Signals

THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY NEWSLETTER

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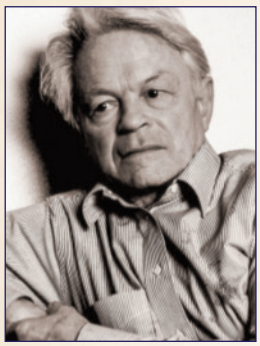
In Memoriam



Jean Lindenmann
1924 – 2015

by Otto Haller

Jean Lindenmann died in Zürich on January 15, 2015, a few months after his 90th birthday. He will be best remembered for his very early work on viral interference, although he did seminal work in other fields as well. The discovery of interferon by Isaacs and Lindenmann was a true scientific breakthrough in cell biology (1, 2). It was the result of a comparatively short and extremely productive collaboration that took place at the National Institute for Medical Research, Mill Hill, London, in 1956/57.

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Paula Pitha-Rowe
1937-2015

by William G. Nelson, M.D., Ph.D.

Paula was a long time member of the ICIS/ISICR and was the 1996 Milstein Awardee. I think she attended almost every annual meeting and served the society as Chair of the Awards Committee. I hope to have a more personalized tribute for the next newsletter but I can speak for the society when I say that we have all been saddened by this news and she will be fondly remembered for her science, her collegiality and her friendship.

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Future Meetings

2015 Meeting
Cytokines 2015
Oct. 11-14, 2015,
Bamberg, Germany

2016 Meeting
Cytokines 2016
Oct. 16-19, 2016
San Francisco, CA

ICIS
International Cytokine & Interferon Society

In Memoriam

Jean Lindenmann
1924 – 2015

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Jean Lindenmann was born on September 18, 1924, in Zagreb, Yugoslavia (present-day Croatia). The family moved to Switzerland and he grew up in Zürich where he studied medicine. Thereafter he became an assistant to Hermann Mooser at the Institute of Hygiene of the University of Zürich where he received training in bacteriological diagnostics. Moreover, poliomyelitis was a constant theme at the Institute, and Lindenmann became interested in viruses. He was especially intrigued by the phenomenon of viral interference, which was poorly understood and aroused his curiosity. He could show that heat-inactivated influenza virus particles attached to erythrocytes were still able to induce interference, suggesting that viral interference did not require infectivity and was presumably not due to consumption of some essential components in cells. In 1956, Lindenmann obtained a one-year fellowship from the Swiss Academy of Medical Sciences to learn virology at the National Institute for Medical Research at Mill Hill in London under C.H. (later Sir Christopher) Andrewes (1896-1988). A surprise meeting with Alick Isaacs who worked on viral interference next door marked the unexpected beginning of a close collaboration that culminated in the description of interferon. The circumstances and the details of the ingenious experimental set-up that led to this discovery have been commemorated by Lindenmann and others on various occasions (3). Suffice it to say that, despite some initial skepticism, interferon was rapidly accepted as an antiviral substance by the scientific community. The Institute immediately realized the potential clinical usefulness of the new antiviral substance and filed a patent application.

In 1957, Lindenmann returned to Switzerland, working first at the Institute in Zürich and later at the Swiss Federal Office of Public Health in Bern, where a new direction in interferon research opened up by chance. Lindenmann was in charge for the licensing of a pertussis vaccine. For this work he used mice of a particular inbred strain, A2G, which were recommended for a novel vaccine protection assay. One day, he used some spare mice for a side project with influenza virus and realized that the virus grew poorly in these animals although they produced almost no interferon. Surprisingly, A2G mice appeared to be naturally immune to influenza viruses due to a genetic predisposition (4).

Lindenmann moved to the United States in 1962 where he assumed a position as Visiting Assistant Professor at the Department of Microbiology (headed by Emanuel Suter) of the University of Florida, Gainesville. He continued to work on A2G mice and their exceptional influenza resistance together with Paul Klein (then a Ph.D. student and now Professor emeritus at the University of Florida). They determined that resistance was specific for influenza (orthomyxo-) viruses and was governed by a single dominant gene which they called Mx (now Mx1) for „myxovirus resistant“. The nature of the Mx resistance, however, remained a mystery. The analysis of the underlying mechanism kept Lindenmann and some of his students and collaborators busy for many years to come. In fact, it took 18 years to find out that interferon was at the center of the resistance phenotype. The telling experiment was made back in Zürich when Ion Gresser provided a potent antibody to mouse interferon. After injection into Mx-bearing mice before infection, the antibody completely wiped out resistance. Mx1 turned out to be an interferon-inducible gene and the gene product presumably had selective antiviral activity for orthomyxoviruses. Lindenmann hesitated a bit in the beginning to accept interferon as an explanation for the specific resistance of his beloved A2G mice but eventually turned into an ardent proponent of the new idea. The new view was that Mx was just one example of a diverse set of effector proteins each with different antiviral specificities that together formed the overall antiviral state targeting many different viruses (5). The next logical step was to identify the interferon-induced Mx1 protein. In excellent collaborations with Michel Horisberger at the Research Department of Ciba-Geigy (now Novartis) in Basel and with Charles Weissmann at the Institute for Molecular Biology I of the University of Zürich, the Mx1 gene product was eventually identified and the gene molecularly cloned (6,7). Peter Staeheli was the first person to witness that the mouse Mx1 protein had intrinsic and specific antiviral activity against influenza viruses when expressed without the help of interferon from a constitutive promoter in transfected cells (7). The Mx field has since considerably expanded, as summarized in a recent review on Mx that was dedicated to Jean Lindenmann on the occasion of his 90th birthday (8).

In Memoriam

Jean Lindenmann
1924 – 2015

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In an interesting twist of events, A2G mice became key players in yet another exciting story. While working with Paul Klein in Florida, Lindenmann noted that mouse Ehrlich ascites tumor cells grew readily in the peritoneal cavity of A2G mice. He also realized that the tumor cells remained susceptible to infection with influenza viruses and that the inoculated virus killed the tumor but not the host. The infected animals survived and were cured due to the cytolytic power of the virus. Moreover, animals that had survived the process of viral oncolysis proved to be solidly immune against a challenge with the same tumor cells. Somehow the immunogenicity of tumor cells was increased by viral infection. Lindenmann speculated that viral oncolysates produced in tissue culture could be used as protective anti-tumor vaccines. The procedure worked in the mouse model with allogeneic tumors but could not satisfactorily be extended to syngeneic tumors and was dropped. Nevertheless, the concept of enhancing anti-tumor immunity with the help of viruses was a great stimulus for other researchers developing immunotherapies for cancer patients.

Lindenmann was appointed Associate Professor for Experimental Microbiology at the University of Zürich in 1964 and was promoted to Full Professor five years later. The Lindenmann laboratory started small and remained comparatively small for many years, even after its transformation into the Institute for Immunology and Virology in 1980, with Lindenmann as Director. In addition to work on Mx resistance and postoncolytic immunity, Lindenmann´s interests turned toward understanding immune recognition of transplantation antigens, T cell immunity, idiotypes and, in general, the immunological network.

He was a gifted teacher and textbook author who was able to entertain and transmit his excitement to his students. He was also a great lecturer and writer who was knowledgeable about almost any subject in science, art, history and philosophy. He communicated his views to a larger public via regular essays that appeared in the lay press. His scientific achievements were honored with prestigious awards, among them the Cancer Prize of the Swiss Cancer League in 1964, the Robert Koch Prize in 1973, the Marcel Benoist Prize in 1977 and the European Virology Award of the European Society for Virology in 2007. Lindenmann had a long scientific career and much enjoyed the celebrations to mark the 50th anniversary of the discovery of interferon that were held in Oxford, Paris, and Nuremberg in 2007. He will be remembered as a superb intellectual, creative scientist, stimulating lecturer, and generous person with a great sense of humor.

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Otto Haller is Professor emeritus at the University of Freiburg, Germany, and a member of the Board of Directors, University Hospital Zürich, Switzerland. Jean Lindenmann was his mentor at the University of Zürich for many years.
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In Memoriam

Paula Pitha-Rowe
1937-2015

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Below is the letter issued by Dr. William Nelson, Johns Hopkins University.

Death of cancer scientist Paula Pitha-Rowe, Ph.D

It is with great sadness that I announce the death of Paula Pitha-Rowe, Ph.D., Professor of Oncology, Molecular Biology and Genetics, and Biology. Paula was an internationally renowned scientist whose pioneering research helped increase the understanding of how viruses play a role in cancer. She was 77 years old. As one of the first basic scientists in the comprehensive cancer center at Johns Hopkins and Department of Biology, Paula also was the thirteenth female faculty member in the School of Medicine to attain the rank of Professor in 1985.

Paula was a worldwide leader in understanding natural cellular responses to infection and the relationship between viruses and cancer. Much of her research focused on the role of antiviral responses in HIV (human immunodeficiency virus) and Kaposi's sarcoma as well as other cancers.

Her research has revealed a crucial role by a family of genes called IRF involving antiviral responses and inflammation, which appears to play a role in the initiation of cancer. Using genetically modified mice that are missing a critical component of the immune response, she developed mouse models to further study IRF mechanisms. This work is leading to clinical advances in vaccines and drug treatments of viral infections associated with cancer.

Paula also identified the ISG15 gene, an inhibitor of a cellular pathway used by HIV-1, the AIDS-causing human immunodeficiency virus, to produce virus particles and interfere with HIV-1 replication. "Viruses are clever, and many have found a way to limit production of natural defense proteins like ISG15," said Paula in 2007. She led research of new compounds that promote ISG15 expression as a potential therapy for HIV-1 that has become resistant to existing antiviral drugs. She found that ISG15 might also inhibit replication of other viruses, including Ebola and influenza.

Paula was the first full-time research scientist recruited to the nascent cancer program at Johns Hopkins, where she helped steward cancer research, with her own work on virology and interferon, and as a mentor and leader, as the cancer program grew into the Sidney Kimmel Comprehensive Cancer Center.

"Paula was not only a scientific colleague, she was a dear friend. She was one of the first basic scientists in our cancer center, and that was also the direction I sought for my career. She approached science in a way that I wanted to, and so I looked to her as a role model. In recent years, her discoveries impacted my work as an epigenetics scientist in ways I could have never anticipated. She will be greatly, and for me very personally, missed," said Stephen Baylin, M.D.

Paula received her doctoral degree in 1964 from the Czech Academy of Sciences in Prague, Czech Republic. Her training included fellowships at the National Research Council in Canada, Curie Institute in Paris, and the Salk Institute. She joined the Johns Hopkins faculty in 1971. Among her many honors, Dr. Pitha-Rowe was the 2005 recipient of the G. J. Mendel Honorary Medal for Merit in Biological Sciences. She was an elected fellow of the American Association of the Advancement of Science (AAAS), an honor that recognizes distinguished scientists who have worked to advance science or its applications.

Paula spent her last days teaching the Biology Department's Virology course and taking care of her grandchildren – two activities she loved.

