunny Shin, *University of Pennsylvania, Perelman School of Medicine*
Immunity to Bacterial Pathogens

Carolina B. Lopez, *University of Pennsylvania School of Veterinary Medicine*
Immunity to Viruses

E. John Wherry, *University of Pennsylvania, Perelman School of Medicine*
Immunologic Memory

David B. Weiner, *University of Pennsylvania, Perelman School of Medicine*
Vaccination

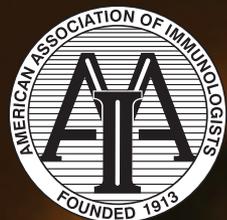
Vijay K. Kuchroo, *Brigham & Women's Hospital, Harvard Medical School*
Autoimmunity

Michael J. Lenardo, *NIAID, NIH*
Genetic Approaches to Immune-Mediated Diseases

Andrew C. Chan, *Genentech, Inc.*
Bench to Bedside to Bench: Current Issues in Immunology

For complete course details and registration, visit:
www.aai.org/Education/Courses

For assistance, contact (301) 634-7178 or meetings@aai.org. Overseas applicants are advised to apply early for visas; for details, visit www.aai.org/Education/Courses/Visa.html.



2013 Advanced Course in Immunology

July 28–August 2, 2013 • Seaport World Trade Center, Boston, Massachusetts

Director: Leslie J. Berg, Ph.D., *University of Massachusetts Medical School*

Don't miss the premier course in immunology for research scientists!

This intensive course is directed toward advanced trainees and scientists who wish to expand or update their understanding of the field. Leading experts will present recent advances in the biology of the immune system and address its role in health and disease. This is not an introductory course; attendees will need to have a firm understanding of the principles of immunology.

Faculty

Marc K. Jenkins, *Center for Immunology,
University of Minnesota Medical School*

Anatomy of the Immune Response

Jonathan C. Kagan, *Children's Hospital Boston,
Harvard Medical School*

Innate Immunity

Wayne M. Yokoyama, *Washington University
School of Medicine*

*NK Cells — Their Receptors and Function
in Health and Disease*

Michael C. Carroll, *Immune Disease Institute,
Harvard Medical School*

Molecular and Cellular Mediators of Inflammation

Shannon J. Turley, *Dana Farber Cancer Institute,
Harvard Medical School*

Dendritic Cells

Frederick W. Alt, *Children's Hospital Boston,
Harvard Medical School*

*The Generation and Modification of Lymphocyte
Antigen Receptor Genes*

Shiv Pillai, *Massachusetts General Hospital Cancer
Center, Harvard Medical School*

B Cell Development

Avinash Bhandoola, *University of Pennsylvania,
Perelman School of Medicine*

T Cell Development

Thorsten R. Mempel, *Massachusetts General Hospital,
Harvard Medical School*

Lymphocyte Trafficking

Kenneth L. Rock, *University of Massachusetts
Medical School*

MHC-Restricted Antigen Presentation to T Cells

Leslie J. Berg, *University of Massachusetts
Medical School*

Signaling from Antigen Receptors

Brian A. Cobb, *Case Western Reserve University
School of Medicine*

Glycoimmunology

Charlotte S. Kaetzel, *University of Kentucky College
of Medicine*

Mucosal Immunity

David M. Center, *Boston University School of Medicine*

Asthma and Allergy

JoAnne L. Flynn, *University of Pittsburgh School
of Medicine*

Immune Response to Pathogens

Ann Marshak-Rothstein, *University
of Massachusetts Medical School*

B Cell Tolerance and Autoimmunity

Vassiliki A. Boussiotis, *Beth Israel Deaconess
Medical Center, Harvard Medical School*

T Cell Tolerance and Autoimmunity

Megan Sykes, *Columbia University College
of Physicians and Surgeons*

Transplantation

Robert Schreiber, *Washington University
School of Medicine*

Tumor Immunology

Susan M. Kaech, *Yale School of Medicine*

Lymphocyte Memory

Linda C. Burkly, *Biogen Idec*

Immunotherapeutics

Dennis W. Metzger, *Albany Medical College*

Vaccines

Support in part for this AAI course has been generously provided by the Society for Glycobiology.

For complete course details and registration, visit:

www.aai.org/Education/Courses

For assistance, contact (301) 634-7178 or meetings@aai.org. Overseas applicants are advised to apply early for visas; for details, visit www.aai.org/Education/Courses/Visa.html.

FOCUS ON PUBLIC AFFAIRS

AAI Holds Second Annual Public Policy Fellows Program Capitol Hill Day

The 2012–13 class of AAI Public Policy Fellows flew to Washington in early March to participate in the second annual Public Policy Fellows Program Capitol Hill Day. Despite a perilously snowy forecast, the official closure of the federal government, and a virtually empty downtown, the AAI fellows braved the weather and had a very full and productive day on Capitol Hill.

The 10 AAI fellows (listed below) were joined by AAI Committee on Public Affairs Chair Elizabeth Kovacs and AAI Advocacy Programs Subcommittee Chair Michael Princiotta. The program opened on the evening of March 5 with a training dinner. The featured guest speaker at the dinner was Hugh Auchincloss, AAI '83, principal deputy director of the National Institute of Allergy and Infectious Diseases (NIAID), who graciously accepted an invitation to speak for the second consecutive year. Auchincloss discussed the role of NIAID and NIH and participated in a lively conversation with the AAI fellows.

The fellows visited offices of their own congressional delegations, as well as those of other fellows. In addition to meeting with staff, fellows met personally with six senators and five members of Congress. The AAI fellows advocated for predictable and sustained funding for NIH, including a budget of at least \$32 billion in fiscal year 2013. They also stressed the damaging effect that sequestration will have on biomedical research and urged lawmakers to stop these devastating cuts.

2012–13 AAI Public Policy Fellows

- Ling Cao, M.D., Ph.D., *University of New England*
- Kory Alderson Hallett, Ph.D., *Oak Ridge Institute for Science and Education Fellow at DOE; University of Wisconsin–Madison*
- Stephanie James, Ph.D., *University of Colorado School of Medicine*
- Joshua Obar, Ph.D., *Montana State University*
- Hannah Phipps-Yonas, Ph.D., *University of Arizona College of Medicine*
- Melanie Ragin, Ph.D., *Fort Valley State University*
- Jillian Richmond, Ph.D., *Massachusetts General Hospital/Harvard Medical School*
- Mark Rubinstein, Ph.D., *Medical University of South Carolina*
- Adam Soloff, Ph.D., *Medical University of South Carolina; University of Pittsburgh School of Medicine*
- Dina Weilhammer, Ph.D., *Lawrence Livermore National Laboratory*



Hugh Auchincloss



AAI Fellow Joshua Obar chatting with Sen. Max Baucus



L–R: Melanie Ragin, Sen. Tim Scott, Adam Soloff, Mark Rubinstein



L–R: Mark Rubinstein, Sen. Angus King, Ling Cao, Hannah Phipps-Yonas, AAI Director of Public Policy and Government Affairs Lauren Gross, Jillian Richmond

Congress Completes FY 2013 Spending Bills

Nearly halfway through FY 2013, Congress reached agreement on a continuing resolution (CR) to fund the federal government through the end of this fiscal year (September 30, 2013). The CR caps discretionary spending at \$1.043 trillion in compliance with the American Taxpayer Relief Act (the Fiscal Cliff agreement). It does not eliminate or modify sequestration (automatic across-the-board cuts).

The CR includes a \$71 million increase for NIH, which is nearly offset by a 0.189 percent across-the-board reduction to the section of the bill that funds the Departments of Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS). Because the resulting ~\$30.7 billion NIH budget is subject to sequestration, NIH will experience a cut of ~\$1.56 billion (5.1 percent).

This final version of the CR was approved by the Senate on March 20 (by a vote of 73 to 26) and the House on March 21 (by a vote of 318 to 109) but not before consideration of several amendments. Sen. Tom Harkin (D-IA), chair of the Senate Labor-HHS Appropriations Subcommittee and a past recipient of the AAI Public Service Award, introduced an amendment that would have increased the NIH budget by \$211 million. However, the Senate rejected the Harkin amendment by a vote of 54 to 45, six votes short of the 60 required for passage.

The Senate did, however, accept an amendment offered by Sen. Tom Coburn (R-OK) to prevent the National Science Foundation (NSF) from funding political science projects unless they are certified by the NSF director as "promoting national security or the economic interests of the United States." The amendment was accepted by voice vote, indicating no apparent opposition.

President, Congress Roll Out FY 2014 Spending Plans

Although presidents typically release their budgets on the first Tuesday in February, this year, amid a number of fiscal challenges, the president delayed release of his fiscal year (FY) 2014 budget until April 10, 2013. Despite this delay, and in part because current law requires withholding salaries from members of Congress unless their chamber passes a budget resolution, the House and Senate moved forward with their FY 2014 budget proposals in March. Descriptions of the three budget plans are below.

Any budget resolution that passes the House, Senate, or both chambers of Congress is nonbinding and serves only as a framework for that fiscal year's appropriations bills.

FY 2014 President's Budget

On April 10, 2013, President Obama released his long-awaited budget for FY 2014 (which begins on October 1, 2013). The budget's aim, according to the White House, is to achieve \$1.8 trillion in deficit reduction over the next decade while protecting critical investments in infrastructure, education, and research and development.

Continued next page



The American Association of Immunologists

9650 Rockville Pike
Bethesda, MD 20814-3994
Tel: 301-634-7178
Fax: 301-634-7887
E-mail: infoaai@aai.org
www.aai.org

Member Services

Tel: 301-634-7195
E-mail: members@aai.org

The Journal of Immunology

Tel: 301-634-7197
E-mail: infoji@aai.org
www.jimmunol.org/

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Unlike the House and Senate budget plans, the president's budget includes detailed plans for federal departments, agencies, and programs. It includes a budget of \$31.2 billion for NIH in FY 2014, an increase of \$471 million (1.5 percent) over the FY 2012 level. (Because the FY 2013 appropriations bills were not signed into law until March 2013, the White House made comparisons in its budget based on levels enacted for FY 2012.) The proposal also replaces sequestration (automatic, across-the-board cuts) with other means of deficit reduction, including \$200 billion in savings from discretionary programs (one-half from defense; one-half from nondefense) over 10 years.

The slight boost in funding to NIH would help the agency provide an estimated 36,610 research project grants (RPGs), an increase of 351 RPGs. The budget also includes funding for the following new and existing programs:

- an additional \$80 million in research grants for drug development and therapies for Alzheimer's disease
- \$40 million for the new Big Data to Knowledge (BD2K) program, through the Common Fund
- \$40 million for the new Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative
- a \$40 million increase for the Cures Acceleration Network (for a total budget of \$50 million and part of a proposed ~\$91 million increase for its NIH home, the National Center for Advancing Translational Sciences)
- \$32 million for two new diversity initiatives: the Building Infrastructure Leading to Diversity (BUILD) program and the National Research Mentoring Network (NRMN)
- a \$14 million (1.8 percent) increase in the National Research Service Award (NRSA) program to increase the stipend level by 2.7 percent (although supporting slightly fewer trainees than in FY 2012)

FY 2014 House Budget

The House Republican Budget Resolution was introduced by Rep. Paul Ryan (R-1st, WI), chair of the House Budget Committee, on March 12, 2013. It was approved by the House Budget Committee on March 13 (by a vote of 22–17) and by the full House on March 21 (by a vote of 221–207).

This is the third budget released by Chairman Ryan. Unlike his previous budget plans, which would have required 25 years to balance the federal budget, this plan seeks to balance the budget within a decade. The plan would accomplish this goal and modify sequestration, in part, by making “\$4.6 trillion in spending reductions over the next ten years,” including up to \$1.1 trillion in nondefense discretionary spending (from which NIH is funded).

FY 2014 Senate Budget

Sen. Patty Murray (D-WA), chair of the Senate Budget Committee, introduced the Senate Democratic Budget Resolution on March 12. The Senate Budget Committee approved the resolution (by a vote of 12–10) on March 14, and the full Senate approved the resolution on March 23 (by a vote of 50–49).

The Senate Budget Resolution fully replaces sequestration and sets significantly higher funding levels for discretionary spending. In total, the Senate Budget Resolution would achieve “\$240 billion in responsible savings across [nondefense] discretionary spending” over 10 years.

Like the House Budget Resolution, the Senate Budget Resolution includes no specific budget for NIH, but the 113-page plan released by Murray does include a section on the importance of investing in life sciences research.

