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OCTOBER 2019 VOLUME 7 NO. 2



#### A Message from the Outgoing President

It has been an honor to serve as President of our Society, and I want to take this opportunity to thank everyone for the success of our conferences and for making our Society stronger than ever. At a time when politicians may distort scientific findings, I encourage you to reach out to your communities and explain how science matters.

There have been many discoveries and technical advancements that will impact our daily lives: CRISPR-Cas9 applications, the microbiome in health and disease, microfluidic systems and single cell sequencing, immune T cell engineering. Cytokines and interferons are integral to all biological processes.

This year I look forward to meeting you in Vienna... new relationships will be forged, and old ones renewed. Many thanks to Georg Schett and co-organizers for planning Cytokines2019, and to Chris Hunter and Kate Fitzgerald for organizing a terrific Cytokines2018 meeting in Boston. Cytokines 2020 will be hosted by Michael Gale in Seattle and Cytokines 2021 will be hosted by Simon Jones in Cardiff. We all benefit from the leadership of volunteers that tirelessly ensure the success of our annual meetings.

At our conferences we recognize some of the great accomplishments of our members and encourage the achievements of young investigators. We thank Philip and Cheryl Milstein for their continued support of the Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research, Young Investigator Awards, and Travel Awards. Many thanks to BioLegend for sponsoring an Award in memory of William E. Paul for major contributions to cytokine biology. Robert Fleishmann has continued to provide The Christina Fleishmann Award to Young Women Investigators, and Robert Pestka and PBL Assay Science provides the Sidney & Joan Pestka Graduate and Post-Graduate Awards. I'd like to also acknowledge the European Federation of Immunological Societies (EFIS) and the European Journal of Immunology (EJI) for sponsoring the EFIS/EJI Travel Awards for Trainees. Their generosity is appreciated and inspiring.

I have seen how the inner workings of the Society rely on those of you who serve on ICIS Committees: Executive, Council, Meetings, Awards, Publications, Nominations, Development, Finance, Standards, Nomenclature, Communications & Membership. There is not enough room on this page to thank each of you individually. Know that you are appreciated and critical in steering the course of the Society by generously devoting your time. Our future is bright with Kate Fitzgerald taking the helm in 2020; her leadership as President will continue to build the Society. One person in particular who deserves many thanks is Joan Oefner, our Managing Director, for her capability, unbridled enthusiasm and friendship.

My research adventures have been enriched in many ways by sharing ideas with members of our Society from various parts of the globe. Together we have demonstrated that science does not need to be under the same roof to produce fruitful collaborations.

With Best Wishes, Mic Drop,

anci

President 2018-2019

**Future** Meetings Cytokines 2020, November 1 - 4 2020 Hyatt Regency Seattle, Seattle, USA

**Newsletter Editors:** 

**Howard Young** Marta Catalfamo Di Yu / Zhian Chen

**Managing Director:** Joan Oefner



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The Milstein Awards – 30 Years of Support Leading to New Treatments in Immunology, Rheumatology, Cancer, Infectious Disease and Inflammation

The ICIS recognizes two world leaders in deciphering the role of innate immunity in the host immune response.



## AKIKO IWASAKI, PHD

WALDEMAR VON ZEDTWITZ PROFESSOR OF IMMUNOBIOLOGY: MOLECULAR, CELLULAR AND DEVELOPMENTAL BIOLOGY; AND DERMATOLOGY; INVESTIGATOR, HOWARD HUGHES MEDICAL INSTITUTE, YALE UNIVERSITY, NEW HAVEN, USA

The ICIS Awards Committee have chosen Akiko Iwasaki, PhD as one of the two recipients of the 2019 Seymour & Vivian Milstein Award for Excellence in Interferon and Cytokine Research in recognition of her outstanding contributions to the field of immunology, particularly involving interferons and cytokines. Dr. Iwasaki has made major discoveries in the areas of innate anti-viral immunity and mucosal immunity that have resulted in paradigm shifts in our understanding of the immune response and vaccine design. Specifically, Dr. Iwasaki has revealed fundamental mechanisms spanning the activation, function and pathologic roles of type I interferons, from pregnancy to aging. A large body of her work is dedicated to revealing various aspects of interferons and cytokines in viral immunity and host physiology. Her work has direct relevance in several important infectious agents including herpes simplex virus (HSV), influenza virus, rhinovirus, Zika virus and human immunodeficiency virus (HIV).

Akiko Iwasaki received her Ph.D. from the University of Toronto (Canada) in 1998, and her postdoctoral training from the National Institutes of Health (USA) (1998-2000). She joined Yale University (USA) as a faculty in 2000, and currently is an Investigator of the HHMI and Waldemar Von Zedtwitz Professor of Department of Immunobiology, of Department of Molecular Cellular and Developmental Biology, and of Dermatology. Akiko Iwasaki's research focuses on the mechanisms of immune defense against viruses at the mucosal surfaces. Her laboratory is interested in how innate recognition of viral infections lead to the generation of adaptive immunity, and how adaptive immunity mediates protection against subsequent viral challenge.

#### PRESTIGIOUS. IMPORTANT. CELEBRATED

The continued generosity of the Milstein family through the Milstein Foundation, has made a difference to medical research. They have supported the recognition of significant medical breakthroughs by pioneering scientists, as well as ensured the success of our future scientific leaders. Vivian and Seymour Milstein initiated the Milstein Awards for Interferon and Cytokine Medical Research, and their children, Philip and Constance Milstein continue their legacy as generous donors. Their support has made a significant impact on promoting medical science that will benefit the health of society in many years to come. This is the 30th year of the prestigious Milstein Awards, the Milstein Young Investigator Awards, and the Milstein Travel Awards. We are grateful of their selfless philanthropy.

Dr. Iwasaki was the first to demonstrate that DNA viruses are recognized by Toll-like receptor 9 (TLR9), to produce type I interferons and cytokines. This discovery has been replicated and extended by others and is now widely regarded as an underlying mechanism by which TLR9 signals bifurcate to activate interferons vs. cytokines.

She was the first to identify the critical role of autophagy in innate immune recognition of viruses and in antigen presentation. Specifically, she showed that autophagy is required in pDCs to produce type I IFNs. Prior to this work, the role of autophagy in antiviral defense was confined to degradation of viruses. Her studies revolutionized this area of immunology, opening the doors to new ways of thinking about how cells recognize viruses and trigger the appropriate immune responses to fight them.

In a series of studies, Dr. Iwasaki and colleagues demonstrated the NLR inflammasome pathway to be the critical innate sensor responsible for generating protective immune responses against influenza viruses. Her group identified a viral gene responsible for triggering of the inflammasomes, revealed the importance of commensal bacteria in this process, and showed that the cytokine IL-1 is the initiator of adaptive immune responses.

Dr. Iwasaki's recent work demonstrated that interferon induction depends on temperature. At the core body temperature, interferon induction is engaged maximally, whereas the lower temperature found in the nasal cavity dampens this response. These studies provided a possible explanation to the long-standing question as to why we catch the cold virus in cold weather, and have attracted extensive public attention.

Dr. Iwasaki's research revealed that type I interferons play a detrimental role in the context of congenital exposure to Zika virus. On the other end of the spectrum, her work shows that aging significantly impairs interferon induction due to degradation of TRAF3.

Through a series of studies. Dr. Iwasaki demonstrated the critical role of CD4 T cells in antiviral immunity, both as direct antiviral effectors and as gatekeepers for CD8 T and antibody access to restricted tissues. She showed that CD4 T cells mediate migration of CD8 T cells and antibodies through the secretion of cytokine IFNgamma. Her group has contributed to expanding the role of CD4 T cells as an orchestrator of other immune effector mechanisms.

Finally, Dr. Iwasaki made a breakthrough discovery that vaccines against local infections can be improved by establishing memory T cells at the exposure site. Her new method, Prime and Pull, which relies on recruitment of T cells through chemokines such as CXCL9 and CXCL10, has strong potential for clinical use. Dr. Iwasaki is now collaborating with several academic and industrial partners to improve the efficacy of vaccines using her new approach.

It is clear from this that Dr. Iwasaki has made a large impact in several key areas of modern immunology. Her studies are characterized by originality and high impact. Her publications are highly cited and highly regarded by her colleagues. Most importantly, her discoveries have led the way to understand the immune response to important pathogens, with major implications for basic science and medicine.

## **2019 ICIS** THE SEYMOUR AND VIVIAN MILSTEIN AWARDEES for Excellence in Interferon and **Cytokine Research**



## HAO WU, PHD

ASA AND PATRICIA SPRINGER PROFESSOR OF STRUCTURAL BIOLOGY. DEPARTMENT OF BIOLOGICAL CHEMISTRY AND MOLECULAR PHARMACOLOGY, HARVARD MEDICAL SCHOOL, AND PROGRAM IN CELLULAR AND MOLECULAR MEDICINE, BOSTON CHILDREN'S HOSPITAL, BOSTON, USA

The ICIS Awards Committee have chosen Hao Wu, PhD as one of the two recipients of the 2019 Seymour & Vivian Milstein Award for Excellence in Interferon and Cytokine Research in recognition of her unparalleled contributions to the molecular mechanisms of cytokine signaling. Her in-depth mechanistic elucidation of many important protein complexes, in particular those used by the tumor necrosis factor receptor (TNFR) family, the Toll-like receptor/interleukin 1 receptor (TLR/IL-1R) family and the inflammasomes, not only changed how we understand cytokine-induced programmed cell death and immunity, but also presented a new paradigm for immune cell signaling.

Dr. Wu received her pre-medical training at Peking University from 1982 to 1985 and studied Medicine at Peking Union Medical College from 1985 to 1988. She obtained her Ph.D. degree in Biochemistry from Purdue University in 1992, working in the laboratory of Professor Michael Rossmann. After performing postdoctoral training at Columbia University in the laboratory of Professor Wayne Hendrickson, she became an Assistant Professor at Weill Cornell Medical College in 1997 and was promoted to Professor in 2003. In 2012, Dr. Wu moved to Harvard Medical School as the Asa and Patricia Springer Professor of Structural biology in the Department of Biological Chemistry and Molecular Pharmacology, and Senior Investigator in the Program in Cellular and Molecular Medicine of Boston Children's Hospital.

Dr. Wu has received a number of honors, including the Howard Hughes Medical Institute pre-doctoral fellowship, the Aaron Diamond postdoctoral fellowship, the Pew Scholar award, the Rita Allen Scholar award, New York Mayor's Award for Excellence in Science and Technology, the Margaret Dayhoff Memorial Award from the Biophysical Society and most recently, the Dorothy Crowfoot Hodgkin Award from the Protein Society. She serves on the Scientific Advisory Council of the Cancer Research Institute and the Editorial Board of Cancer Cell.

Over two decades of research at Weill Cornell and Harvard. Hao has achieved an integrated understanding of protein signaling complexes generically denoted as "signalosomes". She is internationally recognized for uncovering several fundamental themes in signal transduction of the immune system using structural biology approaches. Most notably, Hao revealed that, under physiological as well as pathological conditions, proteins of the death domain (DD) superfamily may assemble into higher-order structures with helical symmetry by a nucleated polymerization mechanism. She drew parallels between DD helical assembly and cytoskeletal filaments, and discovered that DD assembly is stabilized by three types of evolutionarily conserved protein-protein interactions. She then related these higher-order structures to their crucial signaling roles, where the assembly process concentrates signaling molecules such as caspases and kinases, rapidly amplifies signals, and mounts all-or-none threshold responses. Beyond providing structural and molecular basis for many key pathways in programmed cell death and immunity, her discoveries also spawn the development of therapeutics against diseases ranging from autoimmune disorders to cancer.

The following are a few studies highlighting Hao's seminal research achievements:

To begin with, her lab provided insightful analysis on receptorbinding and ubiquitin ligase activity of TRAF proteins. She solved the first structure of a TRAF family member, TRAF2, and its complexes with peptides from a number of intracellular receptor tails and with TRADD (Park et al. Nature 1999; Ye et al. Molecular Cell, 2000; Park et al. Cell 2000). These structures not only revealed the trimeric structural architecture of TRAFs, but also defined sequence motifs for TRAF2 interaction that have been used widely by biologists to search for binding sites of TRAFs in proteins. She continued her work to TRAF6, a unique TRAF family member that is involved in the signaling of TLRs and IL-1Rs in addition to TNFRs. Her work identified a TRAF6-binding motif that is different from those used for TRAF2, and that is used widely for finding binding sites of TRAF6 in proteins (Ye et al., Nature 2002, Yin et al., NSMB 2009). TRAFs have RING domains that may serve as ubiquitin ligases. Her work illuminated the field by showing that only the RING domain of TRAF6, but not of TRAF2, can interact with E2 ubiquitin conjugating enzymes, rebutting an earlier misbelief in the field with regards to the ubiquitin ligase activity of TRAF2 (Yin et al. Biochemistry 2009). She further dissected the interaction between TRAF2 and cIAP1/cIAP2, suggesting that the apparent ubiquitin ligase activity of TRAF2 comes from the associated cIAP proteins (Zheng et al. Molecular Cell 2010).