She is survived by a son, Ian Pitha, M.D., Ph.D., Assistant Professor of Ophthalmology at the Wilmer Eye Institute; a daughter, Ulla Pitha, in investment management in Baltimore; a daughter-in-law, Heather Sateia, M.D., Instructor in Internal Medicine at Johns Hopkins; and two grandchildren, Calla Pitha and Miles Pitha. She also is survived by a younger sister who lives in California and a sister and brother who live in the Czech Republic as well as numerous nieces and nephews in the United States and the Czech Republic.

The family will hold a private burial. Plans for a memorial service with friends and scientific colleagues will be scheduled later this spring.

Sincerely,

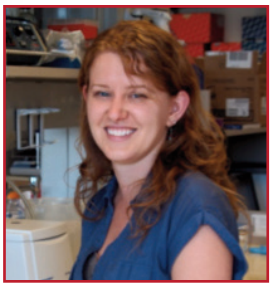
William G. Nelson, M.D., Ph.D.
Marion I. Knott Professor and Director
Sidney Kimmel Comprehensive Cancer Center

2014 MILSTEIN YOUNG INVESTIGATOR AWARDEES

DOMINIC DE NARDO

Institute of Innate Immunity • University Hospital University of Bonn

Dr Dominic De Nardo received his PhD in 2009 from the University of Melbourne, Australia, where he developed a keen interest in macrophages and the innate immune system while working on mechanisms of Toll-like receptor activation. In 2010 he accepted a postdoctoral position with Prof Eicke Latz at the Institute of Innate Immunity in Bonn, Germany, where his research focuses on understanding the mechanisms controlling activation and regulation of innate immune receptors and signaling pathways, and their roles in inflammation during health and disease. During his postdoc Dominic identified the molecular mechanism underlying the ability of HDL to reduce inflammation, co-authored several studies published in journals such as Nature Immunology and Immunity, was invited to edit the innate immunity section of Current Opinion in Immunology and secured funding to lead a junior group. In late 2014 Dominic will return to his homeland to continue his research in the laboratory of Dr Seth Masters within the Inflammation Division at the Walter and Eliza Hall Institute of Medical Research in Melbourne.



STACY HORNER

Molecular Genetics and Microbiology • Duke University Medical Center • Durham, NC

Dr. Stacy Horner is currently an Assistant Professor in the Molecular Genetics & Microbiology and Medicine departments at Duke University Medical Center. She received her Ph.D. in 2007 from Yale University under the mentorship of Dr. Daniel DiMaio. Her postdoctoral fellowship, which was supported by the Irvington Institute Fellowship Program of the Cancer Research Institute, was with Dr. Michael Gale Jr. at the University of Washington. Her postdoctoral research focused on understanding innate immune regulation by hepatitis C virus (HCV), a global human pathogen. During this time, she identified the mitochondrial-associated ER membrane (MAM; a subdomain of the ER located adjacent to mitochondria) as a membrane platform that organizes innate immune signaling to RNA viruses and serves as the intracellular site of immune regulation by HCV. Her current research focuses on understanding the organization and regulation of antiviral innate immunity and how RNA viruses, including HCV, evade innate immunity. Research in her laboratory uses an interdisciplinary approach, combining techniques from cell biology, virology, biochemistry, and systems biology to reveal the viral and host strategies that coordinate and regulate innate immunity to RNA viruses, with the ultimate goal of developing new immunomodulatory strategies for virus treatment and prevention.

2014 MILSTEIN YOUNG INVESTIGATOR AWARDEES

MARIA LIASKOS

Centre for Innate Immunity and Infectious Diseases • MIMR-PHI Institute of Medical Research • Melbourne, Australia

Dr Maria Kaparakis-Liaskos obtained her Ph.D from the Department of Microbiology and Immunology at the University of Melbourne in 2005, under the supervision of Professor Richard Strugnell. Since graduating, Dr Liaskos' research interests have focused on understanding the mechanisms underlying the induction of inflammation and pathology in response to bacterial infection, and in particular, to the gastric pathogen Helicobacter pylori.

Dr Liaskos undertook her post-doctoral studies in the laboratory of Associate Professor Richard Ferrero at Monash University, where she examined innate immune responses to Helicobacter pylori. During this time, she and her colleagues identified bacterial outer membrane vesicles as a novel mechanism whereby all Gram negative bacteria, irrespective of their mode of infection, could be detected by the intracellular pathogen recognition receptor, NOD1.

In 2009, Dr Liaskos joined the Centre of Innate Immunity and Infectious Diseases, at Monash Institute of Medical research, now named the MIMR-PHI Institute of Medical Research. Her current research focuses on understanding the role of NOD1 in responding to bacterial infections and in the development of pro-inflammatory cytokine responses. Her recent research has identified the intracellular location of NOD1, as well as the mechanisms whereby NOD1 detects Gram negative bacterial peptidoglycan, resulting in the generation of autophagy and the production of pro-inflammatory cytokines by the host. These recent findings elucidate the cellular processes underlying NOD1-driven pathology and have the potential to advance the design and development of therapeutics against NOD-Like Receptor (NLR) driven disease states.

2014 MILSTEIN YOUNG INVESTIGATOR AWARDEES

SETH MASTERS

Inflammation Division • The Walter and Eliza Hall Institute • Victoria, Australia

Dr. Masters completed his PhD at the Walter and Eliza Hall Institute (WEHI), which resulted in the first structure of the SPRY/B30.2 domain. In 2006 Dr Masters started a postdoc with Dan Kastner at the NIH who previously discovered mutations in the SPRY/B30.2 domain of the protein Pyrin, which cause familial Mediterranean fever. During this postdoc he was part of a team that discovered a new inflammatory disease caused by mutations affecting the IL-1 receptor antagonist (IL-1Ra). Starting in 2009, Dr Masters completed a second postdoc at Trinity College Dublin where he continued to work on IL-1. Research here showed that soluble oligomers of IAPP, which are increased in type 2 diabetes, trigger the NLRP3 inflammasome to process IL-1β, which impairs the function of insulin producing beta cells. Dr Masters has now started his own laboratory in the newly formed Inflammation Division at WEHI, and has published on miRNA regulation of the NLRP3 inflammasome and the first mouse models of NLRP1 inflammasome modulation.

KATE SCHRODER

Institute for Molecular Bioscience • The University of Queensland • Brisbane, Australia

Kate Schroder's research focuses on the interactions between host and pathogen during the initial stages of infection and the development of inflammation. She received her PhD in 2005 for studies investigating mechanisms of cross-talk between innate immune signalling pathways (interferon-gamma and Toll-like receptors), in the laboratory of David Hume. Her subsequent postdoctoral position with David Hume and Matthew Sweet investigated the transcriptional programs triggered by macrophage differentiation and Toll-like receptor ligation. A key focus of her postdoctoral studies was to define species differences in the TLR4-dependent responses of human versus mouse macrophages. During her NHMRC CJ Martin Fellow in Jürg Tschopp's group in Switzerland, Kate gained expertise in Nod-like receptor function and inflammasome signalling. She returned to Australia in 2011, and now heads the Inflammasome Laboratory of the Institute for Molecular Bioscience, University of Queensland, as an ARC Future Fellow. Her current research interests include mechanisms of signal integration between inflammasomes and other innate immune pathways (e.g. TLRs), the molecular mechanisms governing inflammasome and caspase activation, the evolutionary biology of inflammasomes, and the cellular mediators of inflammasome-dependent inflammation. The Inflammasome Laboratory integrates molecular and cell biology approaches with in vivo studies to gain a holistic understanding of inflammasome function during infection, and inflammasome dysfunction in human inflammatory disease.

2014 CHRISTINA FLEISCHMANN AWARDEE

SOPHIE BROUGHTON

St Vincents Institute For Medical Research
Victoria, Australia

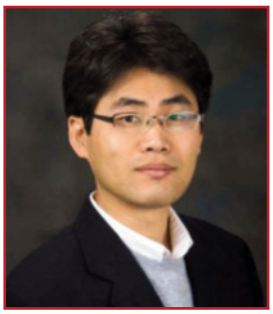
Dr. Sophie Broughton is a Leukaemia Foundation Research Fellow at the Australian Cancer Research Foundation Rational Drug Discovery Centre at St Vincent's Institute of Medical Research, in Melbourne, VIC.

She received her PhD in Structural Immunology in December 2011 at Monash University, Clatyon under the supervision of Professor Jamie Rossjohn and in collaboration with Professor Robert Anderson (Walter and Eliza Hall Institute, Nexpep). Her PhD studies were focused on how T cell receptors (TCR) bind to immunogenic gluten peptides as presented by Major Histocompatibility Complex class II (MHC-II) molecules in celiac disease (CD). She was able to solve the first crystal structure of a CD-associated TCR, and also the first structure of the ternary complex of α-gliadin bound to the MHC-II molecule HLA-DQ8. The culmination of her PhD work was published in the journal *Immunity*.

She now works with Professor Michael Parker and his team on understanding the structural and functional mechanisms of signalling within the beta common cytokine family. She is involved in a number of crystallography-based projects including the structure determination of binary and ternary structures of the IL-3 receptor:cytokine complexes, and IL-3 receptor:Fab complexes. Dr Broughton has recently solved the first structure of the IL-3 alpha receptor and a manuscript based on this work has just been published in *Cell Reports*. Additionally, Dr Broughton has solved the crystal structure of the binary complex of GM-CSF with its alpha receptor, which enabled significant improvement of the existing GM-CSF ternary complex and revealed new insights into conformational changes that occur during cytokine recognition and assembly.

Dr Broughton has so far published 10 papers, 7 since the completion of her PhD in 2011. She has received numerous awards including the 2014 Society of Crystallographers in Australia and New Zealand Rising Star award and the Susan Alberti Women in Research Award (2014). She has also contributed to a number of invited cytokine reviews including *Immunological Reviews, Current Opinion on Structural Biology, Growth Factors, and Cytokine Growth Factor Reviews*.

2014 ICIS JOURNAL OF BIOLOGICAL CHEMISTRY HERBERT TABOR AWARDEE



YEONSEOK CHUNG

Seoul National University
Seoul, South Korea

Dr. Chung received his Ph.D. from the Seoul National University in 2003 with his thesis work focused on understanding the balance between tolerance and immunity in the mucosal immune system. Dr. Chung's research demonstrated that a unique subset of dendritic cells in the gut-associated lymphoid tissues was responsible for cross-priming of intestinal antigens.

Dr. Chung has worked in Dr. Chen Dong's laboratory at MD Anderson Cancer Center as a post-doctoral fellow and later as a junior faculty from 2005 to 2010. His main research interest is to understand the biology of pathogenic T cells in autoimmune diseases in the context of helper T cell subsets and cytokines. Dr. Chung described how sequential cytokine stimulation and transcription factors shape the generation and maintenance of IL-17-producing-inflammatory T cells, follicular helper T cells and follicular regulatory T cells. As a result of his expertise in the area of cellular and mucosal immunology, Dr.Chung was recruited as an assistant professor at the Institute of Molecular Medicine, the University of Texas Medical School at Houston. More recently, he has moved to Seoul National University, South Korea. As an independent scientist, Dr. Chung has been working on how immune systems cross-talk with environmental factors in steady state as well as in disease setting in the context of cytokine and helper T cell involvement. Dr. Chung's research team utilizes genetic and immunologic approaches in diverse animal disease models. He has published 47 research articles in highly prestigious journals such as Nature Medicine, Immunity, Science and Nature Immunology. The outcome of these studies will help us better understand our immune system, and develop novel approaches for the treatment of immune-mediated diseases and cancer.