AAI Submits Testimony on FY 2014 NIH Funding

AAI Committee on Public Affairs Chair Elizabeth Kovacs submitted testimony March 15 on behalf of AAI to the House Departments of Labor, Health and Human Services, and Education and Related Agencies (Labor-HHS) Appropriations Subcommittee. AAI recommends that the subcommittee, which has jurisdiction over NIH funding, provide an appropriation of at least \$32 billion for NIH in fiscal year 2014.

The complete AAI testimony is reprinted at p. 8, below. AAI recently submitted similar testimony to the Senate Labor-HHS Appropriations Subcommittee; the Senate testimony can be accessed on the AAI website at http://aai.org/Public_Affairs/Docs/2013/AAI_Testimony_Senate_LHHS_Appropriations_Subcommittee_FY2014.pdf.

President Obama Launches Brain Initiative

President Obama announced a new large-scale initiative on April 2, 2013, to map the human brain. The new project, formally titled the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, “aims to help researchers find new ways to treat, cure, and even prevent brain disorders such as Alzheimer’s disease, epilepsy, and traumatic brain injury” (see www.whitehouse.gov/the-press-office/2013/04/02/fact-sheet-brain-initiative).

BRAIN is one of President Obama’s “Grand Challenges” of the 21st century: “ambitious but achievable goals that require advances in science and technology to accomplish.” President Obama cites the Human Genome Project as an example of a successful Grand Challenge from years past (see www.whitehouse.gov/blog/2013/04/02/brain-initiative-challenges-researchers-unlock-mysteries-human-mind).

In his FY 2014 budget (detailed above), President Obama includes nearly \$110 million for BRAIN, including \$50 million from the Defense Advanced Research Projects Agency, \$40 million from NIH, and \$20 million from the National Science Foundation. The leading NIH contributor to BRAIN will be the NIH Blueprint for Neuroscience Research, but some funding will come from NIH institutes and centers and from the NIH director’s discretionary fund. At least four private-sector partners have also agreed to make contributions to the initiative.

NIH is establishing a working group, co-chaired by Cornelia “Cori” Bargmann, Rockefeller University, and William Newsome, Stanford University, to define the initiative’s primary scientific goals and to create a plan for achieving those goals.

In a short YouTube video promoting BRAIN (www.youtube.com/watch?feature=player_embedded&v=slQ8ELULNP0), NIH Director Francis Collins explains the primary objective of the initiative: “It aims to bring together nanoscience, engineering, and neurology to make sense of how the brain works—how circuits in the brain allow us to do all the complicated things that currently we don’t understand, that will build a foundation that will help us to understand... the causes and ultimately the way to prevent and cure diseases like Alzheimer’s, schizophrenia, autism, epilepsy, and traumatic brain injury.” Collins also notes that the project is going to take “quite a few years.”



Attendees gather at the steps of the Carnegie Library in support of the Rally for Medical Research

Thousands Gather in Washington to Support Medical Research

The American Association for Cancer Research hosted the “Rally for Medical Research” in Washington, D.C., on April 8. AAI was one of nearly 200 partnering organizations lending support of various kinds to the rally or its cause.

ABC/NPR political analyst Cokie Roberts served as emcee for the event and actress Maura Tierney was a featured speaker. Two members of Congress spoke: Rep. Chris Van Hollen (D-8th, MD), recipient of the 2011 AAI Public Service Award, and Rep. Rosa DeLauro (D-3rd, CT). President Obama and two Republican members of Congress (Rep. Jerry Moran of Kansas and Rep. David McKinley of West Virginia) sent supportive messages, which were read to the crowd.

Speaker Marc Tessier-Lavigne, Ph.D., president of the Rockefeller University and former chief scientific officer for Genentech, Inc., specifically mentioned the need to better understand the immune system and stressed the importance of basic research. Other speakers included patient advocates and representatives from some of the rally’s sponsoring organizations.

At one point, the crowd was led in a mass “text-Congress” moment when all attendees were asked to send text messages to Congress urging more funding for medical research.

To view the full event, please visit the Rally for Medical Research YouTube page: www.youtube.com/watch?v=Y23FFtBWzdY.

AAI was represented at the rally by AAI Director of Public Policy and Government Affairs Lauren Gross and AAI Legislative Assistant Jake Schumacher.

Testimony of Elizabeth J. Kovacs, Ph.D., Chair, Committee on Public Affairs, The American Association of Immunologists (AAI)

Submitted to the House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies, regarding the Fiscal Year (FY) 2014 Budget for the National Institutes of Health

March 15, 2013

The American Association of Immunologists (AAI), the world's largest professional association of research scientists and physicians who are experts on the immune system, respectfully submits this testimony regarding appropriations for the National Institutes of Health (NIH) for Fiscal Year (FY) 2014. AAI recommends an appropriation of at least \$32 billion for NIH for FY 2014 to enable NIH to support existing research projects, fund a limited number of outstanding new ones, and ensure that the brightest students and trainees are able to pursue careers in biomedical research in the United States.

The Irreplaceable Role of NIH in Advancing Biomedical Research

NIH grants support the work of most biomedical scientists.¹ The vast majority of AAI members who work in academia depend on NIH grants to support their research at universities, colleges, and research institutions all around the country; many also teach the medical students and undergraduates who will be the next generation of physicians and researchers. Many AAI members who work in government are employed by the NIH; they depend on the NIH budget—as well as regular interaction with their private sector colleagues—to advance their work.² Our industry members, who generally do not receive NIH grants or awards, nonetheless depend on scientific discoveries that are generated by NIH-funded researchers to catalyze translational research or develop products. No matter where on the spectrum of biomedical science researchers may work, they know that NIH is the lynchpin to, and essential ingredient for, success.

NIH's irreplaceable role in our nation's biomedical research enterprise is indisputable among scientists. And the partnership between government-funded research and advancements in the private sector has never been more clear or more necessary: in a recent article in *Forbes*, three "current and former leaders of major commercial and academic life science institutions" (Marc Tessier-Lavigne, Ph.D., P. Roy Vagelos, M.D., and Elias Zerhouni, M.D.)³ compellingly argue that the "tiny" federal investment in NIH research has reaped "enormous benefits—human and economic" and that "continued investment in basic science is . . . key to our economic competitiveness. America remains the world's leader in biotechnology and pharmaceutical discovery thanks to the

strength of our research universities and other biomedical research institutions, which not only spawn countless biotechnology companies but also have attracted the R&D operations of most major pharmaceutical companies, which are keen to tap into our innovation." Those who suggest that the private sector can or will fill the gap left by inadequate NIH funding miss the essential point made by these internationally recognized scientific leaders: NIH-funded research and NIH leadership provide the foundation upon which commercial discovery and development depend.

Inadequate NIH Funding Threatens Human Health and U.S. Preeminence in Medicine

America's dominance in advancing basic biomedical research, discovering urgently needed treatments and cures, and "growing" brilliant young scientists has been unchallenged for more than fifty years. However, erosion of the NIH budget over the last decade has already led to the loss of grant funding among even the most highly qualified scientists, resulting in the closure of labs, the termination or interruption of important research, and the emigration of talented scientists to other countries that are investing heavily in their futures.⁴ For those scientists who are willing and able to continue, securing funding increasingly consumes their time—time that should be devoted to research and to mentoring the nation's future researchers, inventors, and innovators. And in a relatively new discipline such as immunology, where knowledge is expanding exponentially and the potential for even greater success is palpable, this shrinking of federal resources is both alarming and a squandering of precious prior federal investment.

The Immune System and Its Impact on Disease

The functional immune system recognizes and attacks bacteria, viruses, and tumor cells inside the body. Many infectious agents, including influenza, HIV/AIDS, tuberculosis, malaria, and the common cold, challenge—and sometimes overcome—the defenses mounted by the immune system, resulting in disease. A malfunctioning immune system can attack our normal body tissues, causing "autoimmune" diseases or disorders, including Type 1 diabetes, multiple sclerosis, rheumatoid arthritis,

asthma, allergies, inflammatory bowel diseases, and lupus. The immune system also plays a role in many other diseases and conditions, including cancer, Alzheimer's disease, obesity, Type II diabetes, and cardiovascular disease. Understanding the immune response is also crucial to developing protective vaccines against pathogens that might cause the next pandemic, man-made and natural infectious organisms (including plague, smallpox and anthrax) that could be used for bioterrorism, and environmental threats that could cause or exacerbate disease. Immunologists have made great progress in many of these areas, but solving key scientific questions that lead to prevention and cures cannot occur without investigator-initiated peer-reviewed research supported by a strong, adequately funded NIH.⁵

Recent Immunological Advances and Their Promise for Tomorrow

- **A potential cure for cancer?** NIH-funded scientists have demonstrated that they can remove a specific subset of immune cells (T lymphocytes) from individuals with cancer, genetically modify them in the laboratory to recognize the patient's own cancer cells, and administer those cells to the patient. This personalized immunotherapy has induced complete and partial remissions in patients in a recent clinical experiment. Scientists have also shown similar techniques could induce cures in other types of cancer, including metastatic melanoma (a type of skin cancer), which is one of the ten most common cancers.⁶
- **A way to stop Alzheimer's disease?** Alzheimer's disease (AD) is a neurodegenerative disease of the brain that currently afflicts 5.4 million Americans, mostly over age 65.⁷ While the cause of AD is unknown, researchers have recently found evidence of immune cells present in AD lesions, systemic alteration in the immune system of AD patients, and local inflammation in the brains of those with AD. Such recent discoveries are leading scientists to develop immune based therapies to treat AD patients, including monoclonal antibodies which target AD plaques for destruction, and DNA based vaccines. Such potential treatments are under development in many NIH-funded laboratories.
- **New treatments for emerging zoonotic infectious diseases?** Zoonotic infections (human infections acquired from a different animal species) include avian influenza, SARS, hantavirus, dengue virus, Nipah virus, and West Nile virus. Although the overall incidence remains low, these infections can have high mortality rates and emerge without warning, as evidenced by the 2012 hantavirus outbreak in Yosemite National Park and the severe West Nile virus season.⁸ Developing preventive vaccines for these infections has proven difficult, and current treatments are limited. NIH-funded research on hantavirus and influenza A has shown an association between illness/death and an inappropriately strong immune response caused by an

excessive release of cytokines (hormones of the immune system). Researchers are exploring whether limiting the inappropriate immune response during infection can reduce virus-induced illness and death.⁹

The Importance of Sustained NIH Funding to Research, Scientists, and Our Nation

Despite strong Congressional support for biomedical research and NIH, fiscal pressures in recent years have resulted in flat or reduced NIH funding. After accounting for increases in biomedical research inflation, these budgets have eroded NIH's purchasing power by about 20 percent since 2003. Under sequestration, with its FY 2013 budget cut of about 5.1 percent, NIH's purchasing power will be further reduced. AAI is deeply alarmed about this funding reduction and believes it could irreparably harm ongoing research, weaken the U.S. biomedical research enterprise, and enable global competitors to recruit away our best scientists.

Conclusion

AAI thanks the members and staff of the subcommittee for their strong bipartisan support for biomedical research, and urges an appropriation of at least \$32 billion for NIH for FY 2014 to fund important ongoing research, strengthen the biomedical research enterprise, and support the thousands of scientists across the nation who devote their lives to finding the answers we need to prevent, treat, and cure disease.

References

1. After a highly competitive peer review, NIH distributes most (more than 80 percent) of its \$30.7 billion budget to scientists who conduct research at approximately 2,500 universities, medical schools, and other research institutions across the United States. About 10 percent of its budget supports the work of the approximately 6,000 scientists who work in NIH's own laboratories (<http://nih.gov/about/>).
2. AAI is concerned that a federal policy limits the ability of government scientists to attend privately sponsored scientific meetings and conferences (www.hhs.gov/travel/policies/2012_policy_manual.pdf). Government scientists contribute significantly to scientific advancement in our field. Information exchange among scientists from government, academia, industry, and private research institutes is absolutely essential, and any barriers to the participation of government scientists undermine the best interests of science.
3. Dr. Lavigne is president of The Rockefeller University and former chief scientific officer for Genentech Inc.; Dr. Vagelos is chairman of Regeneron Pharmaceuticals and retired chairman and CEO of Merck & Co., Inc.; and Dr. Zerhouni is president of research and development for Sanofi and former director of NIH. "Legendary Drug

Continued next page

AAI Testimony (continued)

Industry Executives Warn U.S. Science Cuts Endanger The Future," *Forbes* online (3/6/13) www.forbes.com/sites/matthewherper/2013/03/06/drug-industry-greats-say-the-u-s-must-reverse-the-cuts-to-our-investment-in-science/.