On a second thread, her laboratory provided a rigorous and unprecedented detailed analysis of the Myddosome (MyD88-IRAK4-IRAK2) involved in TLR/IL-1R signaling (Lin et al., Nature 2010). The crystal structure of the Myddosome complex surprisingly reveals the helical, nucleated polymerization of DD proteins dictated by shape and electrostatic complementarity, which provides an elegant mechanism for signal transduction. Following this discovery, Hao's group found that this assembly mechanism is also employed by inflammasomes (such as the NLRP3-ASC-Caspase-1 inflammasome), the intricate supramolecular complexes that are activated by diverse microbial and damage- associated signals to trigger immune response (Lu et al., Cell 2014). It turns out that nucleated polymerization is a unified mode of protein assembly and has far-reaching impacts in biology, as Hao's laboratory elucidated with high-resolution structures of a death inducing signaling complex in apoptosis (Wang et al., NSMB 2010) and a signalosome in B-/T-cell receptor pathways (Qiao et al., Molecular Cell 2013). In more recent years, she uncovered how NLR-like proteins such as NLRC4 form inflammasomes using an ATPase-driving disk-like assembly architecture (Zhang et al., Science 2015), and she is now extending this mechanism to the NLRP3 inflammasome. Moving on from conventional signalosomes that function by recruiting downstream proteins, Hao now also investigates complexes that act as effectors of signalosomes. For instance, the recently identified gasdermin family mediates intercellular signaling by forming pores on the plasma membrane to allow cytokine release. To address the molecular mechanism of pore formation, Hao led her group to the functional characterization and structural determination of a gasdermin membrane pore (Ruan et al., Nature 2018), a study that significantly advanced the field of innate immunity.



#### **Honorary Lifetime Membership Award**

Nominations are solicited for Honorary Life Memberships in the ICIS. Each year an individual will be awarded Life Membership as a tribute to his/her contributions to the field. Nominees should be individuals who have made substantive contributions to the cytokine/ chemokine/ interferon field over much of their careers, either in basic, clinical or applied research. Honorary members are esteemed members of the Society and provide us with an historical perspective and valued research tradition.



## KOUJI MATSUSHIMA, MD, PHD

DIVISION OF MOLECULAR REGULATION OF INFLAMMATORY AND IMMUNE DISEASES. RESEARCH INSTITUTE FOR BIOMEDICAL SCIENCES, TOKYO UNIVERSITY OF SCIENCE. CHIBA. JAPAN

Prof. Kouji Matsushima is currently Professor of Division of Molecular Regulation of Inflammatory and Immune Diseases, Research Institute for Biomedical Sciences, Tokyo University of Science. Dr. Matsushima is awarded the 2019 ICIS Honorary Lifetime Membership Award in recognition of his exceptional contributions to cytokine and chemokine research, from basic research to translational research and to clinical therapies. In addition to his major scientific achievement in cytokine and chemokine fields, he served as a senior council member of the ICS (International Cytokine Society) and as president of the Cytokines 2017, 5th Annual Meeting of the International Cytokine & Interferon Society organizing committee.

Dr. Matsushima graduated from Kanazawa University Medical School in 1978 and received his Ph. D. from Kanazawa University, Graduate School of Medicine in 1982. After getting his degree, he immediately joined the National Cancer Institute, USA as a Fellow in the Biological Response Modifiers Program located in Frederick, MD.

The prelude to the discovery of chemokines: There was fierce competition in cDNA cloning research in the 1980s. Dr. Matsushima joined the laboratory of Dr. Joost J. Oppenheim in October 1982. He succeeded in purifying human IL-1alpha and IL 1beta. His purification confirmed the correctness of cDNA cloning of human IL 1 beta precursor by Phil Auron et al. in 1984, and identified the mature and active form of human IL 1beta (cleavage site of ICE/Caspase 1). He also confirmed the biological activities ascribed previously to IL-1, such as thymocyte co-mitogenic activity, stimulation of fibroblast proliferation, endogenous pyrogen activity and acute phase protein-inducing activity.

Purification and cDNA cloning of human interleukin-8 (CXCL8): In the 1970's, leukocyte-derived neutrophil chemotactic factor (NCF) and monocyte chemotactic factor (MCF) were described in the literature, but their molecular nature remained unclear. Before his purification and cDNA cloning of IL-8, IL-1 and tumor necrosis factor had been considered responsible for the chemotactic activity. To his surprise, neither his purified IL-1s nor recombinant TNF alpha displayed the chemotactic activity.

The neutrophil chemotactic activity was detected in the conditioned media that he used for the IL-1 purification. In 1986, Dr. Teizo Yoshimura joined Ed Leonard's laboratory as a postdoctoral fellow and Dr. Matsushima mentioned to Dr. Yoshimura the mysterious and intriguing phenomenon of neutrophil chemotactic activity in the conditioned media of activated human leukocytes, and they decided to characterize and clone the cDNA in collaboration (KM acted as PI). They could easily separate neutrophil chemotactic activity from IL-1 activity by HPLC gel filtration, and succeeded in purifying 400 µg of NCF from 4 L of LPS- stimulated human PBMC conditioned medium. Dr. Matsushima cloned, by himself, from the construction of the cDNA library to DNA sequence analysis, the cDNA from LPS-stimulated human PBMCs based on the amino acid sequence information of the purified NCF, To confirm that the cloned cDNA really did encode the NCF protein, they chemically synthesized 72 amino acids deduced from the cDNA sequence, expressed the recombinant NCF in E. coli. made a monoclonal antibody against the recombinant NCF. Dr. Matsushima published a paper describing the cDNA cloning of NCF in J. Exp. Med. In 1988. Dr. Howard Young can add a personal note to this story as he was in my office a bit late in the day and Dr. Matsushima came rushing in with his x-ray film showing what appeared to be a positive plaque and indeed the one spot turned out to be IL-8.

#### Purification and cDNA sequencing of MCAF/MCP-1(CCL2):

When Dr. Chris Larsen from Denmark joined NCI in 1988, he re-examined the MCF activity in the conditioned media that he used for IL-1 purification, and found that there was too much activity in the media, and that it was necessary to make a 1,000 fold dilution in order to detect MCF activity (it was well known that too high a concentration of chemotactic factor inhibits cell migration). Since MCF activity could be adsorbed by a heparin column in the same way as IL-8, it was really easy to purify MCF from THP-1 conditioned media, and Dr. Matsushima completed the entire purification procedure in a week (J. Exp. med. 1989). However, it took several weeks to obtain partial amino acid sequence information for MCF because of a blockade of the N-terminal by pyroglutamate formation. Dr. Matsushima collaborated with Dr. Masaaki Yamada (Dainippon Pharmaceuticals. Co. Ltd.) in the cDNA cloning of MCF. They successfully obtained international patent rights. Independently,

Dr. Yoshimura, in Dr. Leonard's lab, purified the same MCF protein simultaneously, but independently from different cell line conditioned media. Dr. Matsushima named this molecule MCAF based on its chemotactic and activation effects on monocytes, while Dr. Yoshimura named it MCP-1.

Dr. Matsushima was awarded tenure at the NCI but in 1990 he returned to Kanazawa University, his alma mater and became a professor at the age of 37. In his new position, he began trying to establish the role of chemokines in inflammatory and immune diseases. A number of papers resulted from these efforts, including Prevention of lung reperfusion injury in rabbits by a monoclonal antibody against interleukin-8 (Nature 1993), Prevention of proteinuria by the administration of anti-interleukin 8 antibody in experimental acute immune complex-induced glomerulonephritis (J Exp Med. 1994.), and Intervention of crescentic glomerulonephritis by antibodies to monocyte chemotactic and activating factor (Faseb J. 1996.) Those studies first established the in vivo roles of chemokines controlling cell-type specific leukocyte infiltration during inflammation. He moved to The University of Tokyo in 1996, and made numerous monoclonal antibodies against N-terminal regions of human chemokine receptors using hybridoma technology, and he found that only one clone among several hundred clones recognizing CHO-chemokine receptor transfectants recognized natural CCR4 on human T lymphocytes. He subsequently found that CCR4 is selectively expressed on the CD4+Th2 population and also aberrantly and highly expressed on adult T cell leukemia (ATL) cells (in collaboration with Dr. Osamu Yoshie). He then collaborated with Kyowa-Hakko Co. Ltd., Japan to convert the murine monoclonal antibody to a humanized antibody with potent ADCC activity and succeeded in the clinical development of this novel reagent. This humanized anti-CCR4 antibody (mogamulizumab) has been approved as a therapy for adult T cell leukemia (ATL), and other types of CCR4+T cell leukemia and lymphoma, such as Sezary's syndrome and Mycosis fungoides in the USA, Europe and Japan. In addition, this antibody also turned out to deplete Treg cells (CCR4++) very efficiently. Therefore, numerous clinical trials of this anti-CCR4 antibody particularly in combination with various immune-check point antibodies are being carried out as a means to deplete regulatory T cells in cancer patients.



The ICIS will on occasion bestow this honor on an ICIS member who has made an extraordinary contribution to the Society. The individual will have devoted significant time and energy over a period of years to elevating the goals of the Society in furthering research on interferon, cytokines and chemokines.



## BRYAN R.G. WILLIAMS, PHD, HON. FRSNZ, FAA

HUDSON INSTITUTE OF MEDICAL RESEARCH, CLAYTON, AUSTRALIA

Bryan R. G. Williams, PhD, Hon. FRSNZ, FAA is honored with the 2019 ICIS Distinguished Service award in recognition of his extraordinary contributions to the cytokine research community.

Professor is Williams is Emeritus Director and Distinguished Scientist, Hudson Institute of Medical Research, Professor, Department of Molecular and Translational Science, Monash University. A distinguished researcher and international authority on innate immunity and cancer biology, Professor Bryan Williams has made major contributions to our understanding of the antiviral mechanisms of actions of interferons, advancing their therapeutic utility. His discoveries in the 2-5A-RNaseL pathway, cloning and characterization of protein kinase R, and innate immune signaling pathways have opened new therapeutic opportunities.

Professor Williams received his PhD from the Department of Microbiology at the University of Otago, Dunedin, New Zealand. Following postdoctoral training at the National Institute for Medical Research, Mill Hill, London, he held faculty positions at the University of Toronto and the Hospital for Sick Children, Toronto, Canada. He was Chairman of the Department of Cancer Biology at the Lerner Research Institute, Cleveland Clinic Foundation, USA, from 1991 until joining the Monash Institute of Medical Research as Director in 2006 (now Hudson Institute of Medical Research). He served as Hudson Institute Director and CEO until July 2017.

As the 1990 recipient of the prestigious Milstein Award, the International Society for Interferon Research recognised Professor Williams for his contributions to advancing interferon research for the treatment of human diseases. Elected as an Honorary Fellow of the Royal Society of New Zealand in 1997, Professor Williams served as President of the International Society for Interferon and Cytokine Research from 1998 to 1999. In 2005, he shared the Maurice Saltzman Award from the Mt Sinai Health Care Foundation, for his leadership contribution to the Case Comprehensive Cancer Center and in 2006 received the Dolph Adams Award for the most highly cited review article published in the Journal of Leukocyte Biology. In 2008, he received the Boltzmann Award for international research collaboration, awarded by the European Cytokine Society. In 2013, he was elected as a Fellow of both the Australian Academy of Science and the American Academy of Microbiology.

Professor Williams is Chair of the Board of BioGrid Australia Ltd, and serves on the Boards of Pacific Edge Ltd, Pacific Edge Pty Ltd, Pacific Edge Diagnostics Singapore Pte Ltd, XYnapse Therapeutics Pty Ltd and Cartherics Pty Ltd. He is Chair of the Biopharmaceuticals, Biomaterials and Medical Devices Advisory Committee for Therapeutic Innovation Australia, and is a Member of the Board of Trustees and a Member of the Scientific Advisory Council of the Hope Funds for Cancer Research (Newport, RI, USA).

He is also a Member of the Scientific Advisory Boards of BioGrid Australia Ltd and Pacific Edge Ltd, a Member of the Scientific Review Panel for the Malaghan Institute (New Zealand), a Member of the International Science Advisory Panel for Healthier Lives (New Zealand) and a Scientific Advisor to EnGeneIC Ltd. He is currently Chair of the Award Committee for the International Cytokine and Interferon Society (ICIS) and is a Member of the ICIS Nomination Committee. He is also a Member of the Gottschalk Medal Awards Committee for the Australian Academy of Science, and a Member of the Steering Committee of the Australian Living Organoid Alliance (ALOA).

Professor Williams is an Editor for the Journal of Virology, and serves on the Editorial Boards of the Journal of Interferon and Cytokine Research, Viral Immunology, Cytokine and Growth Factor Reviews and Frontiers in Cancer Genetics, and is a Faculty Member of F1000Prime.