2014 ICIS SIDNEY AND JOAN PESTKA AWARDEE – Graduate Student Award

ANNIE BRUNS

Molecular Biosciences
Northwestern University
Evanston, IL

Annie Bruns is currently a graduate student in the laboratory of Dr. Curt Horvath in the Department of Molecular Biosciences at Northwestern University. Her research focuses on understanding the biological functions of the cytoplasmic RIG-I-like receptor, LGP2, in regard to RNA virus detection, ATP hydrolysis, and its contribution to a fully functional antiviral response.

To better understand the mechanisms of RLR-RNA recognition and the role of ATP hydrolysis in this process, she established an in vitro model system that combined single molecule TIRF microscopy, quantitative biophysical analysis, and protein biochemistry with analysis of signal transduction and interferon gene activation. This combination of experimental techniques revealed that LGP2 utilizes ATP hydrolysis to enhance and diversify its RNA recognition capacity. This property is required for LGP2 to synergize with another RIG-I-like receptor, MDA5, to potentiate IFNβ transcription in vivo. Further investigation of the relationship between MDA5 and LGP2 through in vitro RNA binding experiments and electron microscopy revealed that LGP2 increases the initial rate of MDA5-RNA interaction, and regulates MDA5-RNA filament assembly, providing a potential mechanism for LGP2 co-activation of MDA5 and a biological context for MDA5-RNA filaments in antiviral responses.

Annie has so far published 8 papers since beginning research in 2008, and when she isn't at the bench she enjoys teaching, advocates science communication through storytelling and art, and participates in various science outreach activities with students ranging from middle school to undergraduates.

2014 ICIS SIDNEY AND JOAN PESTKA AWARDEE – Postgraduate Award

AMANDA HUBER

Neurology
University of Michigan
Ann Arbor, MI

Dr. Amanda Huber received her B.S. cum laude in 2004 from Defiance College, Defiance Ohio. She began her graduate work at the University of Cincinnati in 2005 in the lab of Dr. Yaron Tomer, where her work focused on the functional impact of a single nucleotide polymorphism (SNP) in the kozak consensus sequence of the CD40 gene on the etiology of autoimmune thyroid disease.

In 2008 she was awarded the Ryan Fellowship; the highest honor the College of Medicine awards to a graduate student, recognizing outstanding research accomplishments and potential. In 2009, her lab relocated to Mount Sinai School of Medicine, New York, NY. While here, she received an Outstanding Abstract Award from The Endocrine Society in 2011. Additionally, in 2011 she earned her Ph.D. degree in Immunology from the Mount Sinai School of Medicine. Currently, Dr. Huber is a postdoctoral fellow in the Holtom-Garrett Program in Neuro-immunology at the University of Michigan under the mentorship of Dr. David Irani. Her research is devoted to finding factors that contribute to differential therapy outcomes to IFN-β in the demyelinating autoimmune disease Multiple Sclerosis. The goal of her research is to characterize the role of interferon regulatory factor (IRF)-7, type-I IFN, and lymphoid chemokine production. Early this year she and her colleagues reported in Glia that during viral infection in the central nervous system, microglia from mice deficient in IRF-7 produce more of the lymphoid chemokine CXCL13 compared to wild type mice. Translating this to the mouse model of multiple sclerosis, she hypothesized that both endogenous and exogenous IFN-β act by dampening microglial lymphoid chemokine production during disease, limiting pathogenic inflammation within the CNS. Dr. Huber has amassed a total of 18 publications, 7 as first author, and was recently awarded a postdoctoral fellowship from the National Multiple Sclerosis Society.

2015 ICIS Awards

ICIS AWARDS LIST:

1. Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research
2. Honorary Life Membership
3. ICIS Distinguished Service Award
4. The Milstein Young Investigator Award
   Fleischmann Award to Young Women Investigators
6. Sidney & Joan Pestka Graduate and Post-Graduate Award in Interferon Research Sponsored by PBL Interferon Source
7. Journal of Biological Chemistry/Herbert Tabor Young Investigator Award
8. The Milstein Travel Awards

2015 ICIS AWARDS DESCRIPTIONS:

The Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research

http://www.milstein-award.org/

The Seymour and Vivian Milstein Award for Excellence in Interferon and Cytokine Research, represents the pinnacle of scientific achievement in interferon and cytokine research. This Award is bestowed upon a leading biomedical research scientist who has made outstanding contributions to interferon and cytokine research, either in a basic or applied field. Many laureates have made seminal advancements that have enabled the successful treatment of disease or have the potential to lead to significant health benefits. The winner(s) will be an invited speaker(s) at the annual meeting.

Nominations should be communicated to the Awards Committee of the ICIS through the ICIS website (www.cytokines-interferons.org). Deadline for nomination: **June 1**

Honorary Life Membership

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. Honorary Life Members are accorded all rights and privileges of active members, are exempted from Society dues and annual meeting registration fees, and are listed in the dedicated Honorary Life Members section of the Society web site. The winner(s) is elected by vote of the ICIS Council and will be an invited speaker(s) at the next ICIS meeting.

Nominations should be communicated to the Awards Committee of the ICIS through the ICIS website (www.cytokines-interferons.org). Deadline for nomination: **June 1**

ICIS Distinguished Service Award

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.

Nominations should be communicated to the Awards Committee of the ICIS through the ICIS website (www.cytokines-interferons.org). Deadline for nomination: **June 1**

2014 ICIS Awards continued

The Milstein Young Investigator Award

ICIS members who attend the 2014 ICIS meeting in Melbourne and who have received a Ph.D or M.D. within the previous 10 years are eligible. Every year up to five awards are granted to individuals who have made notable contributions to either basic or clinical research. This award is provided by a generous gift of the Milstein Family. ICIS members may either apply themselves or nominate other eligible members for Milstein Young Investigator Awards. A CV and letter of recommendation (including confirmation of eligibility) should accompany the application.

Deadline to submit your 2015 application is **July 3**.

The Christina Fleischmann Award to Young Women Investigators

The rules for this ICIS award are the same as for the Milstein Young Investigator Award (see above) except for gender and the candidate must have received a Ph.D or M.D. degree within the previous 10 years. This award is made possible through the generosity of the Fleischmann Foundation and is dedicated to the memory of ISICR member and outstanding interferon research scientist Christina Fleischmann. This award is open to young women investigators working in cytokine, chemokine and interferon biology.

Deadline to submit your 2015 application is **July 3**.

The Sidney & Joan Pestka Graduate and Post-Graduate Awards for Excellence in Interferon and Cytokine Research Sponsored by PBL InterferonSource

The Sidney & Jsoan Pestka Graduate and Post-Graduate Awards are targeted to graduate students and post-doctoral fellows who have begun to make an impact in interferon and cytokine research. The Awards are designed to fill the gap among the awards currently offered by the ICIS to more senior investigators—The Milstein Young Investigator Award, the Christina Fleishmann Award, Honorary Membership, and The Seymour & Vivian Milstein Award. Candidates must be actively working in interferon/cytokine research. The award includes a $3500 cash award, $1500 travel grant, a $2500 PBL Assay Science product credit for each awardee, and a complimentary one-year ICIS membership. This is an annual award and a recipient may receive an award only once. However, an individual who receives the Graduate Award remains eligible for the Post-Graduate Award. In years where a suitable candidate is not identified, an award will not be bestowed. Applicants should submit a CV, a letter of support from their mentor, including confirmation of trainee status, and a statement of research and accomplishments. No proprietary or confidential information can be included in the application.

Deadline to submit your 2015 application is **July 3**.

The Milstein Travel Awards

ICIS members who attend the annual meeting are eligible for Travel Awards. They are provided through a grant from the Milstein Family based on the scientific merit of the abstract and financial necessity. This award does not exempt payment of the conference registration fee. There are no age restrictions to this award. However, if both senior and junior members from the same laboratory apply for an award, preference is given to the junior member. This award is dependent on availability of funds.

Deadline to submit your 2015 application is **July 3**.

The Journal of Biological Chemistry/Herbert Tabor Young Investigator Award

The Journal of Biological Chemistry/Herbert Tabor Young Investigator Award will be presented at the ICIS meeting in Melbourne. The award, that includes a crystal award and cash prize, honors Herb Tabor, who served for 40 years as the distinguished Editor in Chief of The JBC, and recognizes a young investigator who exemplifies Herb Tabor's values of creativity and scientific excellence. The award will be made to a Melbourne meeting participant based on the excellence of their abstract and other application materials. Postdoctoral researchers and junior faculty members who have not yet received tenure are eligible. A CV and letter of recommendation should accompany the application. Deadline to submit your 2015 application is **July 3**.

NEW ICIS MEMBERS

We welcome these new members to the society and look forward to their participation in the society and the annual meeting.

Ma.del Banas-Lara
LSU
USA

Tyler Barker
Intermountain Healthcare
USA

Nikola Baschuk
La Trobe University
Australia

Subir Biswas
India

Lars Bjork
Karolinska Institutet
Sweden

Alison Browning
Monash University
Australia

Daniel Croker
The University of Queensland
Australia

Michael Farrar
University of Minnesota
USA

Conor Finlay
Trinity College Dublin
Ireland

Terry Fredeking
Antibody Systems, Inc.
USA

Ryann Guayasamin
Yale University
USA

Tang Hu
Barry University
USA

Caleb Huang
Centre for Life Sciences (CeLS)
Singapore

Winnie Kan
Centre for Cancer Biology
Australia

Ronan Kapetanovic
Univ of Queensland
Australia

Yiliu Liu
Lady Davis Institute, Jewish General Hospital
Canada

Toshifumi Matsuyama
Nagasaki University
Japan

Kevin Moore
USA

Eric Pietras
University of California San Francisco
USA

Sarah Pogue
Teva Pharmaceutical Ind, Ltd
USA

MARIA Sanchez-Aparicio
Icahn School of Medicine at Mount Sinai
USA

Smriti Sharma
Inst of Medical Sciences, BHU
India

Kalpana Shrivastava
Medical Histology
Spain

Natalie Sims
St Vincent's Inst
Australia

Elizabeth Jeanne Thatcher
U. of Massachusetts Medical School
USA

Di Yu
Monash University
Australia

Liang Yu
Monash University
Australia

Feng Zhu
NIH/NCI/CCR Cancer & Inflammation Prog
USA

Dr. Robert Friedman receiving a plaque from the ICIS in honor of his outstanding career in Interferon Research. Presented by ICIS member Dr. Robert Silverman at a Festschrift In Honor of Dr. Friedman, held on Friday the 21st of November, 2014 at the USUHS in Bethesda, MD.