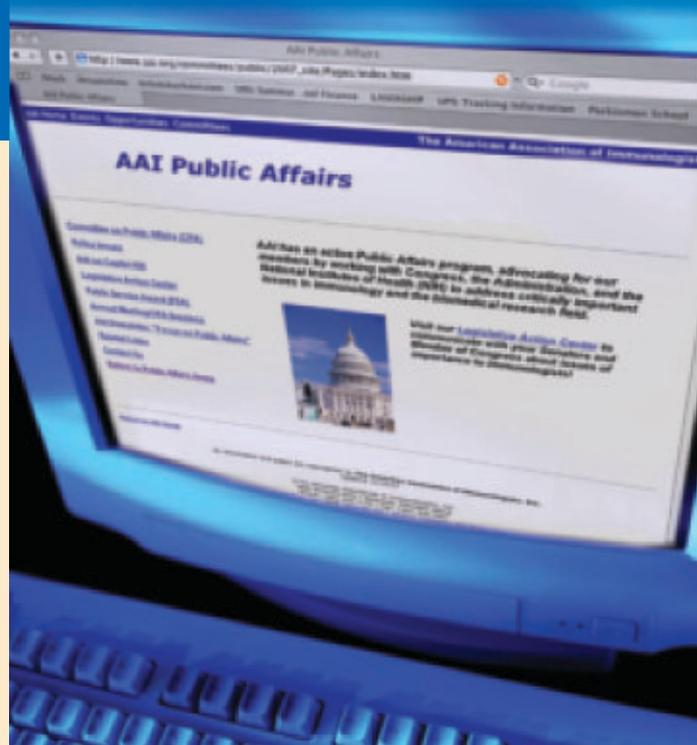
4. See "U.S. cuts could lead to brain drain in medicine," *Baltimore Sun*, 2/23/13, http://articles.baltimoresun.com/2013-02-23/news/bs-md-research-funding-20130221_1_nih-grantsresearchers-head-first-grant. See also Atkinson, et al. 2012, "Leadership in Decline," The Information Technology and Innovation Foundation, www2.itif.org/2012-leadership-in-decline.pdf.
5. NIH should robustly fund and primarily rely on individual investigator-initiated research, in which researchers working in institutions across the nation submit applications to, and following independent peer review, receive grants from, NIH. Biomedical innovation and discovery are less likely to be achieved through "top-down" science, in which the government specifies the type of research it wishes to fund.
6. See Kalos et al. 2011, "T Cells with Chimeric Antigen Receptors Have Potent Antitumor Effects and Can Establish Memory in Patients with Advanced Leukemia," *Science Translational Medicine*, 3: 95 <http://stm.sciencemag.org/content/3/95/95ra73.short>; Porter et al. 2011, "Chimeric Antigen Receptor-Modified T Cells in Chronic Lymphoid Leukemia," *N Engl. J. Med.* 365: 725-733 www.nejm.org/doi/full/10.1056/NEJMoa1103849.
7. See www.alz.org/documents_custom/2012_facts_figures_fact_sheet.pdf. The Alzheimer's Association estimates that up to 16 million people will have Alzheimer's by 2050. And the costs are staggering: "In 2012, the direct costs of caring for those with Alzheimer's . . . will total an estimated \$200 billion... Unless something is done, the costs of Alzheimer's in 2050 are estimated to total \$1.1 trillion (in today's dollars). Costs to Medicare and Medicaid will increase nearly 500 percent."
8. See www.cdc.gov/hantavirus/outbreaks/yosemite-national-park-2012.html and www.cdc.gov/ncidod/dvbid/westnile/index.htm.
9. See Teijaro et al. 2011, "Endothelial Cells Are Central Orchestrators of Cytokine Amplification during Influenza Virus Infection," *Cell* 146: 980-991 www.sciencedirect.com/science/article/pii/S009286741100941X.

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Members in the News

Jim Allison Is First Lloyd Old Immunology Award Recipient

James P. Allison, Ph.D., AAI '78, was honored this spring as the inaugural recipient of the American Association for Cancer Research-Cancer Research Institute (CRI) Lloyd J. Old Award in Immunology. The award, which confers a \$10,000 honorarium, recognizes outstanding and innovative research in cancer immunology that has had a far-reaching impact on the cancer field.

Allison serves as chair of the Immunology Program at the University of Texas (UT) MD Anderson Cancer Center in Houston. He has contributed seminal work elucidating mechanisms of T cell biology and regulation throughout his career. After publishing the first biochemical description of the $\alpha\beta$ T cell receptor in 1982, Allison went on to identify the requirement for costimulation in T cell activation and the inhibitory receptor cytotoxic T lymphocyte-associated antigen 4 (CTLA-4). His lab works to define signaling events in T cell activation and differentiation that can be applied to new strategies for the treatment of autoimmune diseases and immunotherapy of cancer. Allison's work has led to the development and clinical use of an anti-CTLA-4 antibody, ipilimumab, for the treatment of cancer through an approach termed immune checkpoint blockade. Ipilimumab is the first drug to increase survival rates of metastatic melanoma patients, and this approach shows promise for augmenting the immune response to combat multiple, additional types of cancer. Allison's research has exemplified the vital contribution that basic research can make to clinical medicine.

A member of the AAI Council from 1996 to 2003, Allison served as AAI president in 2001–2002. He is a past AAI Distinguished Lecturer and has served on multiple occasions as a major symposium speaker, chair, and abstract programming chair at the AAI annual meeting. He is a past member of the AAI Committee on Public Affairs and AAI Program Committee and has served as an associate and section editor for *The Journal of Immunology* and as an AAI Advanced Course faculty member.

In 2011, he was honored with the AAI Lifetime Achievement Award in recognition of his scientific accomplishments and outstanding leadership and service on behalf of AAI. He was also awarded the AAI-Dana



Jim Allison

Foundation (now AAI-Steinman) Award for Human Immunology Research in 2008. Allison's additional career honors include: member, Institute of Medicine and National Academy of Sciences; Richard Smalley Memorial Lectureship Award, International Society for Biological Therapy of Cancer; C. Chester Stock Award, Memorial Sloan-Kettering Cancer Center; William B. Coley Award for Distinguished Research in Basic and Tumor Immunology, CRI; Advancement of Cancer Research Award, Gilda's Club New York City; Smalley Award, Society for Immunotherapy of Cancer; Centeon Award for Innovative Breakthroughs in Immunology; and NIH Merit Award.

Allison has held a variety of NIH study section and other review panel appointments, including at the National Cancer Institute, National Institute of Child Health and Human Development, and National Institute of Allergy and Infectious Diseases. He serves as director of the CRI Scientific Advisory Council and has held editorial appointments with multiple journals, including *Journal of Clinical Investigation*, *Proceedings of the National Academy of Sciences USA*, *Immunity*, *Journal of Experimental Medicine*, *Developmental Immunology*, *International Immunology*, and *Science*.

A native Texan, Allison earned B.S. (microbiology) and doctoral (Ph.D., biological sciences) degrees from UT at Austin. Following postdoctoral training at Scripps Clinic and Research Foundation in La Jolla, California, he joined the faculty of the UT System Cancer Center Science Park in Smithville.

In 1985, Allison joined the University of California, Berkeley, as a professor in the Division of Immunology, Department of Molecular and Cell Biology. During a 20-year tenure, he held additional Berkeley appointments as director of the Cancer Research Laboratory, director of the Immunology Program, and co-chair of the Department of Immunology. He was named a Howard Hughes Medical Institute Investigator in 1997.

In 2004, Allison was appointed chair of the Immunology Program at the Memorial Sloan-Kettering Cancer Center, where he served until late 2012 and held additional appointments as director of the Ludwig Center for Cancer Immunotherapy and David H. Koch Chair in Immunologic Studies.

Paula Lutz Named College Dean at University of Wyoming

Paula M. Lutz, Ph.D., AAI '88, recently the dean of the College of Letters and Sciences and a professor of cell biology and neuroscience at Montana State University, has been appointed dean of the College of Arts and Sciences at the University of Wyoming (UW). At UW, Lutz will lead the college with the largest enrollment of the university's academic units, offering bachelor's degree programs in 43 disciplines, 42 master's programs, and 11 doctoral programs.



Paula Lutz

Lutz's research has focused on immunotoxicology (effect of lead on the immune system), membrane biochemistry, and surface proteins of B lymphocytes (regulation and cell-surface expression). As her administrative roles have expanded, Lutz has sustained her teaching and research endeavors, including research into the effects of lead on children's immune systems. As an administrator, Lutz is credited with notable achievements in developing innovative teaching and curricular initiatives, programs to advance research and graduate education, diversity enhancement, faculty hiring and career development, budget management, and strategic planning.

In 2002, Lutz became the first female dean (College of Arts and Sciences) at the University of Missouri-Rolla (UMR), where she had previously served as associate dean for graduate studies and research and chair of the Department of Biological Sciences. In the course of her research, teaching, and administrative activities, Lutz has been active in mentoring women, minority scientists, and academicians. At UMR, she helped to create a Women's Leadership Institute, worked with her university's chapter of Women in Science and Engineering, and helped start UMR's Expanding Your Horizons program to encourage interest in science and math among junior high-aged

girls. She was honored with the university's Woman of the Year award, UMR Alumni Merit Award, and more than one dozen outstanding teaching and faculty excellence awards.

Lutz is a past member of the AAI Committee on Public Affairs. She recently served as an elected member of the national Council of Colleges of Arts and Sciences Board of Directors, for which she chaired the Committee on Research Universities. She has served for multiple years as a member of the Autumn Immunology Conference

(AIC) Council, which organizes the annual AIC regional immunology meeting. She is a member of the American Association for the Advancement of Science and an active member of the Society for Environmental Geochemistry and Health, having served as its secretary, secretary-treasurer, and treasurer. Lutz has been a participant, including as invited guest lecturer, at the American Society for Histocompatibility and Immunogenetics annual meeting and regional educational workshop and has served as a member of the External Research Advisory Board of the University of South Dakota.

A chemistry graduate of UMR, Lutz received her Ph.D. in microbiology and immunology from the Duke University Medical Center's Department of Microbiology and Immunology (advisor: Jeffrey Dawson). She trained as a postdoctoral fellow at the University of North Carolina at Chapel Hill and later as a research associate and postdoctoral fellow in the Division of Immunology at Duke. She joined the faculty at UMR (now the Missouri University of Science and Technology) as an assistant professor in 1987. She was appointed associate professor in 1993 and full professor in 2000.

AAI Newsletter: Members in the News—Submissions Invited

AAI welcomes the opportunity to highlight the career achievements and professional honors attained by AAI member scientists. Such publicity not only serves to inspire colleagues but also informs the broader public of immunology's vital and widening role in scientific discovery and transformative medicine.

Help AAI share news of your or another member's noteworthy scientific and/or service recognition or career appointment by contacting mwcuddy@aai.org. Thank you!

Otto Götze, M.D., AAI '72

1935–2013

The following tribute was authored by colleagues Martin Oppermann and Reinhard Würzner. AAI gratefully acknowledges the submission.

Professor Otto Götze, who devoted his scientific and medical life to innate immunity and, in particular, to the alternative pathway of complement, died February 4, 2013, in Göttingen after a long illness at age 77. He was head of the Department of Immunology at the University of Göttingen from 1979 to 2003.

Otto Götze was born on August 2, 1935, in Recklinghausen in the Ruhr area of Germany. His family moved soon thereafter to Hamburg, where Otto spent his childhood and adolescence. He was always proud of his roots, and his attitude was indeed typical for a “Hanseatic” character: straightforward but always a bit stiff, like the winds in that region. Known among those in the lab as Otto, but addressed in his presence as “Herr Götze,” he was authentic, open-minded, and well-respected by co-workers and students, who enjoyed him as an enthusiastic teacher and thoughtful mentor. His peers and professorial colleagues respected him as a constructive and reliable partner endowed with a strong personal and scientific integrity—the principal basis for his high international reputation. Two of his scholars from his time in Göttingen, the authors [Martin Oppermann (MO) and Reinhard Würzner (RW)] here review Otto Götze’s scientific and medical career by dividing his scientific life into four periods.