The 2019 ICIS Distinguished Service Award acknowledges Williams' accomplishments noted above as well as his commitment to the ICIS and to him being an outstanding ambassador for the Society, in every regard.

Since 1983 Bryan has been an active and contributing member of first the ISICR, then most recently, the ICIS. Summarized below, his numerous contributions to the ICIS, beyond his research contributions to the field, some of which are highlighted below:

- 1992 Bryan was chair of the Organizing Committee (with Eleanor Fish and Dan Skup), ISICR Annual Meeting, Toronto, Canada and Co Chair (with George Stark) Organizing Committee, ISICR 2001 Annual Meeting, Cleveland, Ohio
- 1996 1999 President-Elect and then President, International Society for Interferon and Cytokine Research
- 1999 2000 and 2004 Board of Directors of the ISICR

Bryan was a member of the International Scientific Organizing Committees for the following Annual Meetings:

- ISICR-ICS 2006 6th Joint Meeting, Vienna, Austria
- 2008 ISICR/ICS Conference, Montreal, Canada, 12-16 Oct 2008
- 9th Joint Meeting of the ICS/ISICR, Florence, Italy, 9-12 Oct 2011
- Cytokines 2014: 2nd Annual Meeting of the International Cytokine and Interferon Society (ICIS), Melbourne, Australia
- 2016 2018 Member of the ICIS Nominations Committee
- 2017 2019 Co-Chair (with Kate Fitzgerald), ICIS Awards Committee

## 2019 THE ICIS-BIOLEGEND **WILLIAM E. PAUL AWARD** for Excellence in Cytokine Research





## CHEN DONG, PHD

PROFESSOR AND DIRECTOR OF THE INSTITUTE FOR IMMUNOLOGY AND DEAN OF THE SCHOOL OF MEDICINE, TSINGHUA UNIVERSITY, BEIJING, CHINA

The ICIS Awards Committee have chosen Chen Dong, PhD as the recipient of the 2019 BioLegend William E Paul Award for Excellence in Cytokine Research in recognition of his transformative research in immunology, including ground-breaking discoveries in the field of T cell biology and IL-17 family cytokines. Dr. Dong's research focuses on understanding the molecular mechanisms whereby immune and inflammatory responses are normally regulated, and to apply this knowledge to the understanding and treatment of autoimmunity and allergy disorders as well as cancer.

Dr. Chen's lab has made seminal contributions to the field of CD4 T cell subsets. In addition to Th1 and Th2 cells discovered in 1986, Chen and others independently discovered Th17 lineage cells in 2005, which are crucial in inflammatory diseases. His group conducted a series of work to identify the key transcription factors and cytokines in Th17 cell development. His group also characterized the roles of Th17 cells in inflammatory diseases and cancers.

In 2008-2009. Chen and others defined another T cell subset - T follicular helper cells, which critically regulates humoral immunity. He first proposed these cells as a distinct subset of T cells and then independently discovered Bcl6 as the necessary factor for the development of these cells. His group also co-identified the T follicular regulatory (Tfr) cells that inhibit germinal center reactions.

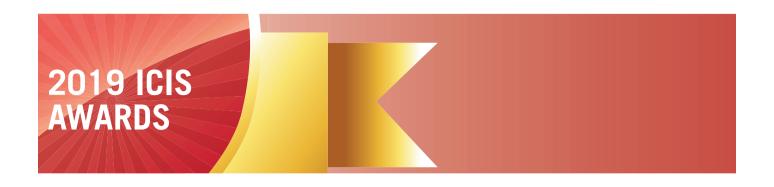
In addition, Chen and his colleagues have systemically analyzed the function of IL-17 family cytokines in the

immune system. They applied mouse genetic approaches to identify key functions of IL- 17A, IL-17F, IL-25/ IL-17E, IL-17C and IL-17B as well as their receptors in inflammatory diseases. They were the first to find Act1 as an adaptor for the signaling of IL-17 family cytokines.

Hence, Chen has conducted groundbreaking and systemic research on T cells and cytokines. These finding have improved our understanding of human diseases and led to novel treatments. For example, antagonizing Th17 cell function has been approved to treat autoimmune diseases psoriasis and ankylosing spondylitis.

He has published more than 200 papers and is a Highly Cited Researcher from 2014 - 2018. He was Young Investigator awardee of the International Cytokine & Interferon Society and was given the American Association of Immunologists BD Bioscience Investigator Award In 2009. He was elected fellow of the American Association for the Advancement of Science in 2011. He currently serves as Editor -in-chief for T Cell Biology Section of Frontiers in Immunology and editorial board member of Immunity.

Chen was a Professor of Immunology and the Director of the Center for inflammation and Cancer at the University of Texas MD Anderson Cancer Center before joining Tsinghua University. He is the founding director of the Institute for Immunology at Tsinghua University, a dynamic immunology research center in the world. Chen became the Dean for the School of Medicine at Tsinghua University in 2016.



### MILSTEIN YOUNG INVESTIGATOR AWARDS



**JUAN LUIS MENDOZA** THE UNIVERSITY OF CHICAGO, CHICAGO, USA

STRUCTURE OF THE INTERFERON GAMMA RECEPTOR COMPLEX REVEALS A MECHANISM FOR DECOUPLING PLEIOTROPY

**Oral Presentation: Sunday 20 October 2019 I 18:35 - 18:45,** in the Opening Session in the Festsaal



**LESIONS** 

SARAH DOYLE TRINITY COLLEGE DUBLIN, DUBLIN, **IRELAND** INTERLEUKIN-18 ALTERS CELLULAR

ORGANIZATION IN CHOROIDAL NEOVASCULAR

Oral Presentation: Wednesday 23 October 2019 | 12:40 - 12:50, in the Session: Cytokine-mediated resident tissue destruction and fibrotic responses - in the Festsaal



**JUAN FUXMAN BASS** BOSTON UNIVERSITY, BOSTON, USA MAPPING OF THE HUMAN CYTOKINE GENE EGULATORY NETWORK

Oral Presentation: Monday 21 October 2019 | 11:10 - 11:35. in the Session: Induction of immune tolerance -fact or fiction? in the Zeremoniensaal



**YUXIN WANG** 

CLEVELAND CLINIC, CLEVELAND, USA PHOSPHORYLATION OF STAT2 ON T404 IS CRITICAL FOR INTERFERON-MEDIATED SIGNALING AND ANTIVIRAL DEFENSE

Oral Presentation: Wednesday 23 October 2019 | 10:15 - 10:25, in the Session: Type I interferons: biology and their role in disease in the Festsaal



RYAN A. LANGLOIS UNIVERSITY OF MINNESOTA, MINNEAPOLIS, USA MODEL FOR STUDYING INTERFERON-MEDIATED CONTROL OF INTER- AND INTRA-SPECIES VIRUS TRANSMISSION

Oral Presentation: Wednesday 23 October 2019 | 10:35 - 10:45, in the Session: Type I interferons: biology and their role in disease in the Festsaal

AND EVOLUTION

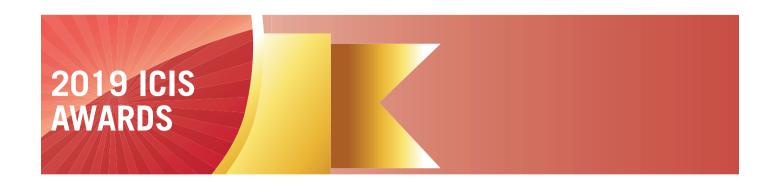
## THE CHRISTINA FLEISCHMANN AWARD TO YOUNG WOMEN INVESTIGATORS



MEIKE DITTMANN, NYU SCHOOL OF MEDICINE, NEW YORK, USA

THE ETS TRANSCRIPTION FACTOR ELF1 TRIGGERS A CRITICAL WAVE OF GENE EXPRESSION IN THE ANTIVIRAL RESPONSE TO TYPE I INTERFERON

Oral Presentation: Wednesday 23 October 2019 I 10:25 - 10:35 , in the Session: Type I interferons: biology and their role in disease in the Festsaal





## THE SIDNEY & JOAN PESTKA POST-GRADUATE AND GRADUATE AWARDS

#### The Sidney & Joan Pestka Post-Graduate Award



**BILLUR AKKAYA** 

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, BETHESDA, USA

TBET PROVIDES SURVIVAL ADVANTAGE TO TREGS DURING SYSTEMIC INTERFERON GAMMA DRIVEN **IMMUNE RESPONSES** 

**Oral Presentation: Monday 21 October 2019 | 14:05 - 14:15,** in the Session: Oral Abstract Session with a focus on T Cells - in the Festsaal

The Sidney & Joan Pestka Graduate Award



**ANUKRITI MATHUR** 

AUSTRALIAN NATIONAL UNIVERSITY, CANBERRA, AUSTRALIA

A MULTI-COMPONENT BACTERIAL TOXIN INCITES HOST INFLAMMATION VIA THE NLRP3 INFLAMMASOME

**Oral Presentation: Wednesday 23 October 2019 I 12:40 - 12:50,** in the Session: Local and systemic effects of IL-1 family cytokines in disease - in the Zeremoniensaal



## SEE WHAT IS HAPPENING IN THE CAREERS AND LABS OF SOME OF OUR PREVIOUS MILSTEIN YOUNG INVESTIGATOR AWARD WINNERS.



#### ANDREAS BERGTHALER

I studied veterinary medicine at the University of Veterinary Medicine in Vienna and performed his graduate studies at the Institute of Experimental Immunology at the University/ ETH Zurich (Dr. Hans Hengartner and Nobel Laureate Dr. Rolf Zinkernagel). After postdoctoral work in the laboratory of Dr. Alan Aderem's group at the Institute for Systems Biology in Seattle I started my own group at the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences in Vienna, Austria.

Our major scientific focus rests on the molecular mechanisms that underlie and drive tissue pathologies in infectious diseases. Integrative approaches of infection models coupled to virological, immunological and pathological readouts are complemented by systems-level technologies such as next-generation sequencing. mass spectrometry and metabolomics. Hypothesis- and datadriven leads are pursued to provide inclusive perspectives on host-pathogen interactions at the organ and organism level. A particular research focus rests on the multi-faceted role of type I interferons (IFN-I) and their role in immunoregulation and immunopathologies. My laboratory uncovered mechanisms

of how the IFN-I induced histone methyltransferase Setdb2 increases susceptibility to bacterial superinfections (Schliehe C et al. Nature Immunology 2015) and how IFN-I induces oxidative stress and tissue damage in viral hepatitis (Bhattacharya A et al. Immunity 2015). Recent discoveries since receiving the Milstein Young Investigator Award include the surprising role of IFN-I signaling competent CD8 T cells in driving infectionassociated cachexia (Baazim H et al. Nature Immunology 2019) and cytokine-induced metabolic rewiring of the liver during viral infection (Lercher A et al. in Revision). My group also investigated the mechanistic basis of Tasmanian devil facial tumor disease, a peculiar disease which already killed an estimated 80-90% of the wild population of the largest carnivorous marsupial species. Our research resulted in a landmark paper describing the hyperactivated ERBB-STAT3 signaling axis and its suppressive effects on MHC class I expression in transmitted cancer cells, providing new molecular and immunological insights into the lack of rejection (Kosack L et al. Cancer Cell 2019). I am also co-founder of the Nasdaq-listed clinical-stage company Hookipa Pharma Inc., which develops viral vectors for immunotherapeutic applications in malignant and infectious indications.

# Where Are They Now?

## SEE WHAT HAS HAPPENED TO PREVIOUS MILSTEIN YOUNG INVESTIGATOR WINNERS!



DUSAN BOGUNOVIC

I was honored by 2015 Milstein Young Investigator Award as an Assistant Professor in Dept. of Microbiology at Icahn School of Medicine at Mt. Sinai in NY, NY, USA. It truly gave me prominence and introduced me to leadership of ICIS and integrated me into this welcoming society. I soon became a part of the Membership Committee, which I now chair with Howard Young. It also galvanized my recognition beyond ICIS. In 2016 I was honored by Young Investigator Award – American Society for Microbiology, in 2017 by Lamport Research Award-Icahn School of Medicine at Mt. Sinai, in 2018 I was selected as the Johnson and Johnson Quickfire Challenge Winner and in 2019 I was honored by Hirschl Scholar Award- Icahn School of Medicine at Mt. Sinai. In 2019, I was also promoted to an Associate Professor of Microbiology, Pediatrics, The Mindich Child Health and Development Institute and Precision Immunology Institute at Mt. Sinai. I continue working in the fields of cytokine biology, with a particular interest in Type I Interferons, human genetics, and inborn errors of immunity. Scientific discovery is wonderful and having a community around one's interest in key to rapid progress. I am looking forward to the upcoming decades.