See the ICIS President, Richard Flavell, give an NIH lecture on "Inflammation, Dysbiosis and Chronic Disease" at https://www.youtube.com/watch?v=O3PCfOEoErQ

ICIS Member spearheads Ebola Clinical Trial

A pilot study to evaluate the safety and efficacy of interferon beta-1a (IFN-ß-1a) in the treatment of patients presenting with ebola virus illness.

Principal Investigators: Eleanor Fish, University Health Network, Toronto, Ontario, Canada. Mandy Kader Konde, CEFORPAG, Conakry, Guinea.

Contact: Eleanor Fish, Phone: 416-340-5380; mail to: en.fish@utoronto.ca

New Member MINIBIOs by Haiying Li

Dr. Rich Robinson, PhD
Assistant Professor
Microbiology and Molecular Genetics
Medical College of Wisconsin, USA

Dr. Rich Robinson received his Ph.D. from Dartmouth (Hanover, NH) in 2007; his doctoral studies focused on regulation of the CD4+ TCR Vβ repertoire by TGFβ1, and were performed in the lab of Dr. James Gorham. He completed his postdoctoral training in TB Immunology at the Trudeau Institute (Saranac Lake, NY) under the mentorship Dr. Andrea Cooper, and then started his independent position at the Medical College of Wisconsin in 2011. The focus of Dr. Robinson's lab is to understand how the gene IL12RB1 promotes TB resistance, how IL12RB1 mRNA sequence variation is introduced at the post-transcriptional level, and the impact of IL12RB1 mRNA sequence variation on TB resistance. For these studies, his lab integrates basic immunology and molecular biology approaches with the TB mouse model.

Dr. Malcolm Starkey, PhD
NHRMC Early Career Fellow School of Biomedical Sciences and Pharmacy
Faculty of Health and Medicine
Priority Research Centre for Asthma and Respiratory Diseases
Hunter Medical Research Institute, University of Newcastle, Australia

Dr. Malcolm Starkey was awarded his PhD in Immunology and Microbiology from the University of Newcastle in 2014 and did short-term post-doctoral training at the National Heart and Lung Institute, Imperial College London. He is currently a National Health and Medical Research Council of Australia early career post-doctoral fellow at the Priority Research Centre for Asthma and Respiratory Diseases in Newcastle Australia. Malcolm's research focuses on early-life respiratory infections (bacterial and viral) and understanding how these infections predispose to the development of chronic diseases (e.g. asthma, emphysema, diabetes) in later life. His research also explores the mechanisms underpinning the development of chronic obstructive pulmonary disease (COPD) and respiratory infection-induced asthma and COPD exacerbations. This is achieved using a combination of clinically relevant mouse models and human primary bronchial epithelial cell cultures.

Dr. Carole Oskeritzian, PhD
Assistant Professor
Department of Pathology, Microbiology and Immunology
USC School of Medicine, USA

Dr. Carole Oskeritzian is an Assistant Professor in the Department of Pathology, Microbiology and Immunology at the USC School of Medicine since the summer of 2012. Using preclinical models mimicking life-threatening anaphylaxis and atopic dermatitis (eczema), Dr. Oskeritzian' s continuously NIH-funded research has identified tissue-resident mast cells and sphingosine-1-phosphate, a signaling lipid metabolite produced by mast (and other, including cancer) cells, on the front line of inflammatory processes. Her laboratory employs pharmacological, molecular and genetic approaches to better understand the inception of inflammation and its epigenetic regulation to prevent rather than cure inflammatory disorders which could lead to cancer.

New Member MINIBIOs by Haiying Li *continued*

Dr. Michael Farrar, PhD
Professor
Center for Immunology
University of Minnesota

Dr. Michael Farrar received his B.S. in Molecular Biology at the University of Wisconsin. He carried out his Ph.D. studies with Dr. Bob Schreiber at Washington University in St. Louis. His thesis work on interferon-gamma receptor signaling established the initial paradigm that cytokine receptors directly recruit and activate STAT transcription factors by direct binding to tyrosine residues in their cytoplasmic tail. Dr. Farrar then carried out postdoctoral studies with Dr. Roger Perlmutter at the University of Washington and subsequently Merck Research Labs where he developed novel chemical-induced dimerization strategies to study signal transduction. Dr. Farrar is currently a professor in the Center for Immunology at the University of Minnesota. His research focuses on three distinct areas of lymphocyte biology. The first major area of interest in the lab involves understanding how cytokine signaling governs the development of regulatory T cells. The second area of focus in the lab is how cytokine receptors and the Jak/STAT5 pathway affect early B cell development, and how perturbations of this pathway interact with other B cell transcription factors to initiate leukemia. Finally, the last area of interest in the Farrar lab is focused on tracking CD4+ T cell immune responses to BCR-ABL+ leukemia. The lab has currently developed tools that allow one to track leukemia-antigen-specific T cell responses and is using these tools to determine how leukemic cells evade the adaptive immune response.

Dr. Natalie Sims, PhD
Associate Director
St. Vincent's Institute, Melbourne, Australia

Assoc. Prof. Natalie Sims directs the Bone Cell Biology and Disease Unit at St. Vincent's Institute and is a Principal Research Fellow at The University of Melbourne. She completed her PhD in 1995 at the University of Adelaide, and carried out postdoctoral studies at the Garvan Institute (Sydney) and Yale University, USA. She defined the roles of Oncostatin M, Cardiotrophin 1, and Leukemia Inhibitory Factor on the development and maintenance of the skeleton, using genetically altered mouse models and in vitro systems. Her current work continues to focus on paracrine control of the skeleton, particularly the way parathyroid hormone, IL-6 and STAT1/3 signalling influence bone formation and destruction. Dr Sims is a board member of the Australian and New Zealand Bone and Mineral Society, and the American Society for Bone and Mineral Research (ASBMR). She is a Senior Editor of the journal Bone, Advisory Editor for Arthritis & Rheumatology, and past Associate Editor of Calcified Tissue International. Her work has been recognised by the ASBMR Fuller Albright Award (2010) and the International Bone and Mineral Society Herbert A Fleisch Award (2013), both for major scientific achievements before the age of 45.

Clinical Trials *by Marta Catalfamo*

Yttrium Y 90 Anti-CD45 Monoclonal Antibody BC8 Followed by Donor Stem Cell Transplant in Treating Patients With High-Risk Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, or Myelodysplastic Syndrome
Principal Investigator: Brenda Sandmaier, MD. Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium. Seattle, Washington, United States
Contact: Brenda M. Sandmaier, MD. Phone: 206-667-4961
ClinicalTrials.gov Identifier: NCT01881464

Intraocular Cytokines in Non-responders to Ranibizumab Treatment for Neovascular AMD
Principal Investigator: Wai-Ching Lam, MD. Toronto Western Hospital, University Health Network, University of Toronto. Canada
Contact: Wai-Ching Lam, MD. Phone: 4166035376
waiching.lam@utoronto.ca
ClinicalTrials.gov Identifier: NCT02218177

Systemic Therapy With Interferon, Interleukin-2 and BRAF Inhibitor
Principal Investigator: Rodabe N. Amaria, MD. University of Texas MD Anderson Cancer Center. Houston, Texas, United States
Contact: Rodabe N. Amaria, MD. Phone: 713-792-2921
ClinicalTrials.gov Identifier: NCT01603212

Comparison of High-dose IL-2 and High-dose IL-2 With Radiation Therapy in Patients With Metastatic Melanoma. (SBRT/IL-2)
Principal Investigator: Brendan Curti, M.D; Steven K. Seung, M.D; Marka Crittenden, MD, PhD. Providence Health & Services. Portland, Oregon, United States
Contact: Christopher Fountain, R.N. Phone: 503-215-2691
christopher.fountain@providence.org
ClinicalTrials.gov Identifier: NCT01416831

Phase I/II Study of De-immunized DI-Leu16-IL2 Immunocytokine Administered Subcutaneously in Patients With B-cell NHL
Principal Investigator: Ryotaro Nakamura, MD. City of Hope. Duarte, California, United States
Contact: Michelle Nelken. Phone: 617-755-4149
michelle.nelken@alopexx.com
ClinicalTrials.gov Identifier: NCT01874288

Aerosol IL-2 for Pulmonary Metastases
Principal Investigator: Aung Naing, MD. M.D. Anderson Cancer Center, Houston, Texas, United States
Contact: Aung Naing, MD. Phone: 713-563-0181
ClinicalTrials.gov Identifier: NCT01590069

AIDS 347: IL-6 Blockade in Treated HIV Infection
Principal Investigator: Benigno Rodriguez, MD. Case Western Reserve University. Cleveland, Ohio, United States.
Contact: Cheryl Smith, 216-844-8052
smith.cheryl@clevelandactu.org
ClinicalTrials.gov Identifier: NCT02049437

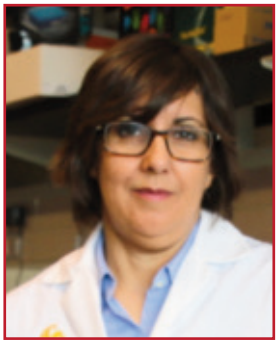
Evolution of Interleukin 7, Fat Mass and Metabolic Profile Before and After Transplantation (IL-7tran)
Principal Investigator: Marie-Christine VANTYGHEM, MD, PhD, Lille University Hospital
Contact: Marie Christine Vantyghem, PhD
+33 3 20 44 45 35, mc-vantyghem@chru-lille.fre
ClinicalTrials.gov Identifier: NCT01414660
Multiple Ascending Dose Trial of MSB0010841 (Anti-IL17A/F Nanobody) in Psoriasis Subjects
Principal Investigator: Study Director, Medical Responsible, Merck KGaA
Contact: Merck KGaA Communication Center. Phone:
+49 6151 72 5200, service@merckgroup.com
ClinicalTrials.gov Identifier: NCT02156466

Intratumoral Administration of L19IL2/L19TNF
Principal Investigator: Mario Santinami, MD. Fondazione IRCCS Istituto Nazionale dei Tumori. Milan, Italy
Contact: Leonardo Giovannoni, MD. Phone:
+39 0577- 588 539, leonardo.giovannoni@philogen.it
ClinicalTrials.gov Identifier: NCT02076633

Anti-TNF Use During Elective Foot and Ankle Surgery in Patients With Rheumatoid Arthritis
Principal Investigator: Mélissa Laflamme, MD, MSc, FRCSC. Centre Hospitalier Universitaire de Québec, CHU de Québe. Canada
Contact: Melissa Laflamme, MD, MSc. Phone:
418-525-4444 ext 46618
ClinicalTrials.gov Identifier: NCT02242474

DNX-2401 With Interferon Gamma (IFN-γ) for Recurrent Glioblastoma or Gliosarcoma Brain Tumors (TARGET-I)
Principal Investigator: Karen Fink, MD, PhD. Baylor University: Charles A. Sammons Cancer Center. Dallas, Texas, United States
Contact: Amy Solis. Phone: 214-820-8685
Amy.Solis@BaylorHealth.edu
ClinicalTrials.gov Identifier: NCT02197169

INTERLEUKIN-7 – COMING OF AGE



Dr. Annette Khaled
Burnett School of Biomedical Sciences
College of Medicine
University of Central Florida

Interleukin-7 (IL-7) is twenty-seven years old – at least if you date from the cloning of the gene in 1988[1]. Mice and humans lacking IL-7, its receptor, or any of its signaling components are extremely lymphopenic[2, 3] - *remember the bubble boy*! So clearly, soon after its discovery, IL-7 emerged as a major player in the immune system. IL-7 deficiency causes a block in the development of double-negative thymocytes, reducing thymic cellularity. It's prominence as an essential factor for a healthy immune system was demonstrated when a key function in the maintenance of naive and memory lymphocytes was discovered in the early 00's[4, 5]. This explains why mutations in IL-7 signaling are associated with so many forms of human disease, from immunodeficiency syndromes to autoimmune diseases, leukemia and even in chronic infections with HIV just to name a few. Elegant studies, using reporter mice, found the major sources of IL-7 to be the bone marrow and thymus[6] with cells in lymph nodes, liver, Peyer's patches, and other intestinal and dermal sites also producers of the cytokine. The availability of IL-7 to drive its diverse functions is thus controlled by combination of factors: production, secretion, degradation and binding to the extracellular matrix. Responsive lymphocytes express the IL-7 receptor (IL-7R), a dimer of the common γ (γc) chain and the unique α chain (CD127), in a manner that is highly regulated. Signals are mediated through the Jak/STAT pathway and intersect with other signaling pathways like PI3 kinase and mTOR[7]. Signals can also be driven through binding of thymic stromal lymphopoietin (TLSP) to CD127. Suffice to say, with all this information, we've learned a lot about IL-7 and explained much of its functions.