The first period extends from 1960—when Otto finished his medical studies at the Universities of Hamburg, Frankfurt, Paris, Munich, and Freiburg, with a doctoral thesis on an immunohematological topic—to 1968. During this time, he received basic clinical training and gained expertise in the laboratory of Herbert Fischer, one of the founding directors of the Max Planck Institute of Immunobiology and Epigenetics in Freiburg. It was a first-author paper in *Nature* on immune hemolysis of terminal complement components¹ that served as Otto’s entrance ticket to endeavors that followed.

In the second period, 1968–1979, Otto joined Hans Joachim Müller-Eberhard, one of the most prominent figures in the field of complement during that time, at the Department of Molecular Immunology of the Scripps Clinic in La Jolla, California. Otto was the recipient of



Otto Götze

a German Research Foundation (DFG) stipend and, therefore, brought his own funding to Scripps. He and his family often recalled memories from this stimulating, formative, and scientifically productive time along the Pacific coast of southern California. Müller-Eberhard’s expanding and “roaring” research group was an ideal setting for an ambitious, young scientist, and the hot complement field was revealing a number of mostly biochemical secrets, often through the work of Müller-Eberhard’s group. A number of complement factors were fractionated and characterized during the period, and a

complement “cascade” came sharply into evidence. Otto’s own, notable insights were reflected primarily in his work on the “alternative” pathway of complement, a concept of antibody-independent activation, which at that time was not readily accepted by the scientific community.² With factors B and D, he characterized central components of this pathway, and his findings formed the core of a model detailing that this pathway was neither alternative nor an escape route but actually the evolutionarily much older, conserved, and, thus, true “classical” pathway.^{3–5} A similar way of danger sensing by nonspecific recognition mechanisms was rediscovered more than 20 years later with the concept of pattern recognition molecules. This second stage of Otto’s career, marked by his seminal work on the alternative pathway of complement, culminated in a one-year appointment as a visiting associate professor at the Rockefeller University in New York.

The third period, 1979–1990, which coincided with his first decade as professor and head of the Department of Immunology at the University of Göttingen, can be summarized as a period of construction. As the first chair at Göttingen in the then-novel discipline of “immunology” (immunology having previously fallen under microbiology there), Otto generated a new research institute that quickly adopted its own identity. His scientific interests at that time focused on two topics. First, in continuing earlier work from his time at Rockefeller, he hypothesized that some complement proteins, e.g., C6, may not only be present in the fluid phase but are also expressed on

Continued next page

the cell surface as integral membrane proteins, which, upon activation-induced aggregation, relay signals into the cell in a manner similar to immunoglobulins.⁶⁻⁷ This fascinating concept, however, could not be verified.

A second interest was the quantitation of complement activation. Together with J. Hinrich Peters, Otto successfully used the monoclonal antibody technology, which was still in its infancy, resulting in an arsenal of anti-complement monoclonal antibodies raised in his lab in that decade.⁸ These reagents, originally generated to characterize membrane complement proteins, later served as valuable tools for complement quantitation in various clinical settings. The methods in hybridoma technology were later published in the form of a laboratory manual.⁹ This book, known as the “green book” for its cover when first published in German, retained that name even when the cover of the subsequent, internationally distributed English version changed to blue.

Two highlights from his scientific achievements with therapeutic implications date to this period. First is the generation of blocking anti-C5a antibodies and their successful application in a pig sepsis model;¹⁰ second is the characterization of an anti-C5 monoclonal antibody (N19-8) which was the first to successfully block both C5a release and activation of the terminal pathway.¹¹ This antibody was the forerunner of Eculizumab, the humanized monoclonal complement blocker that was used to treat almost 400 critically ill patients in Germany during the enterohaemorrhagic *Escherichia coli* O104:H4 outbreak.¹²

Concurrent with these research activities, Otto was establishing a modern, routine diagnostic laboratory for immunological parameters at the university clinics. As in his other endeavors, he quickly made his mark in medical faculty administration as dean and vice dean and as a member of numerous university and clinical boards.

With CD59 yet to be discovered, the role of complement in xenotransplantation and cell regulation completely neglected, and in the absence of anti-complement drugs, many scientists in immunology in the 1980s were convinced that complement was dead! Otto, instead, constantly motivated his co-workers to remain faithful to the originally chosen field of complement, while at the same time advising junior members of his group to develop an independent qualification in a related field such as nephrology, dermatology, or microbiology. At the end of the decade, he received the gold medal of the European Complement Network for his life-long achievements in complement research and on behalf of the European complement society—and one of us (RW) had the pleasure of delivering the laudatory speech.

His fourth scientific period extended from 1990 until Otto's retirement in September 2003, an event marked by an international symposium held in his honor. During this 12-year period, a coincidental exchange of reagents led to a fruitful cooperation with Otto's good friend from his Freiburg period, the late biochemist Kurt Jungermann. Together, they identified the liver as a target of complement activation and, thus, established the modulatory effect of complement on metabolism.¹³

Unlike many colleagues, Otto effectively stopped working in science almost immediately upon becoming an emeritus professor; the 2003 symposium marked the final point in a successful career as an active scientist, as documented in more than 120 publications, including several “citation classics.” Less than 10 percent of his publications were not directly related to complement, illustrating the life-long focus of his scientific interests. The DFG continuously supported his research throughout his career. In addition to numerous medical students who completed their dissertations in his lab, nine Ph.D. students graduated, and three postdocs trained under his guidance. Two of his lab scientists fell in love with one another in his lab and started a family. Together with 23 co-workers, colleagues, and other scholars, they signed the obituary notice.

Otto influenced many scientists who today work not only in immunology but also in related fields, including dermatology, nephrology, transplantation medicine, and microbiology. He encouraged international exchanges on the part of his staff through attendance at international conferences and stays abroad. He kept his scholars on a long leash, displaying confidence that they did not require day-to-day guidance to achieve scientific success. He was a fair senior advisor who fostered, above all, the autonomy of his scholars.

Otto was an outstanding scientist, devoted physician, and engaged teacher—and it was very sad seeing him passing away in the true sense of these words, gradually losing control and orientation over a period of several years. In an address memorializing Otto, one of us (MO) detailed how witnessing Otto's demise brought into sharp focus Otto's own final observation in his valedictory lecture: “We are as confused as ever, but we are now confused on a higher level and about more important things.” It was an expression Otto had often used on various occasions over the years. Otto positively influenced so many scientists; whereas most remain confused with daily scientific problems and less important aspects of life, Otto is now on a “higher level”—he will not be forgotten.

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Hilary Koprowski, M.D., AAI '46

1916–2013

The following obituary appears as published, courtesy of the Philadelphia Inquirer.

Hilary Koprowski, Polio Vaccine Pioneer, Dead at 96

Hilary Koprowski, a virologist and former director of the Wistar Institute who developed the first polio vaccine and helped improve the rabies vaccine for humans, has died.

Koprowski, who was 96 and had been in declining health in recent months, died of pneumonia at his home in Wynnewood, according to his son Christopher Koprowski, chief of radiation oncology at the Helen F. Graham Cancer Center at the Christiana Care Health System.

"Hilary Koprowski left an enduring mark on medical science and the health of humankind, and his many accomplishments serve as a testament to his legacy," said Russel E. Kaufman, president and chief executive officer of the Wistar Institute.

Koprowski raised Wistar's profile during his tenure as director from 1957 to 1991. He then became director of Biotechnology Foundation Laboratories Inc. at Thomas Jefferson University, and was still going to the office two years ago, Christopher Koprowski said. However, his relationship with both employers turned rancorous at the end. He was fired by Wistar in 1991 amid financial problems and later filed age-discrimination claims. He fought Jefferson in court in 2010 over office space after



Hilary Koprowski

his grant funding declined. That suit was dropped and he left in 2011.

"He was charismatic, brilliant beyond anyone else I have ever met," Christopher Koprowski said. "He was a visionary and he was a great leader and he was also a very controversial character."

He said people who got in his father's way found "he could run over them with a bulldozer and he could be very stubborn."

Though Koprowski was the first to develop a polio vaccine—his was an oral version that used live virus—Albert Sabin won the race to get a vaccine licensed in the United States. Later, Jonas Salk developed an injectable vaccine. The other two men became more famous, but Koprowski's work was considered groundbreaking. "He very much enjoyed the fact that he did not achieve the fame of Salk or Sabin," his son said. "He said that that would have stifled him scientifically and invaded his privacy."

A discredited theory blamed clinical trials of his polio vaccine in the Congo for providing the bridge from chimps to humans for the AIDS virus. Scientific experts conclusively debunked the theory in 2001.

Christopher Koprowski said his father had a "kernel of great modesty" about his work. "He didn't think that he was as brilliant as he was. He always would claim to me that he got where he was through hard work purely."

Continued next page

Under Koprowski's leadership, a Wistar release said, scientists there developed the rubella, or German measles, vaccine and a more effective and less painful vaccine for people exposed to rabies.

In the 1970s, Koprowski and fellow scientists developed a technique to produce monoclonal antibodies, which are now used to fight cancer. At Jefferson, he was working on using plants to produce vaccines.

Koprowski was born in Poland and was, his son said, both an academic and a musical prodigy, playing piano. He spoke four languages by age 5. Later, he went to the Warsaw Conservatory and medical school at the same time. He met his future wife, Irena Koprowska, in medical school. They had been married 74 years when she died last year.

The two fled Europe to Brazil in 1939 during World War II. The only work he could find was teaching piano, until he got a chance to study viruses with the Rockefeller Foundation. That is how he became a virologist, his son said. He moved to the United States in 1944 and started

working at Lederle Laboratories soon after. It was there that he began working on the polio vaccine.

He maintained his love of music and played the piano into his 80s. He kept a grand piano at Wistar and played it during holiday parties. He began composing classical music with modern harmonies late in life.

Suzanne Jones was his assistant and office manager for 40 years, but, over the last 20, she said, he called her his boss. "He was the last of the great Renaissance men," she said. "He was a great scientist, a great man, and a great boss."

Over the course of his career, Koprowski published more than 875 scientific publications. He was a member of the National Academy of Sciences and the American Academy of Arts and Sciences.

Survivors include another son, Claude. The family plans a private commemoration of his life.

*By Stacey Burling, Inquirer Staff Writer
POSTED: APRIL 15, 2013*

Karen A. Sullivan, Ph.D., AAI '77

1944–2012

AAI member Karen A. Sullivan, Ph.D., research professor of medicine, Department of Medicine, Tulane University School of Medicine, died on December 28, 2012. The following remembrance was authored by Tulane colleague Laurianne G. Wild, M.D., and appears with her kind permission.

Karen A. Sullivan was born in Bronxville, New York, on January 23, 1944.

She attended Massachusetts College of Liberal Arts, where she received her bachelor of science degree in 1966, graduating cum laude. She received her Ph.D. in microbiology and immunology in 1974 from the Graduate School of Arts and Sciences, Duke University. She completed postdoctoral fellowships in London, England, and in the Division of Laboratories and Research, New York Department of Health, in 1978.

Sullivan began her professional career at the rank of assistant professor and director of the Histocompatibility Laboratory at West Virginia University Medical Center in Morgantown, West Virginia, where she was a faculty member from 1978 to 1980. She spent the next three years on the faculty of the Graduate School of Medical Sciences, Sloan-Kettering Division, Cornell University. In 1983, she accepted a Tulane University School of Medicine appointment as director of the Histocompatibility and Immunogenetics Laboratory (HIL) at the rank of research

assistant professor in the Department of Medicine. In 1987, she was promoted to research associate professor and in 1994 was promoted to research professor of medicine. Karen served as director of the Tulane University HIL for 29 years.

Throughout her professional life, Karen was a member of multiple professional societies, including the United Network for Organ Sharing, The American Association of Immunologists, the American Society of Histocompatibility and Immunogenetics, and the Clinical Immunology Society. She served as chair and member of numerous national committees and on several journal editorial boards, and published more than 30 manuscripts and/or book chapters.

Karen's survivors include two sisters, Dana Sullivan and Megan Sullivan, four nieces, Colleen Sullivan, Maurya Sullivan, Jessica Sullivan, and Siobhan Sullivan, three nephews, James Sullivan, Walter Sullivan, and Bryan Sullivan, and two sisters-in-law, Caterina Sullivan and Sheila Sullivan.

Karen was dedicated to Tulane University for nearly 30 years. She passed away unexpectedly on December 28, 2012, and will be missed dearly by her Tulane family, friends, and colleagues, as well as all of the members of the Sullivan family.