STACY HORNER

I am an Assistant Professor in the departments of Molecular Genetics & Microbiology and Medicine at the Duke University School of Medicine, where I am also the Co-director for the Duke Center for RNA Biology. My research broadly studies the virus-host interactions that control the outcome of infection to viruses in the Flaviviridae family. We focus on defining (1) how these viruses replicate. (2) the mechanisms that regulate antiviral innate immunity to these viruses, and (3) the post-transcriptional RNA regulatory controls to both of these processes. For these efforts, I have received the Ann Palmenberg Junior Investigator Award from the American Society for Virology, the ASM Microbe Junior Investigator Award, the Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease Award, and both the Milstein Young Investigator Award and the Christina Fleischmann Award from the International Cytokine and Interferon Society. I am incredibly passionate about mentoring young scientists of all backgrounds, and so in addition to mentoring undergraduates and PhD candidates in my own lab. I serve as a faculty advisor for our departmental graduate student Women in Science program and have been a member of the Duke Biocore training program. which is committed to promoting diversity and inclusivity in biomedical research. I currently serve on the Membership and Communications Committee for the International Cytokine and Interferon Society.



JOHN SCHOGGINS

I received the Milstein Young Investigator Award in 2013, shortly after I started my independent faculty position in the Department of Microbiology at UT Southwestern Medical School. Over the past 6 years, my lab has continued studying virus-host interactions with an emphasis on the interferon-mediated antiviral immune response. For these efforts, the lab has been awarded an NIH New Innovator Award and received funding awards from The Rita Allen Foundation, The Clayton Foundation, The Burroughs Wellcome Fund, The Welch Foundation, and The American Lung Association. Most of these grants were obtained based on the work of the incredibly talented trainees that have come through the lab. I am thrilled that we have had 4 PhD students defend their theses. Three have moved on to postdoctoral positions, and one has returned to medical school to complete the combined MD/PhD program. As a result of the efforts of these students and the other amazing lab members, I was recently promoted to Associate Professor with tenure. I am grateful for the opportunity to continue working on such an exciting area of interferon biology in a highly supportive and collaborative institution.



DI YU

In 2016, I received the Milstein Young Investigator Award from International Cytokine & Interferon Society (ICIS). I was then recruited to the Australian National University as an Associate Professor in 2017. In Nov 2019, I will be appointed as Professor and join the University of Queensland Diamantina Institute, Brisbane, Australia.

In the Laboratory for T-cell Immune Mechanism Monitoring and Modulation (TIM3), my team is investigating the molecular mechanisms by which T cells control the competence and balance of the immune system, with the aim to design cytokine-based therapies to modulate the immune system to treat autoimmune disease, infection and cancer.



ARI MOLOFSKY

I received my BS in Molecular Biology from the University of Texas in 1999 and MD PhD from the University of Michigan in 2007. Following residency and fellowship training in clinical pathology and hematopathology, I did a research fellowship at UCSF and began my laboratory in 2015 at UCSF. In 2019 I became an Associate Professor, in line, at UCSF. My laboratory goal is to understand the regulation and function of tissueresident immune cells in order to define novel pathways that can be targeted in diverse human diseases, including obesity/ type 2 diabetes, allergic pathologies (asthma, allergy), and neuropsychiatric disease. Our group is focused on type-2 immune-associated lymphocytes, including group 2 innate lymphoid cells (ILC2) and subsets of regulatory T (Treg) cells, and the 'niche' stromal cells and signals involved in their regulation. These tissue resident immune cells are early organizers of tissue remodeling and first responders during tissue damage and infection, positioning them as key mediators of tissue health and disease. Our lab has recently defined a perivascular ILC2 niche in multiple tissues, including lung, adipose tissue. and brain meninges. We are using multimodal approaches such as 3D imaging, single cell transcriptomics, and cytokine reporters to dissect these critical immunemicroenvironment interactions.



The Japanese Society of Interferon and Cytokine Research (JSICR) is sponsoring a session at Cytokines2019, as in Cytokines2018. Three distinguished speakers will speak about their studies on cytokine-mediated diseases after checkpoint blockade.

#### JSICR-sponsored session (Oct 22); Cytokine-related diseases after checkpoint inhibition

Dr. Lucie Heinzerling: She is dermato-oncologist and specialist in the clinical manifestations of cytokinemediated inflammation after checkpoint blockade.

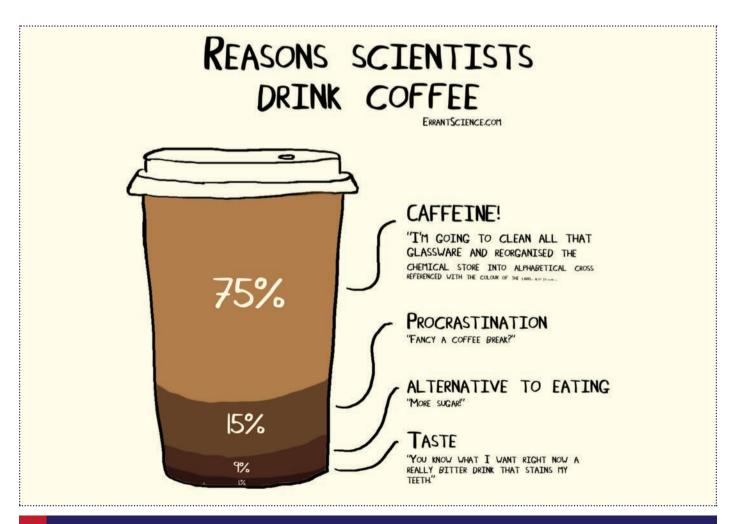
Dr. Taku Okazaki: He is a Professor at Tokushima University. He was also a member of Prof. T. Honios' laboratory, the 2018 Nobel Laureate. His current studies are based upon his previous PD-1/PD-L1 work in the Honio laboratory and his talk will focus on basic research questions in checkpoint inhibitor function.

Dr. Shintaro Iwama: He is a lecturer at Nagoya University and is a clinician specializing in endocrinology. His main focus includes autoimmune diseases (esp. inflammation of pituitary gland) that occur following CTLA-4 blockade and his talk will be on the issues facing clinicians as a consequence of using checkpoint inhibitors.

Oral Presentation: IMMUNE CHECKPOINT RECEPTOR LILRB4: A NEW PLAYER IN REGULATING VIRAL INFECTION, Daniela Verthelyi (United States),

Oral Presentation: INTERLEUKIN-6 IS ASSOCIATED WITH RESISTANCE TO ANTI-PDL1 TUMOR IMMUNOTHERAPY AND PROMOTES THERAPEUTIC RESISTANCE BY INHIBITING CD8+ T CELLS, Nathaniel West (United States)

Akinori Takaoka, President of JSICR







#### www.cytokinesociety.org



The new open access journal *Signals*, owned by ICIS, is open and ready for business (<a href="https://signals.biomedcentral.com">https://signals.biomedcentral.com</a>). The rationale for starting *Signals* came from the realization that many ICIS members, and readers, did not have free access to existing ICIS journals that are publisher owned. As open access, *Signals* is free to any reader from any institution. Springer Nature BMC made an attractive bid to publish the new journal, returning revenues to ICIS, and the Council enthusiastically approved the contract. Jan Vilcek generously donated funds for the initial costs. An outstanding editorial board was assembled (shown below). Revenues will be used to support the annual conference, scholarships, awards and other ICIS functions.

Our aim with *Signals* is to create a journal with significant impact in the areas of immunological signals to include cytokines, chemokines and growth factors, signal transduction, microbial and endogenous danger signals. Original studies can be at the levels of basic, translational and clinical research. *Signals* will publish editorial pieces, letters, interviews and is open to suggestion for other materials of interest to the community.

To launch *Signals* with a significant impact, we are publishing definitive reviews on individual cytokines and chemokines from recognized experts in the field. Thus far we have commitments from these authors and their colleagues: Charles Dinarello (IL-1), Achsah Keegan (IL-4), Tadamitsu Kishimoto (IL-6), Scott Durum (IL-7), Kouji Matsushima and Joost Oppenheim (IL-8), Dario Vignali (IL-35), Michael Dougan (GM-CSF), and Amanda Proudfoot (Rantes CCL5). Other definitive reviews are projected to cover important cytokines and chemokines over the next few years. Although there are many focused reviews available, we believe these definitive reviews on individual cytokines are much needed by the community. We believe these will be highly cited, establishing *Signals* as a vehicle for significant original research findings

It may take a few years for *Signals* to attract many papers that are at the level we are aiming for, but we intend to be quite selective. We are excited about this and extremely grateful to the many enthusiastic ICIS supporters who have contributed to its development. We welcome submissions of work that advances the field of immunological signals, cytokine biology and medicine, and we promise timely review by experts.

Scott K. Durum - Editor in Chief Cristina Bergamaschi - Senior Editor

#### Signals Editorial Board

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We welcome these new members to the ICIS and we look forward to their attendance at the annual meeting and involvement in the society. The ICIS Membership Committee and Council especially thanks the Sponsoring Members noted below. Special thanks to Professor Richard Moriggl, professor for Functional Cancer Genomics in a joint appointment of the University for Veterinary Medicine. Vienna and the Medical University Vienna, for sponsoring four new members! As of August 20, 2019, there are 913 ICIS Members: 436 from the USA and 477 from outside the USA.

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#### Pengcheng Zhou

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Research Advisor: Ting Zheng

## New Member MINIBIOs



Igor E. Brodsky
Associate Professor of Pathobiology
Vice-chair, Immunology Graduate Group
University of Pennsylvania
Philadelphia, USA

Igor E. Brodsky is an Associate Professor of Pathobiology at the University of Pennsylvania School of Veterinary Medicine, and the Vice-Chair of the Immunology Graduate Group at Penn. His lab studies innate immune recognition of pathogenic bacteria, with a specific focus on discovering mechanisms of inflammasome activation and regulation of cell death pathways in response to pathogen virulence activities. Dr. Brodsky obtained his A.B. in Molecular Biology from Princeton University, where he performed undergraduate thesis research on herpes virology with Lynn Enquist. He pursued his PhD training at Stanford University in the laboratory of Dr. Stanley Falkow, where he studied mechanisms of Salmonella resistance to anti-microbial peptides. These studies led to his interest in the area of innate immune recognition of pathogens, which led him to pursue post-doctoral research with Dr. Ruslan Medzhitov at Yale University, where he investigated mechanisms of inflammasome activation and evasion by gram-negative bacterial pathogens. Ongoing work in the Brodsky lab is investigating cross-talk between different cell death pathways and their roles in anti-bacterial host defense, as well as understanding the regulation of inflammatory cytokine gene expression by components of the cell-extrinsic death pathway. The overarching goal of the Brodsky lab is to uncover fundamental mechanisms that govern innate immune recognition of pathogens and corresponding pathogen evasion strategies in order to identify novel areas for therapeutic intervention in the setting of infectious disease. Dr. Brodsky is a recipient of the Burroughs Wellcome Pathogenesis of Infectious Disease award and a Zoetis Award for Veterinary Research Excellence.



Ben Croker Ph.D.
Associate Professor
Division of Allergy I Immunology I Rheumatology
Department of Pediatrics, School of Medicine
UC San Diego
La Jolla, USA
W: www.crokerlab.com

Ben Croker is an Associate Professor at UC San Diego in the Department of Pediatrics where he directs a research program on neutrophil biology, inflammatory cell death, and negative regulation of cytokine signaling. He completed a Ph.D. at The Walter and Eliza Hall Institute of Medical Research in Australia studying the role of SOCS3 in regulation of IL-6 and G-CSF signaling. His postdoctoral studies at The Scripps Research Institute with Professor Bruce Beutler identified an ion channel preventing cardiac arrhythmia and sudden death following pathogen recognition. Dr. Croker was appointed as Assistant Professor at Boston Children's Hospital and Harvard Medical School in 2013, and he joined the Immunology Program at Harvard Medical School in 2014. His lab continues to study genetic regulators of innate immunity and inflammatory cell death in mice and humans.



Sandra Jukić
PhD candidate
Infection Immunology
Research Center Borstel, Germany

I obtained my Bachelor of Science in Biotechnology at the HS Furtwangen University in Villingen-Schwenningen, Germany and my Master's degree in Biology (focused on Biochemistry and Genetics) at the Justus-Liebig-University in Gießen, Germany. Currently I am working on my PhD thesis in the laboratory of Dr. Christoph Hölscher, in the Department of Infection Immunology at the Research Center Borstel, Germany, studying the inflammatory role of Interleukin (IL)-17 cytokines in an autoimmune blistering skin disease. My Project aim is to investigate the exact roles of IL-17A and IL-17F in the pathogenesis of Epidermolysis bullosa acquisita (EBA), using a systemic mouse model to elucidate the function of these cytokines in EBA.