But is that all…

In the last couple years we've become aware of a group of lymphoid-like cells that lack antigen receptors and are part of the innate immune response. These innate lymphoid cells (ILCs) produce cytokines previously associate with helper T cells like interferon-γ (IFN-γ), IL-5, IL-22 and IL-17. In fact, recent nomenclature divides ILCs into three groups that are reminiscent of TH1, TH2 and TH17. Group 1 ILCs are associated with production of IFN-γ, group 2 ILCs make a little IL-4 but more IL-5 and IL-13, while group 3 are more diverse, producing IL-17 and IL-22[8]. Like their adaptive immune system counterparts, ILCs are characterized by signature transcription factors, T-bet, RORγt and GATA-3, in ways that are still being understood. What is known, however, is that, with the exception of conventional natural killer (NK) cells, all ILCs require IL-7 signaling for survival (and maintenance?). In fact, CD127 expression is found on most ILC populations – albeit less than 1% of circulating lymphocytes. CD127+ILC2s are found in the peripheral blood and some CD127+ ILC1s are found in the gut (although their function is still being studied)[9]. Additionally, all ILC subsets express Id2, the transcriptional regulator inhibitor of DNA binding 2. Deletion studies of Id2 suggested that ILCs may arise from a common Id2-expressing (and $CD127^{hi}$?) progenitor. Determining this and *unraveling the molecular cues that control development and function of ILCs* are questions that need answers in order understand the function of ILCs in healthy and disease states.

To that end, two papers in 2014, one published in Cell and another in *Immunity*, brought us closer to understanding what ILCs are about and their connection to IL-7. Klose et al (Cell, 2014) identified an Id2-expressing progenitor that gives rise to all IL-7R+ ILCs of the "helper-type"[10] – called CHILP. CHILP produces the ILC2 and ILC3 lineages and a new, but odd, subset of ILC1 that expresses the NK receptor, NKp46, and requires T-bet, but is distinct from the conventional NK cells. This subset protects against intracellular pathogens by producing IFN-γ and TNF. The significance of this work is that expression of IL-7R+ may drive progenitors into different ILC lineages – with IL-7R+ cells producing the indicated "helper-like" subsets of ILCs and IL-7R- cells following a different differentiation pathway to produce the "cytotoxic/killer-like" ILCs. The second paper by Yagi et al (Immunity 2014) identified more of the molecular controls that guide the development of IL-7R+ ILCs[11]. They reported that GATA-3, a key transcription factor for TH2 cells, is required for the development of all IL-7R+ ILCs as well as for

their later maintenance. Together these two studies suggest that the IL-7R+ subsets of ILCs resemble innate versions of Th subsets, further emphasizing the symmetry between ILCs and the adaptive immunity counterparts, with expression of the IL-7R α chain an important component of the ILC differentiation mechanism.

Differentiation and maintenance of ILC subsets can now be added to IL-7's to-do list, along with generating T cells and supporting naïve and memory populations. How IL-7 does it remains obscure – inducing Bcl-2 for survival or causing chromatin modifications to support lineage plasticity are possibilities. But looming questions remain like - how is the spatiotemporal expression of IL-7 is peripheral tissues controlled? Or under what pathological condition is IL-7 expression enhanced? And what is the link between IL-7R and Id2 and does IL-7 modulate cytokine production by ILCs? Central to the IL-7 knowledgebase is learning how to selectively manipulate IL-7-dependent immune populations to treat disease like chronic infections or autoimmunity. Through it all, one has to appreciate that IL-7 is becoming more interesting and impactful through its pleotropic roles in innate and adaptive immunity. It is not just the cytokine responsible for thymic maturation anymore. IL-7 has grown up.

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Assays for Interferons in the Early Days of Interferon Research

by Bob Friedman, M.D.

In the late 1950s and early 60s investigators studying interferons were faced with several existential problems. The most pressing one was how one assayed for a substance many prestigious scientists claimed didn't exist. Interferons were mocked as imaginons. This was because many labs had not been able to reproduce the original observations of Isaacs and Lindenmann. The reasons for this failure were numerous. Sometimes it was due to the fact that many investigators had no idea how to produce an interferon; in some cases, a preparation that did indeed contain an interferon was assayed on a species of cell which did not respond to that type of interferon; in others substances that inhibited the action of the interferon were present; and finally, some labs had no clue at all about to how to assay interferon.

The last was not puzzling. Interferon assays in the early days depended solely on the ability of a putative interferon preparation to inhibit virus growth. The assays used were laborious, imprecise compared to then current methods employed in chemistry and biology, and the preparations to be assayed were quite impure, and so often contained substances that blocked the antiviral activity of interferon, or were themselves virus inhibitory, and thus led to false positive results. Furthermore, it was difficult to compare results from different laboratories, as each group had its own assay procedure. The later difficulty was partially overcome by the development of international standard interferon preparations, and distributing these to the groups studying interferons.

The most common procedure involved studying the inhibition of virus yield induced by interferon treatment. The method employed by Isaacs and Lindenmann was to study the decrease in influenza virus hemagglutinin formation in chick membrane preparations pretreated with interferon. Since not many labs were as skilled as Isaacs' group at Mill Hill in handling influenza virus, other methods involving the principle of inhibition of virus yield were quickly developed. One method extensively employed was to study the yield of virus plaque formation in an agar overlay system. Cells were treated with dilutions of interferon for several hours before being infected. Several different viruses were employed in such studies. EMC virus, VSV, or Semliki Forest virus was commonly used in such assays which were reasonably easy to perform, fairly accurate and repeatable, but since the viruses used differed in their sensitivity to interferon, and were used on different types of cells treated with different interferons, it was impossible to compare results from the various groups studying interferon, unless interferon standards were included in the assay.

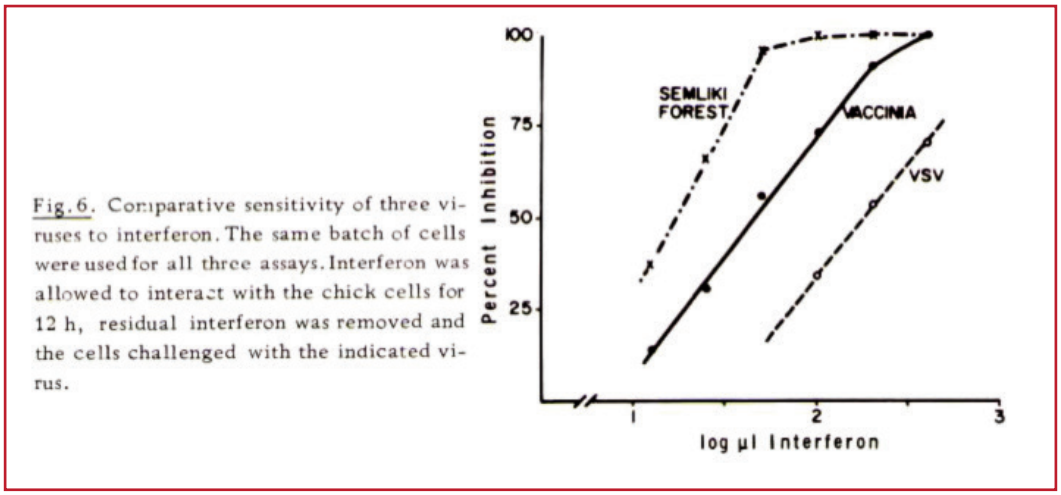

Fig. 6. Comparative sensitivity of three viruses to interferon. The same batch of cells were used for all three assays. Interferon was allowed to interact with the chick cells for 12 h, residual interferon was removed and the cells challenged with the indicated virus.

The Interferon System, Second Edition by William Stewart II, Springer-Verlag, 1981.

Assays for Interferons in the Early Days of Interferon Research

continued

A simpler procedure was to study directly the reduction in virus yield induced by interferon treatment. The disadvantage of this procedure is that it is a two-step one: interferon-treated cells and controls were infected with virus, and the yield of virus assayed by a virus plaque or cytopathic effect (CPE) assay. A variation on this procedure was to look directly at the ability of dilutions of an interferon preparation to inhibit virus CPE by a standard virus dilution.

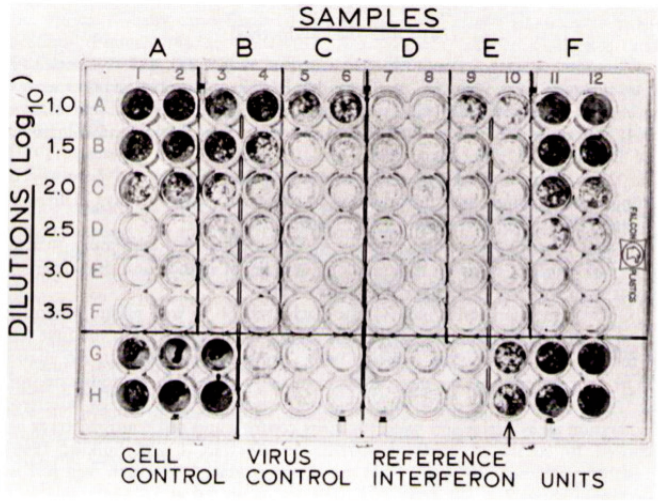

Fig. 3. Microtiter tray assay by CPE-reading method. The titers of the samples estimated from visual microscopic readings were: A, 100 units/ml; B, 60 units/ml; C, 20 units/ml; D, <10 units/ml; E, ~10 units/ml; F, 200 units/ml. Reference interferon assay 1 unit at arrow

The Interferon System, Second Edition by William Stewart II, Springer-Verlag, 1981.