AAI offers condolences to the families, friends, and colleagues of the following members whose deaths were recorded during the past year (since July 1, 2012):

Brigitte A. Askonas, Ph.D., D.Sc.
London, England
AAI '77

Fionula Mary Brennan, Ph.D.
London, England
AAI '12

Robert Guthrie Burrell, Ph.D.
Morgantown, West Virginia
AAI '65

Sheldon G. Cohen, M.D.
Chevy Chase, Maryland
AAI '64

Shreevrat Goenka, Ph.D.
Indianapolis, Indiana
AAI '11

Otto Götze, M.D.
Göttingen, Germany
AAI '72

Shyr-Te Ju, Ph.D.
Charlottesville, Virginia
AAI '80

Hilary Koprowski, M.D.
Philadelphia, Pennsylvania
AAI '46

Norman L. Letvin, M.D.
Boston, Massachusetts
AAI '82

Takayuki Matsumoto, M.D., Ph.D.
Nishinomiya, Japan
AAI '00

Bernardetta Nardelli, Ph.D.
Bethesda, Maryland
AAI '93

Stanley G. Nathenson, M.D.
Bronx, New York
AAI '68

James K. Roche, M.D., Ph.D.
Charlottesville, Virginia
AAI '87

Robert D. Stout, Ph.D.
Louisville, Kentucky
AAI '76

Karen A. Sullivan, Ph.D.
New Orleans, Louisiana
AAI '77

Constantine H. Tempelis, Ph.D.
Berkeley, California
AAI '71

Byron H. Waksman, M.D.
Lexington, Massachusetts
AAI '50

GRIP

Grant Review for Immunologists Program

Get a GRIP: An AAI program designed to help new investigators prepare their NIH grant proposals

AAI is pleased to offer a program to match new PIs with established PIs who have significant, successful grant writing careers. The Grant Review for Immunologists Program (GRIP) invites new PIs to submit an outline or NIH-style abstract to the GRIP coordinator who, with the assistance of a small volunteer subcommittee, will attempt to match the topic of the proposal with the research experience of an established PI. Matches will be made as quickly as possible to allow new PIs to meet upcoming NIH grant deadlines. Participation is open only to AAI members and is strictly voluntary. The program is not intended to supplant internal mentoring programs.

GRIP is now accepting both new PI and established PI participants. Please send your CV and a brief description of either your potential research project (new PIs) or grant reviewing experience (established PIs) to infoaai@aai.org (please write "GRIP" in the subject line).



Program details at www.aai.org/GRIP_rd.htm

100 Years of AAI: A Look Back at Two Early Immunologists in Hawaii

On the occasion of its centennial meeting in Honolulu, AAI reflects on the association's long ties to Hawaii.

“Hawaii,” for most AAI members, including those who attended IMMUNOLOGY 2013™, conjures up images of vast white sand beaches and palm trees swaying in gentle sea breezes. These Edenic images, however, belie the islands’ history as a setting for pioneering immunological research and their longstanding connection to AAI.

In fact, one Hawaiian physician, Archibald N. Sinclair, was among the 52 charter members of AAI in 1913. Sinclair, an established authority on tuberculosis, pioneered an immunological-based method for its treatment.

Another early AAI member in Hawaii, Nils P. Larsen, spearheaded massive reforms to improve public health on the islands as early as the 1920s.

We profile below the lives and careers of these two distinguished early AAI members.

Archibald Neil Sinclair, M.B.C.M., AAI '13 Career Overview

Archibald N. Sinclair was born in New York City on January 20, 1871, just two years after his parents emigrated from Scotland to the United States. Before he was 10 years old, the family moved to Hawaii, when his father, a building contractor, was hired to help build ‘Iolani Palace, the residence commissioned by King Kalākaua, the last Hawaiian king. The family remained in Honolulu after construction of the palace was completed in 1882, and Sinclair attended Oahu College (now known as the Punahou School), a college preparatory school that includes President Barack Obama among its alumni.

After graduating from high school in 1889, Sinclair moved to his parents’ homeland and studied medicine at the University of Glasgow. Upon earning his M.B.C.M.



‘Iolani Palace, 1898

Hawaii State Archives, Digital Collections, Photograph Collection

(Bachelor of Medicine, Master of Surgery) in 1894, he practiced medicine in Yaxley, England, for three years before returning to Hawaii. He began a private practice in Waianae, Oahu, in 1897, but by 1901, he had fully dedicated himself to public health. That year, he was named city physician of Honolulu, a position he held until 1908, and was appointed the first medical superintendent of the Leahi Home, the recently opened tuberculosis sanitarium in Honolulu, where he was to spend the rest of his career. He served

concurrently as acting assistant surgeon for the U.S. Public Health Service from 1900 to 1919 and as physician in charge of the tuberculosis bureau and the bacteriological department of the Territorial Board of Health from 1911 to 1916. Resuming his private practice in 1916 while retaining his position at the Leahi Home, Sinclair continued to specialize in the treatment of tuberculosis and other pulmonary ailments until his death on October 21, 1930.¹

Well-respected among Hawaiian physicians, Sinclair was twice elected president of the Hawaiian Territorial Medical Society, first from 1907 to 1908 and again from 1926 to 1927.

Making the Case for Tuberculin

A remarkable clinician whose case studies were reported in the *Journal of the American Medical Association*,² Sinclair garnered a national reputation for his success in treating tuberculosis with tuberculin. He first presented his “Case for Tuberculin” before the Hawaiian Territorial Medical Society in 1914.³ The use of tuberculin to treat pulmonary tuberculosis was one of the most controversial immunological issues of the day and had been among the topics debated at the first AAI annual meeting held

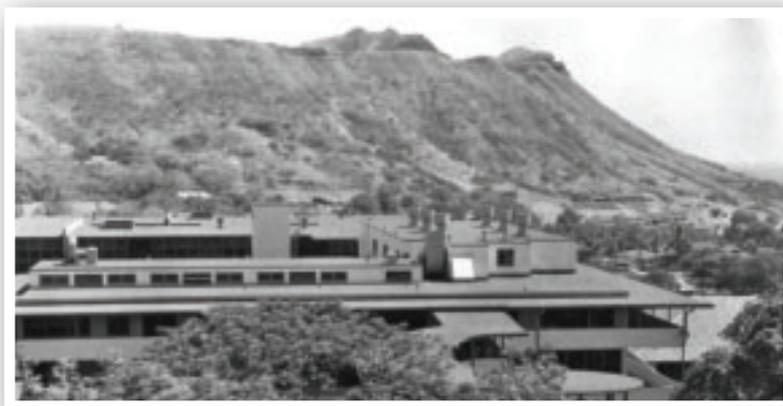
1. “Sinclair, Archibald N.,” *Men of Hawaii: A Biographical Reference Library, Complete and Authentic, of the Men of Note and Substantial Achievement in the Hawaiian Islands*, vol. 2, ed. by John William Siddall (Honolulu: Honolulu Star-Bulletin, 1921), 363; “Archibald Neil Sinclair,” In Memoriam—Doctors of Hawaii—XI, *Hawaii Medical Journal and Inter-Island Nurses’ Bulletin* 17, no. 2 (1957): 152; Gwenfread Allen, *The Story of Leahi: Fifty Years of Service, 1901–1951* (Honolulu: Trustees of Leahi Hospital, 1951), 10; “Dr. Archibald Neil Sinclair House,” Nomination Form, National Register of Historic Places, U.S. National Park Service, <http://pdfhost.focus.nps.gov/docs/NRHP/Text/83003557.pdf>.
2. A. N. Sinclair, “Yersin-Roux Serum in the Treatment of Plague,” *Journal of the American Medical Association* 56, no. 5 (1911): 332–35; A. N. Sinclair, “The Diazo and Urochromogen Reactions in Pulmonary Tuberculosis,” *Journal of the American Medical Association* 66, no. 4 (1916): 247–48.
3. A. N. Sinclair, “The Case for Tuberculin,” *Transactions of the Medical Society of Hawaii* 23 (1914): 79–97.

in Atlantic City, New Jersey, the same year that Sinclair reported his positive findings.⁴ The reason for the controversy was that prior attempts to use tuberculin as a treatment, notably those by Robert Koch in the 1890s, had low success rates and often produced unexpected, negative outcomes, even death. Sinclair conceded that tuberculin treatment was a very complicated, precise process that was ineffective if not administered properly and “in inexperienced hands, even dangerous.”⁵

He cited two schools of thought on administering tuberculin. He dubbed one method the “rules on the bottle method” for treating each patient with a fixed, and often too intense, recommended dosage. He referred to the other method as the “immunizing” method, which he attributed to Sir Almroth Wright (AAI ’14).⁶ Sinclair, having spent four months at St. Mary’s Hospital in London observing Wright prepare and administer tuberculin in 1911, had further refined the process at Leahi Home.⁷ Sinclair’s therapeutic immunizing method involved administering small, regulated tuberculin doses over a long interval and varying those doses based on Wright’s “opsonic index,” which measured the opsonin content in patients’ blood. There was no single dosage that was suitable for all patients nor could tuberculin be expected to cure all patients. Such promises, Sinclair asserted, were “what makes the patent medicine man his living” and were not made by responsible medical practitioners.⁸

Nevertheless, he was convinced that when meticulously administered, tuberculin produced incomparable results. He reported that 67.6 percent of patients who had received tuberculin treatments were able to leave Leahi and return to work, a dramatic increase from the 27.2 percent able to do so before he began administering tuberculin.⁹ Sinclair encountered harsh opposition from a Hawaiian colleague who declared that Wright’s opsonic index was “not accepted in this country,”¹⁰ but he remained sanguine about the prospects for tuberculin treatment and, in May 1916, traveled to Washington, D.C., to report his findings at the third AAI annual meeting.¹¹

Despite Sinclair’s efforts and optimism, his method of treating tuberculosis was never widely adopted. Most clinicians were concerned that the potential was too great for negative side effects from improper administration.¹² According to Arthur Silverstein (AAI ’63), although



Sinclair Building on the Leahi Hospital campus, built in 1949 and named for Archibald N. Sinclair

Courtesy of Leahi Hospital

Wright’s opsonic index was initially met with a great deal of enthusiasm among some immunologists, particularly those in his native England, “the techniques proved so difficult and unreproducible in practice as to become unfashionable within a decade.”¹³

Nevertheless, Sinclair could take pride in the success he had encountered while treating tuberculosis patients at the Leahi Home. Reflecting on the progress that had been made in the treatment of tuberculosis in the first decade of the twentieth century alone, he noted, “One familiar with the [Leahi] Home and its conditions during the past few years cannot but be struck by the change—a few years ago people looked upon it as the last resort of the hopeless—a walk through its wards encountered almost bed-ridden patients entirely; now it is coming to be looked upon as the hope and salvation of the afflicted, and a walk through its wards will frequently show not a single patient in bed—or at the worst of times but an extremely small percentage of bedridden patients.”¹⁴

Continued next page



Archibald N. Sinclair, ca. 1927

Courtesy of Queen’s Heritage Collection, Queen’s Medical Center

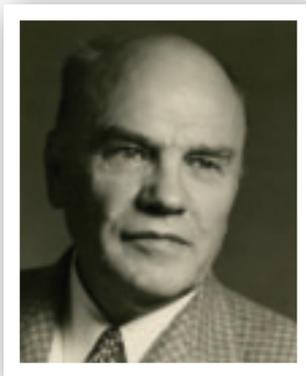
4. “Science at the First AAI Annual Meeting,” *AAI Newsletter*, May/June 2012, 30.
5. Sinclair, “The Case for Tuberculin,” 79.
6. *Ibid.*, 86.
7. *Ibid.*, 85; Allen, *The Story of Leahi*, 12–13, 15.
8. Sinclair, “The Case for Tuberculin,” 97.
9. *Ibid.*, 80.
10. J. T. McDonald, “Discussion,” in *ibid.*, 94.
11. Evidently, tuberculin treatment proved slightly less successful in the two-year interim between presenting his findings at the Medical Society of Hawaii meeting and the AAI meeting. He now reported a success rate of 50.1 percent compared with his earlier rate of 67.6 percent. Abstract of A. N. Sinclair, “Treatment of Tuberculosis Pulmonalis by Tuberculin,” in “Proceedings of the American Association of Immunologists: Third Annual Meeting, Held in Washington, D. C. May 11, 1916,” *The Journal of Immunology* 1, no. 4 (1916): 489–90.
12. “Science at the First AAI Annual Meeting,” 30.
13. Arthur M. Silverstein, *A History of Immunology*, 2nd ed. (New York: Elsevier, 2009), 38.
14. A. N. Sinclair, *Fighting the Great White Plague* (Honolulu: Hawaiian Gazette Co., 1914), 11.