## New Member MINIBIOs Continued



Amanda (Büchau) MacLeod, MD Associate Professor of Dermatology Assistant Professor of Immunology Assistant Professor of Molecular Genetics and Microbiology Associate Residency Program Director for Research Member of the Center for Host-Microbiome Interactions Member of the Center for Microbiome Member of the Duke Cancer Center Affiliate of the Regeneration Next Initiative Duke University, Durham, USA

Dr. Amanda MacLeod received her MD from Heinrich-Heine University in Düsseldorf, Germany and postdoctoral training at the University of California San Diego and The Scripps Research Institute. She joined the faculty at Duke University as an Assistant Professor in September 2014 before being promoted in March 2019. She is a nationally and internationally recognized translational dermato-immunologist with expertise in the regulation of innate antimicrobial immunity in the context of host-pathogen/microbiome interactions, inflammation, injury, and cancer in the skin. Specifically, her research focus lies in understanding the immunobiology and regulation of cutaneous innate antimicrobial peptides and proteins, specifically antiviral proteins, in the context of perturbed skin barrier function and wound healing. Her laboratory discovered that IL-27 activates cutaneous wound healing responses and activation of innate immunity genes. She and her team also recently identified novel regulators of host defense proteins and identified functional non-classical roles for these host defense effectors in the skin. My lab also investigates how innate immune cells and their products play critical roles in allergy and perturbed barrier function (such as eczema, non-healing wounds, hidradenitis suppurativa) and their most recent work has led to identifying effector molecules and pathways of the neuro-immune axis of cutaneous innate antimicrobial (dys-)regulation. Dr. MacLeod is currently funded by the NIH through R01 and R21 grants and has received multiple awards, including those from NIH (K08 Award), Dermatology Foundation, Duke Pinnell Center for Investigative Dermatology, the Duke Physician-Scientist Award and others. She also serves as an Associate Review Editor for Frontiers in Immunology, on the review board (ad hoc or standing) for the NIH, Leo Foundation, and other national and international grant agencies. She is a member of the Education Committee of the Society for Investigative Dermatology, Wound Healing Society, American Association for Immunologists, American Association for the Advancement of Science, and the Women's Dermatological Society. She also works as a consultant for Silab.



Alessio Mylonas, Ph.D. Post-doctoral fellow EPFLausanne, Switzerland https://www.linkedin.com/in/alessio-mylonas/

I earned my PhD from the department of Dermatology at the University Hospital of Lausanne, under the mentorship of Professors Curdin Conrad and Michel Gilliet. There, I worked on the immuno-pathological mechanism of a side-effect of anti-TNF therapies called paradoxical psoriasis. By establishing a unique mouse model, we could identify plasmacytoid dendritic cell activation and type-I interferons as key drivers of skin inflammation. During a short postdoc, my interests shifted to the pathogenesis of a debilitating skin disease called rosacea, and we described how the skin microbiome activates a pathological cascade during flares of the disease. Work supported by three competitive grants awarded to Prof. Conrad and myself, elucidates fundamental components of the pathogenic pathway, and provides novel actionable targets for the treatment of this disease. Currently, I am fascinated by the role of the microbiome in the induction of inflammation during the pathogenesis of Alzheimer's disease, in work that I am undertaking at the Swiss Federal Institute of Technology (EPF) Lausanne, under the European Union's Horizon 2020 ad-gut.eu framework.



Richard Siegel, M.D., Ph.D.
Global Head, Translational Medicine
Co-Head, Translational Research
Autoimmunity, Transplantation and Inflammation

Novartis Institutes for BioMedical Research Basel, Switzerland

Richard Siegel, MD, PhD is Global Head, Translational Medicine Discovery and Profiling, for the Autoimmunity, Transplantation and Inflammation disease area in the Novartis Institutes of Biomedical Research in Basel, Switzerland. Richard joined Novartis in 2018 after 20 years in the NIH intramural research program where he was Chief of the Autoimmunity Branch, conducting basic and translational research in cytokine biology focused on the TNF superfamily of cytokines and their receptors. Since 2010 he was also Clinical Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, overseeing the clinical activities and research program that encompasses interventional and natural history studies of genetic autoimmune and inflammatory syndromes and more common rheumatologic and dermatologic diseases. He was involved in discoveries of pathogenesis and treatments of multiple syndromes, including ALPS, TRAPS, and CAPS, and also somatic mutations in the bone overgrowth condition Melorheostosis. Richard obtained his bachelor's degree at Yale, his MD and PhD at the University of Pennsylvania School of Medicine and trained in Internal Medicine and Rheumatology at the Hospital of the University of Pennsylvania. He has received numerous honors including election to the American Society of Clinical Investigation and American Association of Physicians, and has authored more than 150 publications. Maintaining a presence in in laboratory research, Richard also co-leads the Translational Research group in the ATI division of NIBR, and is committed to bridging the gap between laboratory and clinical research to discover new treatments and improve the lives of patients with autoimmune and inflammatory disease.



**Le (Christy) Ying, Ph.D.**Postdoctoral Researcher
Centre for Innate Immunity and Infectious Diseases
Hudson Institute of Medical Research, Australia

Dr. Le (Christy) Ying is a postdoctoral researcher in the laboratory of Prof. Richard Ferrero at Hudson Institute of Medical Research, Melbourne, Australia. She completed her PhD in Tea Science at University of Zhejiang University, China, in 2018. During her PhD study, Dr Ying focused on the potential role of bioactive compounds from tea extracts in cancer prevention. Then she came to the laboratory of Prof. Bryan Williams at Hudson Institute, as a PhD visiting student from Sep 2016 to April 2018. There, she started the new research projects in cancer immunology, and she developed a novel strategy to stratify gastric cancer patients for treatment and determined prognosis using the integration of several immune markers, including Programmed Death-Ligand 1 (PD-L1). After that, Dr Ying moved to the laboratory of Prof. Richard Ferrero, as her first position after PhD. Her current project is on and defining the potential role of Nod-like receptor family member-NLRC5 in gastric MALT lymphoma during Helicobacter infection.



Elina Zuniga UCSD La Jolla, United States

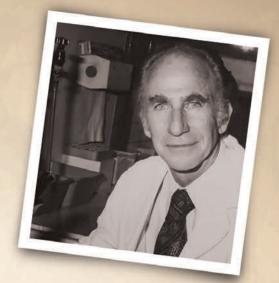
Elina Zuniga received her Ph.D. in Biochemistry from the National University of Cordoba, Argentina. She conducted postdoctoral research at The Scripps Research Institute where she held two post-doctoral fellowships from Antorchas Foundation and PEW Charitable Trust, respectively. After joining UCSD in 2007 she has received a Hellman Foundation Scholar Award, The Vilcek Finalist Prize for Creative Promise, the Leukemia and Lymphoma Society Scholar Award and the American Cancer Society Scholar Award (a lifetime honor). In 2018, the American Association of Immunologists also recognized her scientific achievements and exemplary career with the Vanguard Lecture.

# In Memorium

## Ion Gresser

1928-2019

by Jan Vilcek and Howard Young



## lon Gresser, a virologist who transformed understanding of the roles of interferons, may be best remembered for showing that in mice, interferon- $\alpha(IFN-\alpha)$ can produce acute and chronic disease.

At he time Gresser began these studies, interferon was considered to be a selective antiviral substance, harmless to uninfected cells and organisms, and there was no indication that cytokines would play a role in pathogenesis. That belief was shattered with the 1975 Nature publication with the simple title "Lethality of interferon preparations for newborn mice." Gresser subsequently demonstrated that antibodies to IFN- $\alpha$  can protect young mice from death caused by infection with lymphocytic choriomeningitis virus. This study can be considered a stepping-stone for the therapeutic application of antibodies to cytokines in the treatment of human disease, which was introduced much later and revolutionized the management of some autoimmune diseases.

Since its first description by Alick Isaacs and Jean Lindenmann in 1957, interferon was believed to be important in an organism's resistance to viral infection and was thought to have the potential to become as useful in the treatment of viral diseases as penicillin and other antibiotics had turned out to be for infections caused by bacteria. Gresser made substantial contributions to the body of knowledge about interferon that is now taken for granted. His early studies of mouse models of viral infections established that injections of IFN- $\alpha$  can indeed protect mice from viral infection. Gresser was among the first investigators to explore the potential of interferons in the control of malignancies in animal models, showing that it can protect mice not only from leukemias caused by viruses but also from solid tumors and metastatic cancer. Those findings contributed to the original optimism about the potential usefulness of interferons not only in the treatment of viral infections but also in the control of cancer in humans. Unfortunately, those expectations were generally not borne out by later clinical trials. Although interferon therapies would show moderate efficacy in the control of some viral infections, such as chronic active infection with hepatitis virus B or C, and even more modest results in some malignancies, the benefits fell short of the initial expectations. More surprising at the time was the first demonstration, by Gresser and colleagues in 1973, that IFN-α enhances the expression of histocompatibility antigens and modifies the surface of uninfected cells, and that it has other immunomodulatory actions. Those last findings were among the first demonstrations that interferons have actions separate from their antiviral activities and broadened the scope of interferon research.

A native of New York City, Gresser developed early on an appreciation of science and the arts. His mother, Gisela Kahn Gresser, was a classicist and prominent chess player who dominated women's chess for more than three decades, winning nine national titles between 1944 and 1969. His father, William Gresser, a successful attorney, moonlighted as a serious musicologist. Ion Gresser — who too retained a life-long passion for the piano and classical music — completed his undergraduate studies at Harvard University. In addition to science, he was interested in history, European literature and Russian. After his graduation from Yale School of Medicine and an internship at Bellevue Hospital in New

York City, he joined the army and served as head of an infectious disease laboratory at the army post in Camp Zama, Japan. There he developed an active interest in virology and published his first papers on Japanese encephalitis and Asian flu — a passion that blossomed during a postdoctoral fellowship in the laboratory of John F. Enders, the Harvard-based virologist and co-recipient of the 1954 Nobel Prize in physiology or medicine. While working in Enders' lab, Gresser also published his first paper devoted to interferons.

A Francophile, Gresser moved to Paris in the early 1960s, first joining the laboratory of another interferon pathfinder, Charles Chany, at the Hôpital St. Vincent de Paul, and soon thereafter establishing his own laboratory at the Institut de Recherches Scientifiques sur le Cancer in Villejuif, outside Paris. Eventually, Gresser ended up spending decades at the Villejuif laboratory, and it was there that he conducted all of his many original studies for which he became known. Although he retired from his position at Villejuif many years ago, he continued to publish reviews, as well as original research in collaboration with others. His very last paper, co-authored with Pierre Lebon, Yanick Crow and Jean-Laurent Casanova, appeared in March of this year, only weeks before his passing.

Arguably, the most important contribution of Gresser and his colleagues was the demonstration of harmful effects of interferons in animal models, as well as the clear evidence that interferons contribute to pathogenesis, including the pathogenesis of viral infections. Among the most surprising discoveries was that injection of mice with potent sheep immunoglobulin directed against IFN-α markedly inhibits the manifestations of disease caused by infection with lymphocytic choriomeningitis virus (weight loss, liver-cell necrosis and death), despite the fact that the treated mice had 100-fold more of the virus in their serum than did mice that were not treated with the anti-interferon immunoglobulin. At the time of their publication in 1977, these findings not only were completely unexpected and counterintuitive but also presaged the advent of the dramatic beneficial effects of anticytokine therapies in humans, such as those achieved with the use of monoclonal antibodies to the cytokine TNF in the treatment rheumatoid arthritis, Crohn's disease and some other autoimmune disorders. This discovery alone would be sufficient to earn Ion Gresser a lasting abode in the pantheon of medical science.

#### Jan Vilcek

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#### **Howard A. Young**

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# In Memorium

## **Professor Derek Burke CBE**

1930-2019

by Dr. David Secher



As someone who worked with Derek over many years, I wanted to say something today about his career as a scientist. My name is David Secher and from 1970-1986, I worked at the Medical Research Council Laboratory of Molecular Biology in Cambridge.

Derek's scientific career spanned the whole spectrum: university laboratory research, industrial R&D management, senior administration and government advice. In all these areas, he showed insight, integrity, compassion and an enthusiasm for discovering the truth. When faced with irrational objections, he was polite and persistent, even when feeling frustrated by political lack of interest in evidence and expert opinion.

Derek's career as a scientist started off with eight years of chemistry at Birmingham University and at Yale, where he studied Caribbean sponges – and met and married Mary. When they returned to the UK in 1955, Derek (who was then 25) was offered a job at the National Institute of Medical Research in Mill Hill, to work with Alick Isaacs on the biochemistry of the Influenza virus. Two years later, Isaacs, with Jean Lindenmann, discovered Interferon and, by 1958, Derek was publishing papers on Interferon with Isaacs. Interferon is an important biologically active protein, and for a while it was seen as a potential cure for both the common cold – and for cancer. So this was an exciting new area, and Interferon remained the focus of Derek's research for the rest of his career, at Mill Hill, then at Aberdeen and at Warwick University, where he was the founding professor of biological sciences. His interest in Interferon continued throughout his subsequent career in business and university administration and his last papers, written only last year, were on the discovery and use of Interferon. I was pleased to be asked to sub-edit those papers and honoured to be his co-author on the final one.