Several other types of assays were developed by investigators studying interferon. In one, the metabolic inhibition assay, cells treated with interferon dilutions were infected with a cytopathic virus, and after 4 to 6 days the pH of the culture fluid was evaluated. If the cells had been destroyed by the virus, the pH remained close to neutral; if interferon had protected the cells, the cellular metabolism turned the pH acid. In another method viral-induced hemadsorbtion was evaluated by lysing the red blood cells that had adsorbed to cells, and assaying the amount of hemoglobin released. Cells protected by interferon pretreatment had less hemadsorbtion produced by viral infection than did controls.

One method that at this time was employed extensively deserves special mention. The fluid overlay procedure involved adding a 100-200 plaque forming units of vaccinia virus to interferon preparations, and after 48 hrs staining the monolayer of cells with crystal violet. The plaques formed by vaccinia virus in the monolayer are very easy to read. This is a relatively simple procedure to perform, but extensive studies with it indicated that non-specific inhibitors of virus growth often gave rise to false results.

Even with the employment of standards, interferon assays at these early stages were very messy procedures. Really acceptable studies in this area had to await the development of the assays in use at the present time.

WWW

BiERapp

http://bierapp.babelomics.org/

Welcome to the gene/variant prioritization tool of the BIER (the Team of BioInformatic for Rare Diseases). This interactive tool allows finding genes affected by deleterious variants that segregate along family pedigrees, case-controls or sporadic samples.

Try an Example
Here you can try all the filtering options and discover the gene affected in a test family.

Analyze your own families or case-control data
Here you can upload your VCF file containing the exomes to be analyzed. Define the thresholds of allele frequencies, pathogenicity, conservation; the type of variants sought; and define the type of inheritance and the segregation schema along the family.

Biomet Toolbox

http://biomet-toolbox.org/index.php?page=home

The BioMet ToolBox Version 2.0 (1) is a web-based resource for exploiting the capabilites of metabolic networks described in genome scale models using flux analysis and random sampling, powered by RAVEN, gene set analysis and basic microarray analysis using PIANO, thereby providing an integrated analysis to identify coregulated subnetwork structures within the metabolic network and also for identifying statistically significant gene sets enabling biological interpretation.

CHOPCHOP

https://chopchop.rc.fas.harvard.edu

CHOPCHOP is a web tool for selecting the optimum target sites for CRISPR/Cas9- or TALEN-directed mutagenesis.

CHOPCHOP can be run with as few as three basic input options, or with additional advanced parameters. The basic input comprises: (i) a gene name, genomic coordinates or a pasted sequence (including RefSeq and ENSEMBL gene IDs); (ii) a growing list of organisms and (iii) the choice between CRISPR/Cas9 or TALEN mode. The advanced options provide the user with more flexibility when choosing target sites.

If you use our tool please cite: Tessa G. Montague; Jose M. Cruz; James A. Gagnon; George M. Church; Eivind Valen. (2014). **CHOPCHOP**: a CRISPR/Cas9 and TALEN web tool for genome editing. *Nucleic Acids Res. 42*. W401-W407

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COGERE

http://mips.helmholtz-muenchen.de/cogere

Background

Understanding how regulatory networks globally coordinate the response of a cell to changing conditions, such as perturbations by shifting environments, is an elementary challenge in systems biology which has yet to be met. Genome-wide gene expression measurements are high-dimensional as these are reflecting the condition-specific interplay of thousands of cellular components. The integration of prior biological knowledge into the modeling process of systems-wide gene regulation enables the large-scale interpretation of gene expression signals in the context of known regulatory relations.

Description
COGERE (modeling of condition-specific gene regulation; Latin cogere = to collect) is a method for the inference of transcriptional and miRNA-mediated post-transcriptional condition-specific gene regulatory networks in human and mouse.

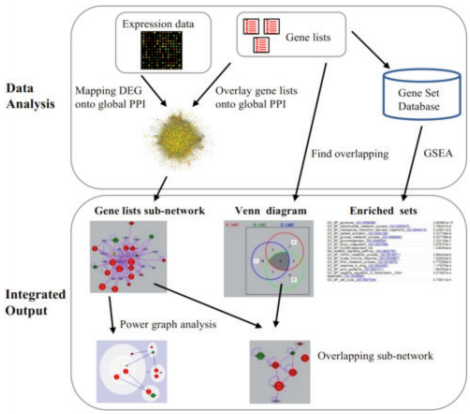
COGERE integrates existing knowledge of regulatory interactions from multiple sources, such as curated data, data obtained from mining of all available biomedical text, data from major studies (e.g. ENCODE, CLIP-Seq) and sequence-based predictions, to a comprehensive model of prior information. **COGERE** infers condition-specific regulation by evaluating the mutual dependency between regulator (transcription factor or miRNA) and target gene expression using prior information. This dependency is scored by the non-parametric, non-linear correlation coefficient $\eta 2$ (eta squared) which is derived by a two-way analysis of variance. **COGERE** allows the inference of regulatory networks from a variety of experimental designs: mRNA expression with or without miRNA expression from the same or different samples for at least two conditions.

https://s3-us-west-2.amazonaws.com/mayo-bic-tools/mace/index.html

ChIP-exo allows for precise mapping of protein-DNA interactions. It uses λ phage exonuclease to digest the 5' end of protein-bound and formaldehyde-crosslinked DNA fragments and thereby creates a homogenous 5' border at a fixed distance from the protein binding location. After sequencing, the 5' ends of reads align primarily at two genomic locations corresponding to two borders of protein binding site. (Rhee & Pugh, 2011 Cell; Rhee & Pugh, 2011 Nature; Mendenhall & Bernstein, 2012 Genome Biol.) MACE is a bioinformatics tool dedicated to analyze ChIP-exo data that operates in 4 major steps: 1) Sequencing depth normalization and nucleotide composition bias correction. 2) Signal consolidation and noise reduction using Shannon's entropy. 3) Single base resolution border detection using Chebyshev Inequality. 4) Border matching using Gale-Shapley's stable matching algorithm.

NetVenn

http://wheat.pw.usda.gov/NetVenn/



NetVenn is a network-based web platform for the comparison and analysis of gene lists by combining Venn diagram and gene set enrichment. The tool can integrate gene sets with differentially expressed gene on interaction network. Power graph analysis is available for the gene lists network.

NetWork Analyst

http://www.networkanalyst.ca/NetworkAnalyst/

NetworkAnalyst is designed to support integrative analysis of gene expression data through statistical, visual and network-based approaches:

Data inputs: one or more gene/protein lists with optional fold changes; one or more gene expression tables from microarray or RNAseq experiments.

Statistical analysis: for single data - paired comparisons, time series, common reference, and nested comparisons; for integrating multiple data sets - p values, fold changes, effect sizes, vote counts, and direct merge.

Network construction: zero-order, first-order, higher-order interaction network or minimum interaction networks;

Network analysis & visualization: interactive visual exploration - zooming, searching, highlighting, point-and-click; network customization - layout (supporting four automatic layout algorithms, as well as manual drag-and-drop), background color, edge size/shape, node size/color/visibility; topology analysis - hubs, modules, shortest paths; in situ functional enrichment analysis based on pathways or gene ontology; network editing - node deletion, module extraction, and image exporting.

Visual analytics: interactive heatmaps and chord diagrams for data exploration.

TriplexRNA

A database of cooperating microRNAs and their mutual targets

http://www.sbi.uni-rostock.de/triplexrna/index.html

The workflow integrates methods of miRNA target prediction; triplex structure analysis; molecular dynamics simulations and mathematical modeling for a reliable prediction of functional RNA triplexes and target repression efficiency.

EARLY REFLECTIONS ON INTERFERON AND NEW CYTOKINES

Norwood Hill, M.D.
Consultant to Antibody Systems, Inc.

I first learned about the interferon that had been discovered by Alec Isaacs and Jean Lindemann during two summer virology fellowships in 1959 and 1960 when I was a medical student at Baylor College of medicine. My mentors were Dr. Joseph L Melnick and his associate Heather Donald Mayor PhD. Dr. Mayor knew Dr. Isaacs while she was earning her PhD at the University of London in 1954. I read the original paper. In addition we discussed interferon at some of our conferences. It was recognized that interferon might prove useful for treating virus diseases.

Years later, in the mid-1970s, I was involved in conducting phase I and phase II clinical trials in leukemia and cancer. Some of the drugs tested were produced at the Wadley institutes of Molecular Medicine . One of these, L-asparaginase, was actually produced in a 1000 liter fermenter especially constructed just for that project. I mention this because it again became useful for producing recombinant proteins several years later.

Interferon became a renewed interest for me and my colleagues when we learned of reports from a small study in New York that direct injection of breast cancers tumors might be having some benefit. We also learned that Hans Strander in Sweden seemed to be finding some benefit with the administration of interferon to patients with osteogenic sarcoma and juvenile laryngeal papilloma. The interferon was being produced by Dr. Kari Cantell in Helsinki Finland at the Red Cross blood center. Since Wadley included the major regional blood center for the Dallas region, we were in an excellent position to start interferon production at our institute. Lee Fikes, head of the Fikes foundation and a member of the Wadley Board of Trustees agreed to provide a grant to establish Wadley's interferon production laboratory. Gordon Dorn PhD, Wadley's chief of microbiology, sent his colleague, Jeffrey Land PhD, to Helsinki to obtain materials including the Sendai virus that was used to stimulate interferon production. By 1978, we were able to report two cases of childhood acute lymphatic leukemia who responded with substantial reduction of leukemic blasts when treated intravenously with high doses of alpha interferon.

One of the leukemia patients was a four-year-old girl who also had non-A, non-B hepatitis with SGOT levels of about 250 units. Over 21 days, the SGOT was reduced to 40. She may have been one of the first patients responding to interferon with what later became known as hepatitis C. I reported these results at the South Central Association of blood Banks meeting in February 1978. The results were published along with additional cases in the proceedings of an international conference on interferon held at Wadley in the fall of 1979.

Soon after our report, we were contacted by Mary Lasker's nephew, James Fordyce, from the Lasker foundation regarding their interest in interferon and possible expansion of production at Wadley that could include other institutes such as MD Anderson hospital. Mr. Fordyce was friends with Bob Swanson. Fordyce, Jordan Gutterman of MD Anderson and Bob Swanson, founding CEO of Genentech, visited our production laboratories. We agreed to harvest white cells from our tissue cultures in the middle of the night during maximum interferon production, flash freeze the cells, and trans-port them by FedEx to Genentech in South San Francisco California. The object was to obtain the alpha interferon gene from producing cells. Unfortunately, their frog oocyte assays for interferon mRNA were not working properly at the time. Eventually Genentech had success in obtaining the gene from a California patient's leukocytes. Our arrangement with Genentech did not involve monetary payments to Wadley. However, Genentech provided materials and training to personnel and Dr. Amanullah Khan's Department of Immunotherapy so that we could get into monoclonal antibody research.