Nils Paul Larsen, M.D., AAI '23

A Religious Upbringing

Although Nils P. Larsen did not call Hawaii home until well into adulthood, his impact on Hawaiian medicine and public health was no less significant than Sinclair's. Born in Stockholm, Sweden, on June 15, 1890, Larsen was the sixth of seven children born to a tailor struggling to support his growing family. Overpopulation and successive crop failures were impoverishing life in Sweden, impelling approximately 330,000 Swedes to immigrate to the United States during the 1880s. When Nils was only three years old, the Larsen family joined the ranks of those who hoped to find a better life in the New World. After settling briefly in Peeksville, New York, Nils's father, a devout man, relocated the family to Bridgeport, Connecticut, where he helped start a church for the Swedish Evangelical Mission Covenant, a Lutheran denomination founded in Chicago in 1885. While attending public school in Bridgeport, Larsen held part-time jobs to help support his family, including work in a steel mill during the summers of his high school years.¹⁵

Larsen attended the Massachusetts Agricultural College (now the University of Massachusetts, Amherst), where he intended to study forestry. Although he began to abandon the formal religious dogmas embraced by his pious father, Larsen remained committed to the Christian ideal of helping others that lay at the heart of the Social Gospel movement of the era. He became actively involved in student religious groups on campus, including the YMCA and the College Christian Association. While attending one religious conference, at which missionaries relayed accounts of their travels, Larsen learned that there was only one doctor for every one million people in China. He decided then that he wanted to become a physician, not out of any special yearning to solve scientific problems but out of his deep-seated commitment to social justice and community service.¹⁶



Nils P. Larsen, ca. 1955
Courtesy of Queen's Heritage
Collection, Queen's Medical Center

Early Career, War, and Marriage

After graduating from Massachusetts Agricultural College in 1913, Larsen attended Cornell Medical School in New York City, earning his M.D. in 1916. He then interned in the pathology department at New York Hospital and took additional courses in biological chemistry at Columbia University. When the United States entered the First World War in April 1917, Larsen was commissioned as a first lieutenant in the Medical Corps of the U.S. Army and was deployed to Belgium the following May. While in Belgium, he received news that his younger sister had died of tuberculosis. Absorbing this loss during the influenza pandemic that ravaged families across the globe likely motivated his later work to combat tuberculosis.

In the spring of 1919, Larsen was promoted to major, awarded the Silver Star for his valor during combat, and released from active duty. That summer, he made his first trip to Hawaii, where he visited his older brother David, a plant pathologist, who was now a manager of a sugar plantation. Following his vacation, he returned to New York to teach at Cornell Medical School and serve as assistant visiting physician in pediatrics at Bellevue Hospital. These years in New York, from 1919 to 1922, proved to be some of Larsen's most productive for clinical research and writing. He published case studies on allergic reactions, asthma, and pneumonia in the *Journal of the American Medical Association* and *The Journal of Immunology*.¹⁷

In September 1921, Larsen married Sara "Sally" Lucas, whom he had met two years earlier during his Hawaiian vacation. Although the two had not kept in touch following Larsen's return to New York, Sally was apparently impressed by Larsen during his visit to Hawaii and contacted him upon her arrival in New York from Honolulu to start a confectionary. The extent to which the confectionary materialized is unclear, but, within months, the couple wed.

Sally's mother appears to have been equally decisive and proactive as her daughter. Upon learning of an opening for a pathologist at Queen's Hospital in Honolulu, she mentioned Larsen to the administrators. If she was seizing upon a possible means of bringing her daughter back to Hawaii, she succeeded. Larsen was offered the position in July of 1922 and promptly accepted it.¹⁸

15. Janine A. Powers, "Worlds Beyond Medicine: Nils P. Larsen's Impact on Hawai'i," *Hawaiian Journal of History* 39 (2005): 92–93.

16. *Ibid.*, 93–94.

17. Russell L. Cecil and Nils P. Larsen, "Clinical and Bacteriologic Study of One Thousand Cases of Lobar Pneumonia," *Journal of the American Medical Association* 79, no. 5 (1922): 343–49; Nils P. Larsen, Royce Paddock, and H. L. Alexander, "Bronchial Asthma and Allied Conditions: Clinical and Immunological Observations," *The Journal of Immunology* 7, no. 2 (1922): 81–95; Nils P. Larsen, A. V. R. Haigh, Harry L. Alexander, and Royce Paddock, "The Failure of Peptone to Protect against Anaphylactic Shock and Allergic Conditions," *The Journal of Immunology* 8, no. 5 (1923): 409–24.

18. Powers, "Worlds Beyond Medicine," 96; Janine A. Powers, "From Medicine to Art: Nils Paul Larsen (1890–1964)" (Ph.D. diss., University of Hawaii, 2003), 22.

At Queen's Hospital

Larsen immediately impressed the administrators of Queen's Hospital. In 1924, he was appointed the hospital's medical director, a position he held until 1942. Named for Queen Emma, its most enthusiastic champion, Queen's Hospital was founded in 1859 to provide medical care to a rapidly dwindling Hawaiian population.

Occupying a major port of call on trade routes across the Pacific, the Hawaiian population was, at that time, besieged by diseases borne by foreigners, most recently a smallpox epidemic that swept across the islands in 1853.¹⁹ At the time of Larsen's appointment more than 60 years later, the hospital had failed to keep pace with the medical advances on the mainland.

Larsen immediately set out to modernize Queen's Hospital. His first reform was to arrange weekly clinics in which medical practitioners from all over the island came together to share and discuss their cases, including the week's deaths. Often, Larsen recruited notable visiting physicians to lecture and consult with the local doctors, and word of the effectiveness of his clinics began to spread nationally, earning Larsen praise in the pages of the *New York Times*.²⁰ He also significantly improved living conditions for the nurses—usually women who were recruited from plantations—raising \$125,000 for the construction of new nurses' quarters in 1931.²¹

Reforming Hawaiian Public Health

Larsen's reforms extended well beyond the walls of Queen's Hospital. He made several significant contributions to improving public health in Hawaii. Shocked by the high infant-mortality rate on the islands, Larsen spearheaded a clean-milk campaign in November 1922. His investigations into the Hawaiian milk industry uncovered widespread unsanitary conditions and resulted in new laws regulating milk production. The successful campaign became a national story when it was reported years later in *Reader's Digest*.²² In the late 1920s, he also called for "preventorium," camps where pre-tubercular children would receive medical care and be provided with a proper diet. With the support of Archibald Sinclair and others at Leahi Home, the first preventorium in Hawaii opened its doors in 1930.²³



Queen Emma, ca. 1880

Photo by A. A. Montano; Hawaii State Archives, Digital Collections, Photograph Collection

Perhaps Larsen's greatest reforms came in his work with the Hawaiian Sugar Planters' Association. In 1928, he criticized the planters for allowing their workers to live in substandard conditions. Improvements in living conditions and diets could prevent the suffering and even death caused by diseases such as beriberi and gastroenteritis, argued Larsen. He soon convinced planters that these reforms were not only a moral obligation but also a sound economic investment. New meal plans were implemented, and health centers were established on plantations where workers could receive treatment and consultation on nutrition, hygiene, and even birth control.²⁴

A Change of Direction

In 1939, Larsen contracted typhus and was hospitalized for 20 days. Shortly after his recovery, he wrote to Hans Zinnser (AAI '17, president 1919–1920) at Columbia University, an authority on typhus and author of *Rats, Lice and History*. The playfully familiar tone of his letter suggests that Larsen knew Zinnser from his time in New York: "I had occasion recently to meet your good friend with whom you have been so intimately associated . . . throughout your professional life—namely typhus fever."²⁵

The typhus left Larsen with angina, for which he decided to seek treatment in Boston. The decision was a fortunate one, for he and his wife departed Hawaii on December 5, 1941, just two days before Pearl Harbor was attacked. When he returned in 1942, he stepped down from his position as medical director of Queen's Hospital and began a private practice.

Larsen continued his research and began pursuing new topics, including the effects of diet on aging.²⁶ He also became interested in native Hawaiian medicine, pointing out that the traditional remedies of the *kahuna lapa'au*, Hawaiian medicine men, were often more scientific than those of the nineteenth-century Western doctors who so easily dismissed them as primitive. Larsen even developed a supplement made of taro, a plant

Continued next page

19. Richard A. Greer, "The Founding of the Queen's Hospital," *Hawaiian Journal of History* 3 (1969): 110–45.

20. Russell Owen, "Massie Will Take Stand Again Today," *New York Times*, 18 April 1932, 5; "Cited for Hawaiian Work: Dr. Nils Paul Larsen to Receive Cornell Alumni Award," *New York Times*, 14 April 1952, 21.

21. Powers, "Worlds Beyond Medicine," 100–101.

22. *Ibid.*, 99; Blake Clark, "Plantation Babies Okay Now," *Reader's Digest*, January 1947, 127–30.

23. Powers, "Worlds Beyond Medicine," 99–100.

24. *Ibid.*, 101–104.

25. *Ibid.*, 106.

26. *Ibid.*, 110–11; Nils P. Larsen, "Animal Fat Diet and Atherosclerosis," *Hawaii Medical Journal and Inter-Island Nurses' Bulletin* 14, no. 6 (1955): 485–90; Walter Sullivan, "Survey of 500,000 Will Study Role of Diet in Heart Disease," *New York Times*, 31 August 1961, 1.

common in the traditional Hawaiian diet that he believed promoted dental health.²⁷ Perhaps it was his eagerness to synthesize Eastern and Western traditions that made him popular with Hawaiians and won him election to the 1950 Constitutional Convention charged with preparing for Hawaiian statehood.²⁸

Although he officially retired in 1955, Larsen continued to treat patients until his death of a heart attack, at the age of 73, on March 19, 1964.²⁹



Queen's Hospital, ca. 1925

Courtesy of Queen's Heritage Collection, Queen's Medical Center

Hawaii—A Researcher's Paradise

Speaking before the Hawaii Medical Association at Queen's Hospital in April 1935, Nils Larsen noted, "The type of observations possible here are endless and many of them cannot be made anywhere else in the world."³⁰ Not only Larsen but also Archibald Sinclair before him and dozens of AAI members since have taken advantage of the unique setting Hawaii offers for immunological research. Even immunologists who were far removed from the islands geographically have long benefited from the presence of AAI members there, as when Arthur F. Coca (AAI '16) and Ella F. Grove (AAI '24) obtained tropical pollen samples from Larsen for their "Studies in Hypersensitiveness" in 1924.³¹

Hawaii may be at once an island paradise and, in the words of Larsen, "the best biological test tube in the world."³²

27. Powers, "Worlds Beyond Medicine," 107–10.

28. Arthur V. Molyneux, "Nils Paul Larsen, M.D.," *Hawaiian Medical Journal* 23, no. 5 (1964): 388.

29. Ibid.; Powers, "Worlds Beyond Medicine," 111.

30. Nils P. Larsen, "Cancer," *Transactions of the Hawaiian Territorial Medical Association* 45 (1935): 48–52, quote from 48.

31. Arthur F. Coca and Ella F. Grove, "Studies in Hypersensitiveness. XIII. A Study of the Atopic Reagents," *The Journal of Immunology* 10, no. 2 (1925): 445–64.