The scientific highlight of Derek's career (and mine) was the paper he and I co-authored in 1980 on a new method for the purification of Interferon. This paper was the culmination of more than three years of collaboration. In 1976 I had given a lecture at Warwick on the production of monoclonal antibodies, a revolutionary technology invented the previous year, and for which my colleagues César Milstein and Georges Köhler won the Nobel Prize in 1984. I was one of the first people in the world to learn this technique and I was interested in applying it to a "real-world" clinical problem. A few days after the lecture, Derek phoned me to ask if I would be interested in a collaboration to make a monoclonal antibody to Interferon. He explained that his lab could do the testing and mine would make the antibodies. If we were successful, it would not only be a major first for the technology, but it could open the way to large-scale production of Interferon for clinical use. I estimated the project would take three months. Two years later and countless attempts resulted in zero progress. I was considering giving up, when Derek called me to say that he was taking sabbatical leave and would like to have a go at doing the delicate bio-assays for Interferon activity himself, rather than delegate this work to a more junior member of staff. In December 1979 and after several more failures, we agreed to give it one more go and then give up. The experiment was done before Christmas and Derek and I spoke after the holiday to break the code and analyse the results.

To our amazement a positive result was seen! Further growth and re-testing of the antibody, which we called NK2, confirmed its activity and within three months we had prepared sufficient antibody to show that it could purify, for the first time, sufficient quantities of Interferon to allow for clinical trials. We also prepared an article, Secher & Burke, that was published in the most prestigious scientific journal, Nature, on 12 June 1980 and that has been referred to in other publications 358 times, more than any other article by either Derek or me. I also submitted a patent application on the same day that I submitted our manuscript, 6 March, but that is another long story!

The article created quite a storm, scientifically and commercially. Unknown to us, the Swiss pharmaceutical firm, Hoffman-la-Roche had been working on a similar project and were only weeks behind. Interferon was a "hot" topic because there had been hints of clinical activity against certain tumours and the pharmaceutical and investment communities had hopes that it might turn out to be a wonder drug for common forms of cancer. It was a very exciting time for both of us.

The close contact with the pharmaceutical industry and the immediate prospects of clinical application impacted on both our future careers. In 1982 Derek moved to Toronto to take up the position of Vice-President and Scientific Director of Allelix Inc. There Derek built up a team of around 200 scientists and developed a strategy for this start-up biotechnology company. (I too left the academic world and in 1986 went to work for a biotechnology company, Celltech, in Slough.)

The products that resulted from our collaboration remained on the market into the present millennium, but, sadly, the clinical use of Interferon has turned out to be limited to certain rare tumours and its effectiveness in treating viral diseases such as colds and flu is limited by its side effects of "flu-like symptoms". The era of Interferon-hype ended and Interferon is now regarded as just one of a family of biologically active proteins called cytokines.

The very close collaboration – and the intense aftermath – resulted in our forming a strong friendship that continued till Derek's death. My wife Sandra and I visited Derek and Mary in their homes in Leamington Spa, Hethersett, Cambridge and Norwich. In Cambridge, I was able to arrange for Derek to have dining privileges in my college, Gonville & Caius, and for many years Derek was a regular and popular guest at High Table, always remembering people's names and taking a close interest in their lives. This year he helped me with my latest article in the Times Higher. I was pleased that he liked it and on 7 March he wrote "Please keep up the good work." Derek was a good friend and I shall miss him dearly.

Dr. David Secher Gonville & Caius College Cambridge, UK

# REVIEWS OF INTEREST

by Zhian Chen and Di Yu

#### Interferon- $\lambda$ orchestrates innate and adaptive mucosal immune responses.

Ye L, Schnepf D, Staeheli P. Nat Rev Immunol, 2019 Jun 14. doi: 10.1038/s41577-019-0182-z. [Epub ahead of print] Review. PMID:31201377

#### Cell-state dynamics and therapeutic resistance in melanoma from the perspective of MITF and IFN pathways.

Bai X, Fisher DE, Flaherty KT. Nat Rev Clin Oncol. 2019 Apr 9. doi: 10.1038/s41571-019-0204-6. [Epub ahead of print] Review. PMID:30967646

#### Fine-Tuning Cytokine Signals.

Lin JX, Leonard WJ. Annu Rev Immunol. 2019 Apr 26;37:295-324. doi: 10.1146/annurevimmunol-042718-041447. Epub 2019 Jan 16. PMID:30649989

#### Targeting immune cell circuits and trafficking in inflammatory bowel disease.

Neurath MF.

Nat Immunol. 2019 Aug;20(8):970-979. doi: 10.1038/s41590-019-0415-0. Epub 2019 Jun 24. Review. PMID:31235952

#### Innate immunity to intracellular LPS.

Rathinam VAK, Zhao Y, Shao F. Nat Immunol. 2019 May;20(5):527-533. doi: 10.1038/s41590-019-0368-3. Epub 2019 Apr 8. Review. PMID:30962589

#### The Cytokines of Asthma.

Lambrecht BN, Hammad H, Fahy JV. Immunity. 2019 Apr 16;50(4):975-991. doi: 10.1016/j.immuni.2019.03.018.

PMID:30995510

#### Interleukin-1 and Related Cytokines in the Regulation of Inflammation and Immunity.

Mantovani A, Dinarello CA, Molgora M, Garlanda C. Immunity. 2019 Apr 16;50(4):778-795. doi: 10.1016/j.immuni.2019.03.012.

Review

PMID:30995499

#### Cytokine Networks in the Pathophysiology of Inflammatory Bowel Disease.

Friedrich M, Pohin M, Powrie F. Immunity. 2019 Apr 16;50(4):992-1006. doi: 10.1016/j.immuni.2019.03.017. Review. PMID:30995511

#### IL-10 Family Cytokines IL-10 and IL-22: from Basic Science to Clinical Translation

Ouyang W, O'Garra A. Immunity. 2019 Apr 16;50(4):871-891. doi: 10.1016/i.immuni.2019.03.020. PMID:30995504

#### Pleiotropy and Specificity: Insights from the Interleukin 6 Family of Cytokines.

Murakami M, Kamimura D, Hirano T. Immunity. 2019 Apr 16:50(4):812-831. doi: 10.1016/j.immuni.2019.03.027. Review.

PMID:30995501

#### The IL-17 Family of Cytokines in Health and Disease.

McGeachy MJ, Cua DJ, Gaffen SL. Immunity. 2019 Apr 16;50(4):892-906. doi: 10.1016/j.immuni.2019.03.021. Review.

PMID:30995505

#### GM-CSF, IL-3, and IL-5 Family of Cytokines: Regulators of Inflammation.

Dougan M, Dranoff G, Dougan SK. Immunity. 2019 Apr 16;50(4):796-811. doi: 10.1016/j.immuni.2019.03.022. Review

PMID:30995500

#### Cytokine Circuits in Cardiovascular Disease.

Williams JW, Huang LH, Randolph GJ. Immunity. 2019 Apr 16;50(4):941-954. doi: 10.1016/j.immuni.2019.03.007.

PMID:30995508

#### The Immunobiology of the Interleukin-12 Family: Room for Discovery.

Tait Wojno ED, Hunter CA, Stumhofer

Immunity, 2019 Apr 16:50(4):851-870. doi: 10.1016/j.immuni.2019.03.011. Review.

PMID:30995503

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Lazear HM. Schoggins JW. Diamond

Immunity. 2019 Apr 16;50(4):907-923. doi: 10.1016/j.immuni.2019.03.025. Review.

PMID:30995506

## Targeting Interleukin-6 Signaling in Clinic.

Kang S, Tanaka T, Narazaki M, Kishimoto T. *Immunity.* 2019 Apr 16;50(4):1007-1023. doi: 10.1016/j. immuni.2019.03.026. Review. PMID:30995492

## Transforming Growth Factor- Signaling in Immunity and Cancer.

Batlle E, Massagué J. *Immunity.* 2019 Apr 16;50(4):924-940. doi: 10.1016/j.immuni.2019.03.024. Review. PMID:30995507

### Systemic effects of IL-17 in inflammatory arthritis.

Beringer A, Miossec P.

Nat Rev Rheumatol. 2019

Aug;15(8):491-501. doi: 10.1038/
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21. Review.

PMID:31227819

### Rediscovering MIF: New Tricks for an Old Cytokine.

Harris J, VanPatten S, Deen NS, Al-Abed Y, Morand EF. *Trends Immunol.* 2019 May;40(5):447-462. doi: 10.1016/j.it.2019.03.002. Epub 2019 Apr 5. Review. PMID:30962001

## Immunomodulatory TGF- Signaling in Hepatocellular Carcinoma.

Chen J, Gingold JA, Su X. *Trends Mol Med.* 2019 Jul 25. pii: S1471-4914(19)30169-8. doi: 10.1016/j.molmed.2019.06.007. [Epub ahead of print] Review. PMID:31353124

## T-cell positioning by chemokines in autoimmune skin diseases.

Richmond JM, Strassner JP, Essien KI, Harris JE. *Immunol Rev.* 2019 May;289(1):186-204. doi: 10.1111/imr.12762. Review. PMID:30977191

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Silk AW, Margolin K. Hematol Oncol Clin North Am. 2019 Apr;33(2):261-274. doi: 10.1016/j. hoc.2018.12.004. Epub 2019 Jan 28. Review. PMID:30832999

## Biological Roles of Neutrophil-Derived Granule Proteins and Cytokines.

Cassatella MA, Östberg NK, Tamassia N, Soehnlein O. *Trends Immunol.* 2019 Jul;40(7):648-664. doi: 10.1016/j.it.2019.05.003. Epub 2019 May 30. Review. PMID:31155315

## The role of cytokines in the regulation of NK cells in the tumor environment.

Konjevi GM, Vuleti AM, Mirja i Martinovi KM, Larsen AK, Juriši VB. *Cytokine*. 2019 May;117:30-40. doi: 10.1016/j.cyto.2019.02.001. Epub 2019 Feb 18. Review. PMID:30784898

## Naturally occurring and synthetic constitutive-active cytokine receptors in disease and therapy.

Floss DM, Scheller J. Cytokine Growth Factor Rev. 2019 Jun;47:1-20. doi: 10.1016/j. cytogfr.2019.05.007. Epub 2019 May 21. Review. PMID:31147158

Most people say that it is the intellect which makes a great scientist. They are wrong: it is character.

— Albert Einstein



#### **Biomet Toolbox**

http://biomet-toolbox.chalmers.se/

The rapid expansion of systems biology has led to the development of a vast number of mathematical models and integrative strategies. Use of computational modeling has emerged as a powerful descriptive and predictive tool that allows the study of complex systems to investigate biological phenomena and represent the core of systems biology. The role of mathematical modeling and data integration is to generate testable hypothesis, design experiments and enrich the information content of experimental data.

#### JABAWS 2.2

http://www.compbio.dundee.ac.uk/jabaws/

JABAWS is free software which provides web services conveniently packaged to run on your local computer, server or cluster.

Services for multiple sequence alignment include Clustal Omega, Clustal W, MAFFT, MUSCLE, T-Coffee, ProbCons, MSAProbs, and GLProbs. Analysis services allow prediction of protein disorder with DisEMBL, IUPred, Jronn (a Java implementation of Ronn by P. Troshin and G. Barton, unpublished), and GlobPlot; and calculation of amino acid alignment conservation with AACon. The secondary structure for an RNA alignment can be predicted with the RNAalifold program from the Vienna RNA package.

JABAWS web-services can be accessed through the Jalview desktop graphical user interface (GUI) (version 2.8 onwards) or the JABAWS Command Line Interface (CLI) client. In this way you can perform computations on your sequences using the publicly available servers running at the University of Dundee. Alternatively, JABAWS installation allows you to perform analysis limited only by your own computing resources, by running it in your local computer, server or cluster.

#### **EBiAn: Easy Bioinformatics Analysis**

https://www.ig.unesp.br/Home/Extensao/EBiAn/html/ebian.

EBiAn package can perform the main analysis and manipulation of DNA, RNA, proteins and peptides sequences. DEVELOPER Luiz Carlos Bertucci Barbosa (luiz cbb@hotmail.com)

#### **Genes in Space 1.2**

https://www.cancerresearchuk.org/get-involved/citizenscience

Genes in Space is the world's first free mobile game that uses the collective force of players to analyze real genetic data and help beat cancer sooner.

#### **Immune Defense**

http://www.molecularjig.com/

Immune Defense is a Real Time Strategy (RTS) game. The player deploys 7 types of white blood cells against bacteria, parasites, viruses and even cancer... Our goal is to teach the basics of cell biology and biochemistry in an intuitive way. To beat Immune Defense, the player needs to know what proteins do, what receptors do, how cells respond to signals in the environment, how random events lead to predictable behaviors ... Additionally, the player battles HIV, TB, Listeria, a Malaria-like organism and learns exactly how vaccination is helpful, why viruses are difficult to detect and why TB and AIDS are so difficult to overcome.