I knew almost nothing about Genentech until James Fordyce got us in touch with Bob Swanson. But I got a little bit of an education about startups, venture capital, and IPOs when I got a call from San Francisco in October 1980 a few days before Genentech's initial public offering asking how many shares of the stock I would like to buy for the offering. Despite only meeting him one time, Bob Swanson had put me on the list of friends of Genentech. I have recently read

Sally Smith Hugh's book "Genentech" that he remembered who his friends were including excellent treatment of Genentech employees and others who had helped the company. I asked if I could get back to the individual who called. In the next few minutes, I was able to come up with $10,500 together with my brother-in-law that we invested in the offering. Our stock shares doubled the first day. IPOs don't always turn out successfully. But I thought it was kind of neat to have a small stake in the company that became the model for the recombinant DNA industry and a whole new field of pharmaceuticals.

Soon thereafter, the Meadows foundation funded a department of genetic engineering at Wadley, chaired by Arthur Bollon PhD. One of the laboratories principal activities was to treat messenger RNA from interferon producing cells with reverse transcriptase. The resulting DNA was inserted into plasmids to create a library of multiple E. coli clones. This would lead to an interesting experience with another cytokine, tumor necrosis factor. When I received the April 12, 1985 issue of science in the mail at home I was excited to see that Genentech had published the DNA sequence. At work the next day, I had such a busy schedule that I couldn't talk to any of the genetics people during regular hours. However, at about 6:30 PM, I went to the genetics laboratory and found that Susan Berent PhD was simply reading journals while she waited for her husband Rich Torczynski PhD to finish an experiment. She was sitting next to the Gene Synthesis Machine when I showed her the article. She said: "I can program this machine to make the DNA probes tonight". Two or three days later she found the clone that contained the tumor necrosis factor gene. As chance would have it, Dr. Khan's immunotherapy group had been taking small samples of leukocytes from our interferon production laboratory and stimulating them with mitogens instead of Sendai virus. They had developed a small-scale method for purifying tumor necrosis factor. Their assay of the recombinant tumor necrosis factor showed high levels of production. Within about two weeks they had scaled up their purification method and found that it worked quite well on the recombinant TNF from the E. coli grown in a small-scale fermenter. We immediately reactivated the 1000 Liter L-asparaginase fermenter that had not been used for seven years. The chief interferon production tech, Salvador Comparini, had previously been the L-asparaginase production chief and now became the TNF production chief. The method for removing E. coli endotoxin contained in Wadley's L-asparaginase patents did the job perfectly for TNF. In all of our experience with developing cancer drugs, we had never experienced a scale up that had no flaws from start to finish. We did a rough estimate that producing an equivalent amount of TNF in leukocyte cultures was about 10,000 times more expensive than our recombinant material. It was pretty exciting stuff to experience firsthand the power for manufacturing recombinant drugs or diagnostic antigens. And we had produced very large amounts of tumor necrosis factor in just our first fermentation run.

Everything went perfect up to a point. Manufacturing went off without a hitch. Final review by the protocol committee and Institutional Review Board gave us approval to begin clinical trials with intratumoral injection, and we actually began those clinical trials one day before MD Anderson hospital physicians began clinical trials with the Genentech product. Then perfect at every step stopped. Although tumor necrosis factor from mice was quite effective against mouse tumors without noticeable toxicity, that didn't turn out to be the case in humans. Treating patients with the human material turned out to be quite toxic.

An amusing event occurred in the late 1970s or early 1980s at a meeting I attended. Walter Gilbert revealed the sequence for an alpha interferon gene that revealed what the amino acid sequence was. A few minutes later, Christian Anfinsen who had won the Nobel Prize in Chemistry for his expertise in sequencing proteins such as ribonuclease, began his lecture by simply saying: "I have wasted my career". His lecture consisted of progress to date in determining the amino acid sequence of alpha interferon by the abruptly outmoded methods to which he had devoted many years.

Recently, I saw the movie entitled: "The Theory of Everything" which was based on a book written by Jane Hawking, Stephen Hawking's first wife. In it, she describes some Dallas doctors who held out the possibility that some medicine was offered to him for treatment of his amyotrophic lateral sclerosis. I don't know who she was referring to. However, I had received a letter from Stephen's father, a British physician, asking whether interferon could help treat Stephen Hawking's motor neuron disease. This may have been based on some information that Stephen Carter of the Roswell Park Cancer Center had used beta interferon injections with some possible benefit for patients with multiple sclerosis. In addition, Lee Fikes knew a great deal about Stephen Hawking's outstanding early career. To my best remembrance, Lee Fikes had some kind of a communication with Hawking or his father. I looked carefully into the questions raised in Dr. Hawking's letter. However, we could find no information or reason to believe it would be helpful in amyotrophic lateral sclerosis. In addition, we had treated 2 patients with amyotrophic lateral sclerosis with no effect. Therefore, I wrote Stephen's father that our early research experience had only been in the field of cancer, that we had given careful consideration to his inquiry, but we did not feel that it was promising for his son. I don't know if the account in Jane Hawking's book in some way related to misunderstanding this exchange of correspondence. Perhaps she was referring to different set of Dallas doctors.

I have just one more anecdote. Samuel Barron and Jerzy Georgiades at the University of Texas Medical Branch in Galveston were working on gamma interferon. At one point in the early 1980s, Geogiades called me with a request regarding Lipizzaner Stallions in Austria. They were apparently infected with some kind of sexually transmitted virus and he wanted to obtain some human alpha interferon for their treatment even though its activity in horses was

completely unknown. However, he obtained the funds from a mysterious source that would guarantee that the amounts provided would be fully funded. We agreed to send the alpha interferon to Georgiades with the assurance that it was not to be used for human trials. I never heard the outcome for the horses. Needless to say, culturing leukocytes to obtain interferon soon and rather suddenly became obsolete because of the new field of genetic engineering production of proteins.

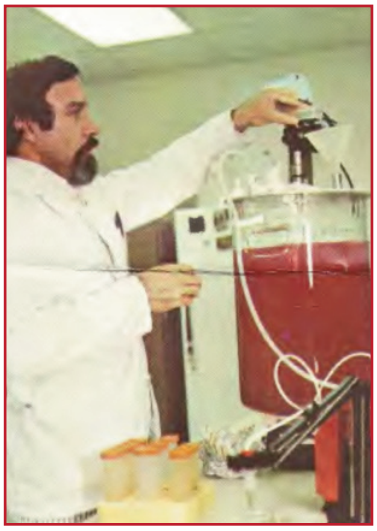
It was great fun to have an involvement with two of the earliest cytokines and to experience firsthand the revolutionary acceleration of the whole field of cytokines with the development of recombinant DNA technology.

Ref: INTERFERON: PROPERTIES AND CLINICAL USES
Edited by:
Amanullah Khan. Department of Immunotherapy
Norwood 0. Hill, President
Gordon I. Dorn, Department of Microbiology
Wadley Institutes of Molecular Medicine

Leland Fikes Foundation Press of Wadley Institutes o
f Molecular Medicine Wes Hicks – Manager

Proceedings of the International Symposium on I
nterferon held at Wadley Institutes of Molecular
Medicine, Dallas, Texas
October 18-20, 1979

Propagation of Sendai virus in 10-day-old chick embryos. The virus was used to stimulate an interferon response by white cell cultures.



Addition of Sendai virus to culture of white cells now suspended in nutrient fluid

Interferon rich culture fluid after removal of cells.

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ICIS COUNCIL MEETING MINUTES

Melbourne, October 26, 2014

Attendees:

Richard Flavell	Michael Tovey
Eleanor Fish	Chuck Samuel
Paul Hertzog	Bryan Williams
Cem Gabay	Scott Durum
Howard Young	phone conference: Sarah Gaffen, Karen Mossman

Announcements:

1. Election results: President elect – Tada Taniguchi – begins two year term Jan 2016. Councilors – Brendan Jenkins, Curt Horvath.

Committee Reports:

2a. Melbourne meeting report (Brendan Jenkins)
Registrants – 515 (as of 10-21), about half Australian. Fewer attendees from Asia than hoped for. Brendan noted that efforts were made to address gender equity, but a much greater percentage of women speakers declined the invitations.

Total budget $493K minus $20K seed money. $118K came from corporate sponsors. $17K (ASD) profit anticipated. This is less than the $80K profit from San Francisco, the difference is accounted for by $53 K spent on lunches in Melbourne. Seed money will be returned in full.

2015 meeting in Germany also uses a local organizer. Thereafter ICIS will seek a single international organizer (discussed below) to provide continuity in future meetings. Cem Gabay raised the importance of having a dedicated list of sponsors that would be passed on each year.

2b. Financial report (Karen Mossman).
~$300K in bank.
Annual management cost to FASEB $80-84K.
Dues are about $20K annually.

Therefore, annual meeting needs to profit $60-80K in order to pay FASEB management. Generating a meeting profit needs to be communicated to organizers of subsequent meetings (e.g., Bamberg)

The IL-6 meeting in Kiev profited $30K, although it is unclear if these funds have been transmitted to the ICIS.

2c. Awards (Eleanor Fish).
High workload for committee of 4 (90 applications), will expand to 8 members next year. Will streamline application to reduce load, reduce full CVs to Biosketches and eliminate recommendation letters for travel awards.

Milstein family is interested in sponsoring a high profile award, like the Lasker Award. Eleanor Fish will join Rob Pestka to discuss with Milsteins if such a meeting can be arranged. The importance of the Milstein funding for travel awards was emphasized (~$58K this year) so it was felt that the importance of these awards needs to be emphasized in any meeting with the Milstein Family. If the size of the Milstein Award is increased substantially, there was discussion regarding the need for a 5- or 10-year commitment.

2d. Meetings (Cem Gabay)
Conference organizers for future meetings. Two professional organizers are being considered. MCI is a European based, for profit company with extensive contacts on different continents. FASEB is a non-profit that previously organized meeting in Lisbon. Need better accounting of specific costs from each organization.

Past meetings.
San Francisco was considered to be successful both scientifically and financially, with ~$80K profit.

Kiel IL-6 meeting also successful scientifically and financially with ~$30K profit, although location of funds is unclear.

Future meetings.
The Bamberg meeting will be held Oct 11-14, 2015. It is accessible by train from Frankfurt or Munich. The budget aims at zero profit, which poses a problem, since we need profits from meetings (see above). However the budget is based only on registrations so any successful fund raising with represent likely profits. It was pointed out that due to a conflict at the meeting venue, the opening reception will be strictly limited to cocktails, with no food.

A San Francisco meeting was proposed for 2016. There was concern that David Artis was not responding to inquiries about planning, raising questions about his commitment (especially given his recent change in institution). He had proposed John O'Shea as a co-organizer, and Scott Durum will contact John about the situation. Chris Hunter was raised as an alternative organizer, or perhaps a joint organizer.

It was suggested that we should be soliciting individuals from the membership who would be good organizers. This would be easier if we work with a PCO, such that fundraising and meeting logistics are not as burdensome.