32. Larsen, "Cancer," 48.

A Chronological Overview:

300–500 AD—Polynesians first inhabit Hawaiian Islands

1778—British explorer Captain James Cook lands in Hawaii; his published account provides the earliest documentation of European contact with islands

1785—First trading ship lands in Hawaii on way to China; sandalwood trade and whaling soon become major industries

1810—Kamehameha formally establishes Kingdom of Hawaii and proclaims himself king after 15-year struggle with *ali'i* (chiefs)

1819—King Kamehameha II abolishes the *kapu*—the traditional religious and legal system that governed all aspects of Hawaiian life

1820—First Protestant missionaries arrive from the United States

1835—First commercially successful sugar plantation is opened by Ladd and Company

1848—King Kamehameha III enacts the *Mahele*, a land division act that introduces legal provisions for private ownership of land; opens way for rapid growth of sugar plantations

1859—Queen's Hospital, named for Queen Emma, is founded to provide medical care to Hawaiian people

1872—King Kamehameha V dies without heir, ending the House of Kamehameha

1874—Riots during the subsequent succession crisis are suppressed by U.S. and British troops; Kalākaua becomes King of Hawaii

1875—Reciprocity Treaty signed between the United States and Kingdom of Hawaii cedes Pearl Harbor to the United States in return for duty-free importation of Hawaiian sugar into the United States

ca. 1880—Archibald N. Sinclair moves to Hawaii with his family as a young boy

1887—King Kalākaua is forced to sign new constitution that strips monarchy of power by the Hawaiian League, a group of American and British businessmen who favor annexation by the United States

1891—King Kalākaua dies and is succeeded by his sister, Queen Lili'uokalani who calls for new constitution

1893—U.S. Marines arrive in Hawaii at request of the Hawaiian League, making it impossible for Queen Lili'uokalani to continue her rule; although U.S. Congress found no party guilty of overthrow in 1894, Congress issued a joint Apology Resolution in 1993 accepting U.S. responsibility for overthrowing the sovereign kingdom

1894—Republic of Hawaii is established

1897—Sinclair returns to Oahu and opens private practice after spending eight years in the United Kingdom, where he received his medical training

1898—Hawaii is annexed by the United States and becomes the Territory of Hawaii

1901—Sinclair is appointed city physician of Honolulu and the first medical superintendent of the Leahi Home

1919—Nils P. Larsen visits his brother in Hawaii after returning from the First World War

1922—Larsen accepts position as a pathologist at Queen's Hospital and moves to Honolulu from New York; he is soon appointed medical director of the hospital

1930—Sinclair dies in Honolulu at the age of 59

1941—The United States enters the Second World War after the attack on Pearl Harbor

1942—Larsen steps down as medical director of Queen's Hospital and begins private practice

1950—Larsen serves as member of the convention that drafts the Hawaiian constitution in preparation for statehood

1954—Democratic Party takes control of Territorial Legislature and pushes for statehood

1959—Hawaii becomes the 50th state of the United States

1964—Larsen dies of a heart attack in Honolulu at the age of 73

AAI History Online: Web Archive Continues to Expand, Evolve

For a century, AAI has fulfilled its founders' mission "to promote by its concerted efforts scientific research" through its annual meetings, *The Journal of Immunology* (*The JI*), awards, and the activities of its many committees.

In 2011, in anticipation of this year's AAI Centennial, AAI launched the AAI History website, which continues to evolve as a living archive, adding resources produced for, during, and after the celebration of the 100-years milestone during the AAI Annual Meeting in Hawaii, May 3–7, 2013. The following features are being incorporated on the website to chronicle the history of AAI and the role our members and immunology have played in pushing forward the boundaries of knowledge in biology and medicine.

AAI Oral History Project

In spring 2012, the AAI Office of History and Archives began coordinating oral history interviews of past AAI presidents conducted by Dr. Brien Williams, an award-winning professional oral historian. The interviews offer unique insight into the lives, works, and personalities of modern immunologists. The interviews also provide personal reflections on the emergence of the field of immunology during the 20th and 21st centuries.

Notable Members of AAI

Among myriad distinguished AAI members are many who have been awarded the highest honors in the scientific world. The membership of AAI has included 25 Nobel Laureates, 48 Lasker recipients, and more than 200 recipients of a dozen of the most prestigious national and international awards for science and immunology.

The *Ji* "Pillars of Immunology" Commentaries

The Pillars of Immunology feature in *The JI* presents commentaries on published articles that have come to be regarded as classics in the field, along with republication of the original article. To date, articles published from 1953 to 1997 have been featured, affording younger immunologists the opportunity to see what research has come before and how it has led to research today. Additional "Pillars" will be featured in the first issue each month of *The JI*. A web-based Table of Contents lists the commentaries in chronological order of publication for

each original scientific article and provides a full citation for the article and links to its republication on *The JI* website. The Pillars of Immunology commentaries are available in three formats for mobile and tablet devices: EPUB, MOBI, and EPDF—see www.aai.org/JI/Pillars.

History Articles

AAI has published a number of articles in the *AAI Newsletter* exploring the roles AAI and AAI members have played in defining and shaping the field of immunology. These articles highlight famous and some lesser-known members who have influenced both the association and the field. The article appearing in this May/June issue of the newsletter is the most recent example:

100 Years of AAI in Hawaii: A Look Back at Two Early Immunologists on the Islands

Other recent articles:

- *PI in the Scotland Yard of Streptococcal Mysteries: Rebecca Lancefield, Ph.D. (AAI 1933, President 1961–62)*
- *Immunologists during the First World War: One Soldier-Scientist's Experience—Stanhope Bayne-Jones (AAI 1917, President 1930–31)*
- *The 1918–1919 Influenza Pandemic as Covered in The Journal of Immunology*

A complete list of articles on AAI history can be found at www.aai.org/about/history.

Timeline

The illustrated AAI Centennial Timeline, unveiled at IMMUNOLOGY 2013™, chronicles the advances in science and immunology that have been made over the last century by AAI members and other scientists, placing those developments alongside key political and cultural events in U.S. and world history. An online version of the timeline will be made available later this year.

Visit the AAI History website at <http://aai.org/About/History/index.html>. Inquiries regarding issues of historic interest about the field of immunology, AAI history, *The JI*, or AAI members may be directed to AAI Historian/Archivist John Emrich, Ph.D., at: jemrich@aai.org; (301) 634-7941.

High School Teachers in AAI Summer Research Program Present Model Curricula at EB

Participants in the 2012–13 AAI High School Teachers Summer Research Program in Immunology gathered at the Experimental Biology meeting (EB), April 20–24, in Boston, Massachusetts. The teachers showed their enthusiasm and fortitude as they traveled to Boston in the midst of a historic city lockdown and manhunt in connection with the marathon bombings there. Fortunately, this situation was successfully resolved prior to the opening of the meeting on April 20.

The AAI program supports high school teachers' participation in a four- to six-week summer research experience in the laboratories of AAI members. Prior to starting in the laboratory, teachers are supported in attending the AAI Introductory Course in Immunology held in July at the University of Pennsylvania. Following the teachers' mentored lab experiences, an educational consultant assists them with the development of innovative curricula based on their summer projects for use in their own classrooms. The teachers also are given an opportunity to share their projects at a national meeting, and the curricula are archived to be available to the public on the AAI website. Teachers in this year's AAI program participated at EB in professional development activities sponsored by The American Physiological Society (APS) and its "Frontiers in Physiology" program for middle and high school science teachers. This opportunity allowed them to interact with other science teacher fellows from other societies. "We thank APS for this opportunity for these high school biology teachers, and we thank APS K–12 Program Coordinator Margaret Shain for the warm welcome and assistance that she provided the teachers on site at the meeting," said AAI Manager of Educational and Career Development Programs Mary Litzinger.

At EB, the AAI teachers presented posters on their summer research experiences and the classroom exercises that they developed from these research experiences. These presentations included:



The 2012–2013 AAI High School Teachers Program participants at Experimental Biology 2013 (L-R): Amanda Smith, Jared Rashford, Retha Prescod, program director Clinton Mathias, Lesli Horowitz, Stephen Biscotte, Judy Birschbach, Heidi Anderson, Nichole Kellerman

- *B cell modeling of cell communication and signal transduction pathways: how can students visualize cellular discussions?*

Heidi M. Anderson, Paul Laurence Dunbar High School, Lexington, Kentucky

Mentor: Subbarao Bondada, AAI '81, University of Kentucky



Heidi Anderson

- *Exploring the link between regulatory T cells and tumor growth: a lesson in the immune system and cancer*

Judy Birschbach, West Bend East High School, West Bend, Wisconsin

Mentor: Douglas A. Steeber, AAI '97, University of Wisconsin–Milwaukee



Judy Birschbach

- *CD4⁺ T cell differentiation: using computer modeling to explore the management of the adaptive immune response to inflammation*

Stephen Biscotte, Cave Spring High School, Roanoke, Virginia

Mentor: Josep Bassaganya-Riera, AAI '02, Virginia Polytechnic Institute and State University



Stephen Biscotte

■ *Bacteria & viruses & fungi, oh my!*

Lesli Horowitz, Kearny School of International Business, San Diego, California

Mentor: Nicholas Gascoigne, AAI '88, The Scripps Research Institute



Lesli Horowitz

■ *How do forensic scientists use immunology techniques?*

Nichole Kellerman, Walter Johnson High School, Bethesda, Maryland

Mentor: Pamela Schwartzberg, AAI '01, National Human Genome Research Institute, NIH



Nichole Kellerman

■ *Gut punched!*

Retha Prescod, Atlantic Community High School, Delray Beach, Florida

Mentor: Zhibin Chen, AAI '00, University of Miami, Miller School of Medicine

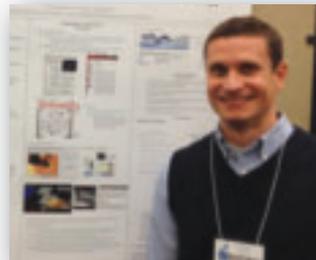


Retha Prescod

■ *Macrophage profiling of challenged, splenectomized mice: an advanced, secondary curriculum unit on cancer immunology*

Jared M. Rashford, Winchester Thurston School, Pittsburgh, Pennsylvania

Mentor: Kyle C. McKenna, AAI '98, University of Pittsburgh



Jared Rashford

■ *Macrophage morphological changes due to iNOS activation by LPS and its implication in chronic asthma*

Amanda Smith, Union City High School, Union City, New Jersey

Mentor: Debra Laskin, AAI '87, Rutgers University



Amanda Smith

Clinton Mathias, AAI '10, assistant professor at Western New England University and director of the AAI High School Teachers Program, said, "It was inspiring to see the research performed by the teachers and the creative ways in which they have applied these experiences to their classrooms. I extend congratulations to all of the teachers and their mentors on a job well done!"

The final curricula developed by the teachers will be available this summer through the archive maintained on the AAI website (www.aai.org/Education/Summer_Teachers/Archive.html).

AAI High School Teachers Summer Research Program in Immunology



Looking for creative ways to help foster the excitement of discovery in the high school science classroom? Consider recruiting an outstanding science teacher to apply for the American Association of Immunologists (AAI) High School Teachers Summer Research Program. Participants enjoy hands-on experience in cutting-edge research, using the latest tools and techniques, and take home a number of new lab exercises for use in their classes.

This national program supports high school science teachers' participation in a 4–6 week summer research experience in the laboratories of AAI members.

Recent past curricula topics include:

- *Where Will Our Next Antibiotic Come From? Investigating the Effects of Plant Extracts on the Growth of E. coli*
- *A Forensic Analysis of Food Poisoning using a Dip-stick Immunoassay*
- *There's No Time to Teach That: Integrating the Immune System, Autoimmunity, Literacy, and Research into an Over-crowded Curriculum*
- *Hiding in Plain Site: The Immune System, Tuberculosis, and Antibiotic Resistance*

For details, visit www.aai.org/Education/Summer_Teachers/index.html or contact AAI Manager of Educational and Career Development Programs Mary T. Litzinger, Ph.D., at: mlitzinger@aai.org or (301) 634-7820.

52nd Midwinter Conference of Immunologists

Scientists and trainees gathered at the 52nd Midwinter Conference of Immunologists (MCI), held January 26–29, at the Asilomar Conference Grounds in Pacific Grove, California. Christel Uittenbogaart, AAI '84, is the executive director of MCI, and Kristin A. Hogquist, AAI '95, and Gregory M. Barton, AAI '09, were chairs of this year's conference.

AAI sponsored the Dan H. Campbell Memorial Lecture, given by Anjana Rao, AAI '90. At the beginning of her lecture on "Signaling in Gene Expression," Rao reflected on the legacy of Campbell, former AAI president (1972–73) and a founder of MCI in 1961.

AAI also sponsored the six Ray Owen Poster Awards, which recognized outstanding poster presentations by graduate students and postdoctoral fellows; the two Ray Owen Young Investigator Awards, which honored outstanding oral presentations by students and postdocs; and an oral presentation session, at which students, postdocs, and early-career faculty gave short research talks. AAI Manager of Educational and Career Development Programs Mary Litzinger represented AAI at the conference.