#### SePIA

RNA sequence processing, integration, and analysis http://anduril.org/sepia/

SePIA is a comprehensive RNA Sequencing workflow standardizing Processing, Integration, and Analysis of large-scale sequencing data. It provides a systematic, pipeline architecture to manage, individually analyze, and integrate both small-RNA and RNA data. SePIA introduces processes for enhanced and streamlined integrated analysis with a modular design that enables robust customization to a given experiment. Furthermore, the underlying pipeline engine supports optimal usage of computational resources.

For method developers, SePIA's modular design makes it easy to extend the workflow with further downstream analysis. For biologists, it provides the advantage of automatically generated, easy to browse-and-query results and data visualizations. All functions and components used in the SePIA workflow and available for use are described in Anduril documentation.

#### **StringTie**

http://ccb.jhu.edu/software/stringtie/

StringTie is a fast and highly efficient assembler of RNA-Seq alignments into potential transcripts. It uses a novel network flow algorithm as well as an optional de novo assembly step to assemble and quantitate full-length transcripts representing multiple splice variants for each gene locus. Its input can include not only the alignments of raw reads used by other transcript assemblers, but also alignments longer sequences that have been assembled from those reads. In order to identify differentially expressed genes between experiments, StringTie's output can be processed by specialized software like Ballgown, Cuffdiff or other programs (DESeq2, edgeR, etc.)

#### rQuant 2.1

#### http://raetschlab.org/suppl/rquant

rQuant is a software of quantitative detection of alternative transcripts with RNA-Seq data. High-

throughput sequencing technologies open exciting new approaches to transcriptome profiling. For the important task of inferring transcript abundances from RNA-Seq data, the author developed a new technique, called rQuant, based on quadratic programming. Our method estimates biases introduced by experimental settings and is thus a powerful tool to reveal and quantify novel (alternative) transcripts.

EBSeq: An R package for RNA-Seq Differential Expression Analysis

Contact email: nleng@wisc.edu, kendzior@biostat.wisc.edu

#### R/EBSeq

#### https://www.biostat.wisc.edu/~kendzior/EBSEQ/

R/EBSeq is an R package for identifying genes and isoforms differentially expressed (DE) across two or more biological conditions in an RNA-seg experiment. Details can be found in Leng et al., 2013. The R/EBSeg package may be downloaded below. A vignette is also available there. It provides the syntax required for identifying DE genes and isoforms in a two-group RNA-seq experiment as well for identifying DE genes across more than two conditions (as noted in the vignette, the commands for identifying DE isoforms across more than two conditions are the same as those required for gene-level analysis). Contact email: nleng@wisc.edu, kendzior@biostat.wisc.edu

#### SBW 2.12.2

#### http://svs-bio.org/

SBW (Systems Biology Workbench), is an open source framework connecting heterogeneous software applications. Researchers in quantitative systems biology make use of a large number of different software packages for modeling, analysis, visualization, and general data manipulation. The Systems Biology Workbench (SBW), is a software framework that allows heterogeneous application components-written in diverse programming languages and running on different platforms-to communicate and use each others' capabilities via a fast binary encoded-message system.

SBW goal was to create a simple, high performance, opensource software infrastructure which is easy to implement and understand. SBW enables applications (potentially running on separate, distributed computers) to communicate via a simple network protocol. The interfaces to the system are encapsulated in client-side libraries that we provide for different programming languages.

#### **CoExpNetViz Comparative Co-Expression Network Construction and Visualization http://**

bioinformatics.psb.ugent.be/webtools/coexpr/

CoExpNetViz takes as input a set of bait genes chosen by you and at least one pre-processed gene expression dataset. You can also specify a negative and positive cutoff value, which will be used to determine if two genes are co-expressed or not. In short the algorithm proceeds in three big steps:

- 1. The co-expression dataset is translated into a co-expression graph using the Pearson correlation coefficient and the cutoff values.
- 2. Non-bait genes (or target genes) are grouped together in homologous families, which results in a graph with two types of nodes: bait genes nodes and family nodes.
- 3. The family nodes are grouped into partitions if the target genes they contain are co-expressed with the same set of bait genes. The output of the algorithm is visualized in Cytoscape.

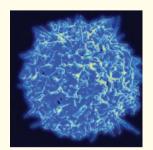
### visANT 5.50 – Integrative Visual Analysis Tool for Biological Networks & Pathways

http://visant.bu.edu/

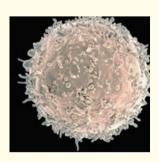
visANT is an integrative visual analysis tool for biological networks and pathways. VisANT is implemented as a java applet which can be run in most common browsers and has been test with Netscape, Internet Explorer with different versions on different platforms.

Bad times have a scientific value. These are occasions a good learner would not miss.

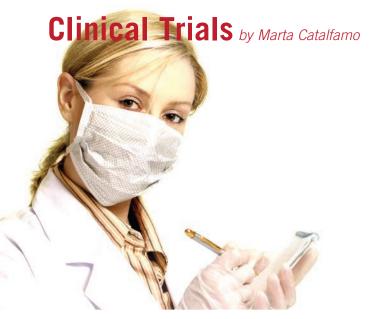
— Ralph Waldo Emerson



T Lymphocyte NIAID



**B** Lymphocyte



### Phase I-II Study of Interferon-gamma in Patients With HER-2 Positive Breast

Principal Investigators: Heather S. Han, M.D H. Lee Moffitt Cancer Center and Research Institute. Tampa, Florida 33612, United States. Contact: Heather S. Han, M.D. Phone: +1 813-745-4933

ClinicalTrials.gov Identifier: NCT03112590

#### Aspirin and Rintatolimod With or Without Interferon-alpha 2b in Treating **Patients With Prostate Cancer Before Surgery**

Principal Investigators: Gurkamal S Chatta, MD. Roswell Park Cancer

Institute, Buffalo, New York 14263, United States.

Contact: Gurkamal S Chatta, MD. Phone: +1 716-845-3863

ClinicalTrials.gov Identifier: NCT03899987

## Modified Virus VSV-IFNbetaTYRP1 in Treating Patients With Stage III-IV

Principal Investigators: Roxana S. Dronca, MD. Mayo Clinic in Florida.

Jacksonville, Florida 32224-9980, United States.

Contact: Roxana S. Dronca. MD. Phone: +1 855-776-0015

ClinicalTrials.gov Identifier: NCT03865212

#### **Intraperitoneal Infusion of Autologous Monocytes With Sylatron** (Peginterferon Alfa-2b) and Actimmune (Interferon Gamma-1b) in Women With Recurrent or Refractory Ovarian Cancer, Fallopian Tube Cancer or **Primary Peritoneal Cancer**

Principal Investigators: Christina M Annunziata, M.D. National Cancer Institute (NCI). National Institutes of Health. Bethesda, Maryland 20892-1360 United States

Contact: Phone: Ann C McCoy, R.N. Phone: +1 (240) 760-6021

ClinicalTrials.gov Identifier: NCT02948426

#### Pembrolizumab and Interferon Gamma-1b in Treating Patients With Stage IB-IVB Relapsed or Refractory Mycosis Fungoides and Sezary Syndrome

Principal Investigators: Michael S Khodadoust, MD. Cancer Immunotherapy Trials Network. National Cancer Institute (NCI). National Institutes of Health. Bethesda, Maryland 20892-1360. United States.

Contact: Alison J. Moskowitz, MD. Phone: +1 212-639-7592 ClinicalTrials.gov Identifier: NCT03063632

#### Peg-Interferon Alpha 2b Combined With Two Intravenous Broadly HIV-1 Neutralizing Antibodies 3BNC117 and 10-1074 (BEAT-2) (BEAT-2)

Principal Investigators: Luis Montaner, MD. The Wistar Institute.

Philadelphia, PA 19104

Contact: Luis Montaner, MD. Phone: 1+(215) 898-3700

ClinicalTrials.gov Identifier: NCT03588715

#### Long-term Follow-up of HLH Patients Who Received Treatment With NI-0501, an Anti-interferon Gamma Monoclonal Antibody

Principal Investigators: Paul Brogan, MD. Great Ormond Street Hospital.

London, United Kingdom, WC1N 3JH

Contact: Cristina de Min, MD. Phone: +41 61 201 1322

ClinicalTrials.gov Identifier: NCT02069899

Recombinant Human Interleukin-7 to Promote T-Cell Recovery After Cord

**Blood Transplant** 

Principal Investigators: David Marin, MD. M D Anderson Cancer Center.

Houston, Texas 77030, United States.

**Contact:** David Marin, MD. Phone: +1 713-792-8750

ClinicalTrials.gov Identifier: NCT03941769

#### HIV Reservoir Reduction With Interleukin-2 (IL2)

Principal Investigators: Benigno Rodriguez, MD, Michael Lederman, MD and Cheryl Smith, MD. Case Western Reserve University. AIDS Clinical

Trials Unit. Cleveland, Ohio 44106., United States. **Contact:** Cheryl Smith, MD. Phone: +1 216-844-8052

ClinicalTrials.gov Identifier: NCT03308786

#### Recombinant Interleukin-15 in Combination With Checkpoint Inhibitors Nivolumab and Ipilimumab in People With Refractory Cancers

Principal Investigators: eraldine H O'Sullivan Coyne, M.D. National Cancer Institute. National Institutes of Health. Bethesda, Maryland 20892-1360. United States

Contact: Ashley B Bruns Phone: +1 (240) 858-3162

ClinicalTrials.gov Identifier: NCT03388632

#### Effect of IL--1 Inhibition on Inflammation and Cardiovascular Risk

Principal Investigators: Priscilla Hsue, MD. San Francisco General

Hospital. San Francisco, California 94110, United States. Contact: Smruti Rahalkar, MAS Phone: +1 415-206-5801

ClinicalTrials.gov Identifier: NCT02272946

#### A Phase II Study of the Interleukin-6 Receptor Inhibitor Tocilizumab in Combination With Ipilimumab and Nivolumab in Patients With Unresectable Stage III or Stage IV Melanoma

Principal Investigators: Jeffrey Weber, MD. NYU Langone Health. New

York, New York 10016, United States.

Contact: Sandra John-Henry Phone: +1 212-263-4432

ClinicalTrials.gov Identifier: NCT03999749

## Research is what I'm doing when I don't know what I'm doing.

- Wernher von Braun



# 32 THINGS YOU SHOULD

http://mentalfloss.com/article/76974/25-things-you-should-know-about-vienna http://www.kaleyann.com/10-fun-facts-vienna/ BY Rachel Chang & kaley@kaleyann.com



Strolling around Austria's biggest city, dubbed the City of Music, is like simultaneously stepping back in time and stepping up in class. You can trace the footsteps of Mozart, Beethoven, Haydn, or Schubert—or waltz along to their compositions at one of the town's many balls. (When you're done, don't forget to refuel with some Viennese coffee and a hot dog.) Read on for more facts to file away about Vienna.

- 1. A military camp called Vindobona was set up where Vienna is now around 50 CE, but the first documents bearing the name Wenia surfaced in 881. It was mentioned as a town in 1137 and the town charter was granted in 1221.
- 2. Napoleon occupied Vienna in 1805 and again in 1809, and both events affected Ludwig von Beethoven. The first interrupted the premiere of what ended up being his only opera, Fidelio. And during Napoleon's May 10, 1809 siege, the prodigy, who was beginning to lose his hearing, hid in his brother Carl's basement with pillows over his ears lest the sound of the shells falling outside cause even more damage
- 3. Vienna technically sits in two different climate zones. It's located right at the border of the moderate middle European transitional climate and the drier Pannonian zone.
- 4. The German name for Vienna is Wien. So yes, that means Austria's most famous dish, the wiener schnitzel, translates to Viennese schnitzel. The proper serving of the dish is breaded veal with a side of parsley potatoes or a potato cucumber salad.
- 5. Vienna's Spanish Riding School, or Spanische Hofreitschule, has kept the renaissance tradition of Haute École equestrian alive for more than 450 years. The name of the institution refers to the horses introduced in the 16th century from Spain's Iberian Peninsula—today's Lipizzaner stallions are descendants of these.
- 6. The famed Vienna Boys Choir's roots date as far back as 1498. Wolfgang Amadeus Mozart worked with the choir and Franz Schubert was once a member. In 1918, the group became a private institution, and their imperial uniforms switched to sailor suits. Now, there are more than 100 boys between the ages of 10 and 14 from 30 countries split into four choirs, giving more than 300 performances a year.
- 7. Over the course of a century, Vienna's population has hovered between 2 million (its peak, in 1910) and 1.48 million (in 1987). As of October 2014, there were approximately 1.8 million inhabitants.
- 8. The Vienna Giant Wheel, or Wiener Riesenrad, was built in 1897 to honor the Golden Jubilee of Emperor Franz Josef I. A year later, in a protest intended to draw attention to the city's poor, a woman

named Marie Kindl hung herself outside one of the cabins. By 1916, a demolition permit was issued, but there wasn't enough money to actually destroy it. In 1944, it was burned down, rebuilt the next year, and put back in rotation in 1947.



- 9. The snow globe was invented in Austria in 1900 when Erwin Perzy was trying to improve on the light bulb—he added water and semolina flakes, in the hopes that the light would bounce off them and cast a brighter glow. That didn't happen, but the effect was striking. Mass production began in Vienna in 1905 by his company, Original Vienna Snow Globes, and the flakes are still falling today. Now run by his grandson, Erwin Perzy III, the family business has made customized globes for Bill Clinton, Ronald Reagan, and First Daughters Sasha and Malia Obama.
- 10. The 521 square miles of the Vienna Woods, or Wienerwald, are home to 2,000 plant species and 150 bird species. At least two endangered species—Ural owls and green lizards—have made the forest home.
- 11. The Austrian city has been home to the Organization of the Petroleum Exporting Countries (OPEC) since 1965. And although the United Nations is headquartered in New York City, one of its primary offices is in Vienna as well. The building serves as home base for the UN's International Atomic Energy Agency and Office on Drug and Crime.
- 12. Vienna is the second most livable city on the planet after Melbourne, Australia, according to the Economist Intelligence Unit's study ranking 30 factors, ranging from safety and education to infrastructure and healthcare.

- 13. Almost 3 million people a year visit the city's most famous church, St. Stephen's Cathedral, or Stephansdom, built in the 12th century. Thirteen bells hang from the tallest tower, which stands 448 feet high and is accessible by climbing 343 steps. But it's the Pummerin bell, in the 224-foot-tall tower, that happens to be the second largest free-swinging European chimed church bell. Composers Joseph Haydn and Wolfgang Amadeus Mozart have both worked in the church.
- 14. Be the belle of the ball: Every year, more than 450 balls take place in the Austrian capital. Viennese Ball Season runs from New Year's Eve to Shrove Tuesday (the Tuesday before Ash Wednesday). That means there's about 2000 hours of ball dancing annually.
- 15. The Vienna Philharmonic's New Year's Concert is one of the hottest tickets in town, with prime seats costing as much as \$1200. This year's show was seen on TV by 50 million viewers in 90 countries. And you have an absolute zero chance of scoring a ticket to ring in 2020. Names must be selected by a random drawing to have the opportunity to purchase tickets—and the entry period closed in February.
- 16. Coffee is about more than just caffeination for Austrians—it's part of their heritage. In fact, in 2011, Viennese coffee houses, which originated in the 17th century, were put on UNESCO's Intangible Cultural Heritage list, as they are a place "where time and space are consumed, but only the coffee is found on the bill."
- 17. The hills may have been alive in Salzburg, but the real-life Maria von Trapp, made famous by The Sound of Music, was actually born in Vienna on January 26, 1905.
- 18. Also born in Vienna? Actor Christoph Waltz, who spent most of his career working in Europe until he landed a starring role in Quentin Tarantino's Inglorious Basterds in 2009. The Austrian-German actor has since appeared in 2011's The Green Hornet, 2012's Django Unchained, 2014's Big Eyes, 2015's Spectre, and is signed on for two more Bond films.
- **19.** Vienna has bragging rights as the only world capital that produces "significant quantities" of wine within its city limits. With 1730 acres of "wine-growing surface," there are more than 320 vintners. Eighty-five percent of the wine produced is white wine grape varietals.
- **20.** By 2050, life expectancy in the city will be 89 years old for women and 85 for men. Comparatively, life expectancy in 2013 was 81 in the country and 71 years globally.
- 21. The 13-mile Danube Island was open in 1981 to reinforce Vienna's flood protection system and has become a prime recreation center, with a 820-foot family beach, a (free!) 53,820-square-foot waterpark, and a climbing park where guests can ascend 33 feet into the air.
- 22. Austria's largest palace, Schonbrunn, has been one of Vienna's most visited sites since 2003. But you can still make the experience personal. The 1798-square-foot, two-bedroom Grand Suite is available for rent—with rates around \$1500 a night. But really, how do you put a price on the ability to say you've stayed overnight in the former imperial home of Emperor Franz Joseph and Empress "Sisi" Elisabeth?



23. If splurging on a palatial stay isn't up your alley, the gardens around Schonbrunn Palace are equally majestic—and free. Open to the public since 1779, the Baroque-style gardens include a labyrinth, a zoo, Roman ruins, Neptune's Fountain, and a Gloriette atop a hill with a sprawling view of the entire grounds.

- 24. The 1949 film The Third Man has been called the "most important" film about Vienna. More recently, Richard Linklater's Before Sunrise was also shot in the capital. And even though the 1984 Oscar-winning Amadeus took place in Vienna, it was shot in the Czech Republic because, according to director Milos Forman, Vienna's "streets are full of boutiques, asphalt, steel, glass and plastic ... besides, Vienna is insanely expensive."
- **25.** When ordering a hot dog from one of Vienna's trademark hot dog stands, get ready to answer whether you prefer the sweet kremser mustard or spicy estragon. Vendors may shorten it to süss (sweet) or scharf (spicy). One of the most popular kiosks is the old city's Würstelstand am Hohen Markt.
- **26.** Vienna is the only capital city in the world to produce significant quantities of wine within its city limits. Home to over 1,700 acres of vineyards and 320 vintners, the Viennese love their wine. While the most popular are white wine varieties such as Grüner Veltliner, Rheinriesling and Weißburgunder, you can also find some nice reds. The best way to enjoy the local Viennese wine is in a heuriger (wine tavern), or by walking along Vienna's Wine Trail.
- 27. Vienna is often called The City of Music, or the World's Capital of Music, as more famous composers have lived here than in any other city in the world. And 4 of the top 10 classical composers in history worked in Vienna between 1750 and 1825. Wolfgang Amadeus Mozart, Ludwig van Beethoven, Joseph Haydn, Franz Schubert, Johann Straus and Johannes Brahms are just a few who called Vienna home.
  - While in Vienna, you can visit the former apartments of many of these famous musicians, which have been turned into museums. And don't miss The House of Music. Here you can "discover the fascinating world of sound and Viennese music in an interactive, playful way".
- 28. Vienna is also called the city of dreams. Sigmund Freud, the father of psychoanalysis, lived and worked in Vienna for much of his career. During this time, he had a significant impact on the city, causing it to be known as the birthplace of psychotherapy.
  The Sigmund Freud Museum is housed in the apartment where he lived and worked for nearly 50 years, until he was forced to flee Austria after the Anschluss.
- 29. The Vienna Zoo, or Tiergarten Schönbrunn, is the world's oldest and only baroque zoo. Built in the gardens of Schönbrunn Palace in 1752, the zoo was once the private menagerie of Emporer Franz Stephen and Empress Maria Theresa.
  Tiergarten Schönbrunn now boasts over 700 different animal species
  - and was voted the best zoo in Europe. Plus, with its original baroque architechture, it is also considered the world's most beautiful zoo.
- 30. The famous French croissants actually has Viennese origins. They are based on the Austrian kipferl, which means crescent in German. Bakers in Vienna made kipferl to commemorate Austria's victory over the Ottoman Turks in 1683, their shape based on the crescents seen on the uniform of the enemy.
  - In 1770, when Maria Antoinette of Austria married King Louis XVI of France, she introduced her favorite pastry to France. The French made a few changes, and called it a croissant.
- 31. Pez, the fun little tablet candies that we all know and love, were invented in Vienna in 1927. The name Pez is an abbreviation on the German word "pfefferminz", meaning peppermint. Because the original PEZ candies only came in that one flavor! The dispenser was invented in 1949, designed to look like a lighter. Smoking was prohibited at that time, so the Pez slogan was "No Smoking PEZing Allowed."
- **32.** Like Berlin, Vienna was also divided into four parts after WWII, and occupied by the United States, France, the United Kingdom and the Soviet Union. The first district of Vienna, the inner city, was administered by all 4 powers. The occupation, and division, of Vienna ended in 1955 with the Austrian State Treaty.

## ICIS Members elected into the National Academy of Sciences



#### Mike-Lenardo NIAID-NIH

Our laboratory investigates the molecular regulation of T lymphocytes, particularly as it relates to immunological tolerance, apoptosis, and autoimmune diseases such as multiple sclerosis, type 1 diabetes mellitus, and similar diseases. We use both molecular biology and cellular immunology techniques to pursue these investigations, with a focus on programs of cell death and survival, including apoptosis, autophagy, and necrosis mechanisms. Our approach has been to use contemporary genomic approaches to discover the molecular basis of new genetic diseases of the immune system that affect activation, tolerance, and homeostasis and to develop novel means of diagnosis and immunomodulation of these diseases. Also, we are attempting to pioneer a means of antigen-specific induction of apoptosis of pathogenic T cells as a means of treating autoimmune disease. Such studies could lead to a better understanding of molecular regulatory mechanisms that are important for human immunological diseases.



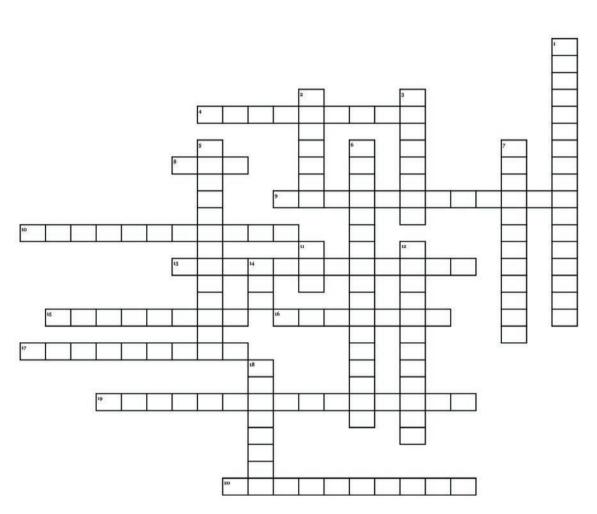
#### Adolfo Garcia-Sastre Mt. Sinai School of Medicine

Research in the García-Sastre lab focuses on a wide variety of viral pathogens, as well as host-pathogen interactions, and vaccine and anti-viral drug development.

A major focus of the lab is on influenza virus research. Influenza viruses are globally important human pathogens infecting up to 500 million people annually. With the recent emergence of highly pathogenic avian influenza (HPAI) strains, there is a pressing need to understand the pathogenesis of influenza A and develop vaccines and therapies. The García-Sastre laboratory investigates the molecular biology of influenza viruses and several other negative strand RNA viruses. Dr. García-Sastre's lab developed reverse genetics techniques that allow for the generation of recombinant influenza viruses from plasmid DNA. This work has led to major breakthroughs in revealing the molecular basis of influenza virus pathogenicity.

Dr. García-Sastre directs the Center for Research on Influenza Pathogenesis (CRIP), one of five NIAID Centers of Excellence for Influenza Research and Surveillance (CEIRS). The CEIRS program is an integrated network of centers that perform influenza virus surveillance and research. CRIP is comprised of a multidisciplinary team of scientists from a number of institutions across the globe.

# IMMUNE SYSTEM



#### Across

- ${\bf 4.}$  Chemical released by the body in response to an injury or allergen
- 8. A sexually transmitted disease
- $\boldsymbol{9.}$  Specialized White blood cells that fight diseases by activating the B-cells
- ${\bf 10.}$  The action or process of recognizing for eign bodies
- 13. The movement of B cells to produce antibodies
- ${\bf 15.}$  The action or process of anti-bodies destroying pathogens
- 16. A substance the body cannot recognize, usually on living
- 17. A type of WBC that fights infection by swallowing pathogens
- 19. Blood cells that fight infection and prevent the growth of cancer
- ${\bf 20.}$  Specific particles created by the immune system to destroy specific disease causing invaders

#### Down

- ${\bf 1.}$  A disease that can be spread by contact with infected people animals water or food
- ${\bf 2.}\,{\rm A}$  special version of a untie Jen that provides immunity against disease
- ${\bf 3.}$  Third and order or level
- ${\bf 5.}$  Physical contact touching and infected individual including sexual contact
- ${\bf 6.}$  A severe allergic reaction that can result in swelling breathing difficulty and sometimes does
- 7. Swelling and redness at the site of infection
- 11. A highly specific attack on a antigen or pathogen by the creation of antibodies
- 12. Specialized white blood cells that fights diseases by talking antigens directly
- 14. A quick and general immune response you're born with
- 18. Any substance that causes an allergic reaction

### MEMBERS IN THE NEWS



Olusegun (Segun) Onabajo, DCEG/NCI

Ofusegun Onabajo was selected as a recipient of a 2019 AAI Early Career Faculty Travel Grant and presented his research at the American Association of Immunologists annual meeting last May!



Feng Zhu – NCI at Frederick Feng Zhu received an AACR-Bristol-Myers Squibb Scholarin-Training Award in this year's AACR annual meeting in Atlanta.

THEY HAVE JUST FOUND THE GENE FOR SHYNESS. THEY WOULD HAVE FOUND IT EARLIER, BUT IT WAS HIDING BEHIND TWO OTHER GENES.

## Future Annual Meetings



8th Annual Meeting 1 - 4 November, 2020 Hyatt Regency Seattle, Seattle, USA