The Ray Owen Poster Awards were given to:

Graduate Students:

Eric Gschweng, University of California, Los Angeles
Amanda Fox, University of California, Davis
Arya Khosravi, California Institute of Technology

Postdoctoral Fellows:

Rebekka Duhén, AAI '13, University of Washington
Kelsey Sivick, University of California Berkeley
Elizabeth Wohlfert, National Institute of Allergy and Infectious Diseases, NIH

The Ray Owen Young Investigator Awards were given to:

Graduate Student

Shivani Srivastava, University of Washington

Postdoctoral Fellow

Judith Mandl, National Institute of Allergy and Infectious Diseases, NIH



AAI Awardees at 2013 Midwinter Conference of Immunologists (L–R): Kelsey Sivick, Elizabeth Wohlfert, Arya Khosravi, Eric Gschweng, Amanda Fox, Shivani Srivastava, Rebekka Duhén (Judith Mandl not shown)



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GRANT AND AWARD DEADLINES

May 30—Lupus Research Institute New Research Grants for Novel Approaches to Lupus

- **Prize/Award:** Annual funding of up to \$100,000, beginning December 2013, for a term of up to three years
- **Eligibility:** Established and new investigators holding advanced degrees and affiliated with institutions of higher learning in the United States
- **Details:** <http://www.lupusresearchinstitute.org/lupus-research/grant-application/2013-novel-research-grants>
- **Contact:** Laura Hack, grants administrator: lhack@lupusny.org; (212) 685-4118

May/June—The Breast Cancer Research Foundation (BCRF)—American Association for Cancer Research (AACR) Grants for Translational Breast Cancer Research

- **Prize/Award:** One-year grants (beginning October 1) providing seed funding for projects with budgets not to exceed \$240,000 with a maximum of 20 percent in indirect costs
- **Eligibility:** Proposals invited by BCRF scientific advisory board (unsolicited requests not accepted)
- **Details:** http://bcrcure.org/action_grantguidelines.html
- **Contact:** bcrf@bcrcure.org

July 1—Abbott Award in Clinical and Diagnostic Immunology

- **Prize/Award:** Cash prize of \$2,500, commemorative piece, travel to American Society for Microbiology general meeting, where laureate presents award lecture
- **Eligibility:** Nominees demonstrating significant contributions to the understanding of the functioning of the host immune system in human disease, clinical approaches to diseases involving the immune system or development, or clinical application of immunodiagnostic procedures
- **Details:** <http://www.asm.org/index.php/awards2/10-awards-a-grants/awards/52-abbott-laboratories-award-in-clinical-and-diagnostic-immunology>
- **Contact:** service@asmusa.org; (202) 737-3600

July 18—American Heart Association National Established Investigator Award

- **Prize/Award:** Five-year award of \$80,000 in annual funding
- **Eligibility:** Mid-career investigators holding a doctoral degree and faculty/staff appointment with current R01 or equivalent funding and a demonstrated commitment to research broadly related to cardiovascular function and disease and stroke or to related clinical, basic science, bioengineering/biotechnology, and public health problems
- **Details:** http://my.americanheart.org/professional/Research/FundingOpportunities/ForScientists/National-Established-Investigator-Award_UCM_321935_Article.jsp
- **Contact:** apply@heart.org; (214) 360-6107

July 18—American Heart Association National Innovative Research Grant

- **Prize/Award:** Two-year award of \$75,000 in annual funding
- **Eligibility:** Investigators holding a doctoral degree and faculty appointment (or equivalent) who are engaged in highly

innovative research broadly related to cardiovascular function and disease and stroke or to related clinical, basic science, bioengineering/biotechnology, and public health problems

- **Details:** http://my.americanheart.org/professional/Research/FundingOpportunities/ForScientists/National-Innovative-Research-Grant_UCM_321936_Article.jsp
- **Contact:** apply@heart.org; (214) 360-6107

July 31—American Association for the Advancement of Science (AAAS) Mentor Awards (Lifetime Mentor Award; Mentor Award)

- **Prize/Award:** Cash award of \$5,000, commemorative plaque, complimentary AAAS annual meeting registration and travel/hotel reimbursement
- **Eligibility:** Mentors of any nationality or citizenship who have demonstrated extraordinary leadership in increasing the participation of underrepresented groups in science and engineering careers and/or impacted the climate of an institution to significantly increase the diversity of students pursuing and completing doctoral studies
- **Details:** <http://www.aaas.org/aboutaaas/awards/mentor/>
- **Contact:** (202) 326-6400

July 31—The Wiley Prize in Biomedical Sciences

- **Prize/Award:** Prize of \$35,000 and luncheon in honor of the recipient
- **Eligibility:** Exceptional scientists or teams who have made breakthrough contributions in pure or applied life sciences research distinguished by excellence, originality, and impact, and who have demonstrated significant leadership in the development of research concepts or their clinical application
- **Details:** <http://www.wiley.com/legacy/wileyfoundation/>
- **Contact:** prizesubmissions@wiley.com

August 1—AAAS Kavli Science Journalism Awards

- **Prize/Award:** Awards in eight categories, with each award comprised of \$3,000 and travel/hotel reimbursement in connection with attending the AAAS annual meeting
- **Eligibility:** Individual science journalists whose outstanding general-audience reporting covering the sciences, engineering, and mathematics has helped foster the public's understanding and appreciation of science
- **Details:** <http://www.aaas.org/aboutaaas/awards/sja/>
- **Contact:** (202) 326-6440

August 1—American College of Rheumatology Research and Education Foundation: Education and Training Awards

- **Prize/Award:** One-year awards in five categories ranging from \$2,000 to \$25,000 in funding; a sixth category offering three-year funding totaling \$180,000
- **Eligibility:** Eligibility by category is detailed at <http://www.rheumatology.org/REF/awards/index.asp>
- **Details:** <http://www.rheumatology.org/REF/awards/index.asp>
- **Contact:** acr@rheumatology.org; arhp@rheumatology.org; foundation@rheumatology.org; (404) 633-3777

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Meetings and Events Calendar

Mark Your Calendar for These Important Dates!

2013

May 28–June 1, 2013

ISIR2013—Building Bridges in Reproductive Immunology

Boston Park Plaza Hotel
Boston, Massachusetts
www.regonline.com/builder/site/Default.aspx?EventID=1144379

June 5–6, 2013

6th International Singapore Symposium of Immunology

Matrix Level 2 Auditorium
Biopolis, Singapore
<http://sgsi.org.sg>

June 15–16, 2013

Making and Breaking the Left-Right Axis: Laterality in Development and Disease Immunology

Fiesta Americana Grand Coral Beach Resort
Cancun, Mexico
www.developmental-biology.org/meetings/index.php?c=Mexico

June 16–20, 2013

17th International Congress of Developmental Biology/72nd Annual Meeting of the Society for Developmental Biology

Cancun Center
Cancun, Mexico
www.inb.unam.mx/isdb/index.html

July 3–5, 2013

AIDS-related Mycoses Meeting

Institute of Infectious Disease and Molecular Medicine
University of Cape Town
Cape Town, South Africa
www.aids-and-mycoses-2013.co.za/

July 7–10, 2013

14th International TNF Conference

Loews Le Concorde
Quebec City, Quebec, Canada
www.tnf2013.com

July 13–18, 2013

AAI Introductory Course in Immunology

University of Pennsylvania,
Philadelphia, Pennsylvania
www.aai.org/Education/Courses/Intro

July 20–24, 2013

The American Society for Virology 32nd Annual Scientific Meeting

Pennsylvania State University
State College, Pennsylvania
www.asv.org

July 21–26, 2013

T Follicular Helper Cells: Basic Discoveries and Clinical Applications

The Chinese University of Hong Kong
Hong Kong, China
www.grc.org/programs.aspx?year=2013&program=tfollic

July 28–August 2, 2013

AAI Advanced Course in Immunology

Seaport World Trade Center
Boston, Massachusetts
www.aai.org/Education/Courses/Advanced

August 22–27, 2013

15th International Congress of Immunology

MiCo—Milano Congressi
Milan, Italy
www.ici2013.org

September 29–October 3, 2013

Cytokines 2013, 11th Joint Meeting of ICS and ISICR

Hyatt Regency San Francisco
San Francisco, CA
www.cytokines2013.com

October 4–8, 2013

ASBMR 35th Annual Meeting

Baltimore, Maryland
www.asbmr.org

October 10–13, 2013

13th International Workshop on Langerhans Cells

Royal Tropical Institute
Amsterdam, The Netherlands
www.lc2013.nl/

December 13–17, 2013

7th International Symposium on CD1 and NKT Cells

Vinci International Congress Centre
Tours, France
www.cd1nkt Symposium-tours.com

2014

February 26–March 2, 2014

2014 BMT Tandem Meeting

Gaylord Texan Hotel & Convention Center
Grapevine, Texas
www.cibmtr.org/Meetings/Tandem/index.html

April 26–30, 2014

Experimental Biology (EB) (APS, ASPET, ASIP, ASN, AAA, ASBMB)

San Diego Convention Center
San Diego, California
Contact: eb@faseb.org

May 2–6, 2014

IMMUNOLOGY 2014™ AAI Annual Meeting

The David L. Lawrence Convention Center
Pittsburgh, Pennsylvania
www.immunology2014.org

May 17–21, 2014

CYTO 2014 (International Society for Advancement of Cytometry)

Ft. Lauderdale, Florida
Contact: rjaseb@faseb.org

June 21–25, 2014

The American Society for Virology 33rd Annual Scientific Meeting

Colorado State University
Fort Collins, Colorado
www.asv.org

September 12–16, 2014

ASBMR 36th Annual Meeting

Houston, Texas
www.asbmr.org

Calendar *(continued)*

2015

February 11–15, 2015

2015 BMT Tandem Meeting

San Diego, California

www.cibmtr.org/Meetings/Tandem/index.html

March 28–April 1, 2015

Experimental Biology (EB) (APS, ASPET, ASIP, ASN, AAA, ASBMB)

Boston, Massachusetts

Contact: eb@faseb.org

May 8–12, 2015

IMMUNOLOGY 2015™

AAI Annual Meeting

New Orleans, Louisiana

www.aai.org/Meetings/Future_Meeting.html

July 11–15, 2015

The American Society for Virology
34rd Annual Scientific Meeting

The University of Western Ontario

London, Ontario, Canada

www.asv.org

October 9–13, 2015

ASBMR 37th Annual Meeting

Seattle, Washington

www.asbmr.org

2016

February 18–22, 2016

2016 BMT Tandem Meeting

Honolulu, Hawaii

www.cibmtr.org/Meetings/Tandem/index.html

May 13–17, 2016

IMMUNOLOGY 2016™

AAI Annual Meeting

Seattle, Washington

www.aai.org/Meetings/Future_Meeting.html

Future AAI Annual Meetings

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2014

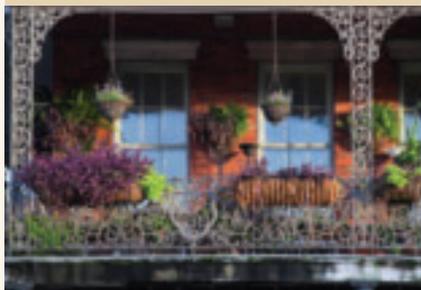


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2015



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May 8–12

New Orleans, Louisiana

2016



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Seattle, Washington

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Commemorative Literature. AAI staff historians and scientists are rigorously researching, archiving, and publishing materials to preserve the proud heritage of the association. Articles posted in the history section of the AAI website, www.aai.org/About/History, include:

- The Founding of AAI
- The Founding of *The Journal of Immunology*
- Immunologists during the First World War: One Soldier-Scientist's Experience
- The 1918–1919 Influenza Pandemic as covered in *The Journal of Immunology*
- The Science at the First AAI Annual Meeting
- Anna Wessels Williams, M.D.: Infectious Disease Pioneer and Public Health Advocate
- Elise Strang L'Esperance, M.D.: Pioneer in Cancer Prevention and Recipient of Lasker Award
- “Studies in Anaphylaxis”: The First Article in *The Journal of Immunology*
- Rebecca Lancefield, Ph.D. (AAI 1933; President 1961–62): PI in the Scotland Yard of Streptococcal Mysteries
- 100 Years of AAI in Hawaii: A Look Back at Two Early Immunologists on the Islands

AAI Website

The www.aai.org/About/History section of the AAI website continues to evolve as a living archive. Current and future resources include:

- Profiles of AAI Nobel and Lasker recipients
- AAI history articles published in the *AAI Newsletter*
- An eBook of commentaries on “Pillars” articles from *The Journal of Immunology*
- Illustrated AAI Centennial Timeline