Special Symposia at other meetings
AAI- Richard Flavell and Sarah Gaffen are co-chairing an ICIS session at AAI (New Orleans, May 2015). Speakers are Andrew McKenzie, Federica Sallusto, Luke O'Neill and Curt Horvath. $5K was dedicated from ICIS to help defray travel costs of speakers. Amount based on precedent in past, advised by Chuck Samuel.

FOCIS (June 2015) - asked if we wanted to give a session and there was positive response from the Council, but no organizer has been identified.

Inflammation Research Association – the IRA has agreed to the ICIS sponsoring a symposium at their annual meeting (Boston, Aug. 8-12, 2015). Registration for speakers will be waived.

2e. Publications (Bryan Williams)
Newsletter- Howard Young currently generates >95% of the content. He needs help. Eleanor Fish suggested that we may wish to approach awardees and ask if they would contribute something for future issues. Sarah Gaffen pointed out that awardees were already asked to write reviews for a special issue of Cytokine (to be published spring 2015). However, Howard emphasized that the newsletter does not publish in depth scientific reviews so there would not be a conflict with Cytokine. A new society-owned journal was proposed (Scott Durum). The two existing "official" journals (JICR and Cytokine) were carried over from the two earlier societies and are owned by the publisher. They contribute very little financially to the society, other than some support for the annual meeting. A society-owned journal can provide a major source of income. It was agreed that this should be pursued, at least in a preliminary fashion, and proposals submitted to the publications committee and the council.

Membership (Sarah Gaffen)
708 members are current. Howard pointed out that the LinkedIn site has over 1000 followers.

Standards (Michael Tovey)
An extensive list of cytokine standards are approved by ICIS and WHO and are available for standardizing against other sources.

Nomenclature
Erik Lundgren is no longer able to chair the Nomenclature Committee and a suitable replacement would be recruited at the meeting. Post meeting note: Sergei Kotenko has agreed to serve as Chair of the Nomenclature Committee.

3. ICIS Leadership (Richard Flavell)
As noted, election results are in (Taniguchi is President-elect. Williams and Horvath are Councillors). 40% of membership voted. Point was made that very few nominees were women, which should be considered in future elections and committee memberships.

4. Other Business
SOP and Policies (Richard Flavell)- will talk with Tada Taniguchi to help guide him over the next year.

Awareness and Visibility (Howard Young)- Possible interactions with the Inflammation Research Association. Howard suggested working with COPE, an online cytokine resource. It was agreed that he should work with the Publications committee on this topic

Respectfully submitted,
Sarah Gaffen and Scott Durum
October 28, 2014

ICIS Awards Committee Report

The Awards Committee completed their reviews of the approximately 60 travel award applications and the different Society Awards in a timely manner, although concerns were raised about the burden of work for each reviewer. The recommendation was made to expand the Awards Committee to at least 8 members. Dr. Bob Silverman resigned from the Committee after many years of service, most recently as Chair of the Committee. The Commiitee acknowledged his incredible support and commitment. The Committee also recommends that in addition to nominations for the Seymour & Vivian Milstein award coming from the ICIS membership, the Awards Committee should consider potential nominees.

Respectfully submitted,
Eleanor Fish
Co-Chair ICIS Awards Committee

ICIS MEETINGS COMMITTEE REPORT

Location: Melbourne Convention center
Date: 26/10/2014 from 11 AM to 2:30 PM

Present:	Absent
Cem Gabay (Chair)	Christine Czarniecki
Stefan Rose-John	Carl Ware
Brendan Jenkins	Curt Horvath
Peter Staehli (voting members)	David Artis
Otto Haller	Leon Platanias
Paul Herzog	
Warren Leonard	
Howard Young (non-voting members)	

PCO selection for the Society Meetings:

Cem Gabay

In order to help the meeting organizers with different logistical issues including fundraising, as well as to maintain the continuity of the information irrespective of the location of future annual meetings and mid-term meetings, the majority of the Committee members agreed with the proposition to work with a professional congress organizer (PCO). Three PCO candidates were interviewed: ASN (based in Australia and PCO of the 2014 Melbourne meeting), MCI (based in Switzerland and PCO of the 2012 Geneva meeting), and FASEB (based in Bethesda, USA, and PCO of the 2009 Lisbon meeting). Brendan Jenkins discussed issues related to the organization of the Melbourne meeting and after significant discussion, the committee members present voted to not further ASN as PCO for ICIS. Both MCI and FASEB have their own specific strengths and weaknesses, and the committee members felt that it was difficult to choose between the two PCOs without additional information. In particular, we would like to have some feedback from their previous clients in Europe and in the US for FASEB and MCI. Cem Gabay will contact FASEB and MCI to obtain a list of associations that worked with these two PCOs for the organization of their meetings. Cem Gabay will then contact the scientific organizers in order to get feedback on the performance of the PCOs. This feedback information will be transmitted by email to the voting committee members, and the committee's recommendation will then be transmitted to the Council for a definitive decision. If possible, the vote will be done by email, but if necessary a TC will be organized. All members agreed that a decision should be obtained rapidly for the organization of the 2016 meeting.

Future Meetings:

Cem Gabay

David Artis had previously agreed to organize the 2016 meeting in San Francisco in collaboration with John O'Shea. Unfortunately, David was not able to come to Melbourne and did not send any details regarding the status of the meeting. Cem Gabay will contact David Artis and John O'Shea. Scott Durum will also contact John. Chris Hunter was also mentioned as a potential organizer or co-organizer for 2016. In any case, a clear commitment from the organizers should be obtained without delay.

Feedback and financial reports of Meetings

Karen Mossman (Treasurer) will make sure that the benefit of the meeting in Kiel returns to the Society.

- Warren Leonard provided the financial report on the 2013 meeting that took place in San Francisco. The meeting was a real success with 612 attendees registered. The Congress made a benefit of $ 85,931 independent of the seed money ($20,000) provided by the Society. Finally some speakers decided to donate their disbursements ($ 6,050) to support future travel awards.

- The mid-term meeting on IL-6 took place in Kiel in May 2014. 160 attendees registered to the meeting and the feedback was excellent. The meeting made a profit of Euro 30,191. Stefan is unsure whether these funds have been transferred to the Society's account.

- Brendan gave a report regarding the current meeting in Melbourne. 515 attendees have registered: A financial benefit of around 20,000 Aus$ is expected independent of the seed money from the Society. Of note, the organizers have spent approximately Aus$ 53,000 to provide lunches to the attendees. This decision has a clear impact on the benefit to the Society but was considered positively by the Committee members as all attendees benefit.

Meeting update

Brendan Jenkins will provide the list of Sponsors to Peter
Cem Gabay will specify to Peter Staehli that the meeting needs to provide a benefit to reinforce the financial situation of ICIS.

Peter Staehli provided an update on the 2015 Annual meeting that will take place in Bamberg from October 11th to 14th. Bamberg is approximately 2 h train from Frankfurt and Munich. The trains from Frankfurt leave directly from

ICIS MEETINGS COMMITTEE REPORT *continued*

Location: Melbourne Convention center
Date: 26/10/2014 from 11 AM to 2:30 PM

the Airport. The organizers made an effort to keep the expenses of the meeting at a reasonable level by working with their local PCO. Several invited speakers are committed and the meeting will last 3 full days following the evening opening session on Oct. 11. The organizers will need to contact sponsors for support to ensure that the meeting provides a financial benefit to the Society. It was noted that due to the change in venue, it will only be possible to serve drinks at the opening redception as there will not be room for food.

Miscellaneous

Cem Gabay will contact FOCIS to obtain more information regarding the organization of the symposium (how many speakers, free registration,…) and will get back to Richard Flavell.

FOCIS has invited ICIS to organize a symposium during the next FOCIS meeting in May 2015. The proposition was circulated among committee members by email. The opinion of the few who responded was positive but asked for additional information.

There is also an invitation from the Inflammation Research Association to sponsor a session at their annual meeting in Boston in August 2015. Kate Fitzgerald will be approached about organizing the session. Registration for the meeting will be waived by the IRA.

ICIS PUBLICATIONS COMMITTEE REPORT

Location: October 26th 2014 Melbourne Convention Centre

Present:	**Absent**
Bryan Williams (Chair)	Karen Mossman
Anthony Sadler	Jeremiah Tilles
Scott Durum (by invitation)	Cassandra Berry
	Meena Subramanyam
	Martin Schiesti
	JICR Editors: Tom Hamilton, Ganes Sen
	Cytokine Editor: Dhan Kalvakalanu
	No response: Steve Swanson, Robin Thorpe.

There were five agenda items:

- A report from the Editors on the Journal, "Interferon and Cytokine Research"- see attached
- A report from the Editor of Cytokine – see attached
- Proposal for a Society sponsored Journal – see attached
- Appointment of new editorial board members for JICR
- Any other business

The Report from the Editors of JICR was tabled and discussed and it was noted that there were 4 review issues of the Journal, and five solicited reviews in addition to the normal submitted manuscripts. The latter increased in number over 2013. The Journal impact factor has also increased and is now standing at 3.9 (2013) up from 3.2 in 2012. The Editors, Drs Sen and Hamilton, were congratulated on their efforts to raise the profile of the Journal. The publishers have also noted their thanks to the Editors (copied to the Committee Chair).

A report from the Editor in Chief of Cytokine was tabled and discussed. It was noted that 10 reviews articles had been published and 3 special issues were planned. The impact factor of Cytokine currently stands at 2.9. Dr Kalvakolanu was commended on his efforts to raise the profile of the Journal.

Dr Scott Durum was invited to present his proposal for starting a Journal to be owned by ICIS. The Journal would be planned around serializing definitive reviews on individual cytokines similar to what had been published by Elsevier several years ago in Cytokine Reference. Dr Durum had discussed this concept with the publications director at FASEB and received enthusiastic support. The Committee recommended that this proposal be taken to the ICIS Council for further consideration.

Proposals for new editorial board members for JICR were considered and Dr Ludmila Prokunina-Olsson and Dr John Schoggins were recommended for appointment.

Respectfully submitted,
Bryan Williams
Chair, ICIS Publications Committee

ICIS Standards Committee Report

Date: October 26, 2014
Location: Melbourne, Australia

The meeting was called to order at 11:00 am on Sunday, September 26th 2014.

Members Present (call-in):	Members excused:
Jorgen Dahlstrom	Anna Costa-Pereira
Robin Thorpe	Amy Rosenberg
Meenu Wadhwa (invited)	Huub Schellekens
Michael Tovey	Martin Schiestl
	Steve Swanson
	Meena Subramanyam

The following topics were discussed:

I. New Cytokine Reference Preparations

Robin Thorpe & Meenu Wadhwa, NIBSC, UK, submitted a report on replacement & new cytokine International Standards & reference preparations.

1. *Replacement Standards*

- The international collaborative study to establish the 3rd WHO International Standard for TNF-α involving 15 laboratories including those of two members of the Committee has been completed and the study results were endorsed by the WHO ECBS in October 2013. The 3rd IS is now available from the NIBSC (www.nibsc.org) code: 12/154.
- The 2nd WHO International Standard for IL-2 is also now available from the NIBSC (www.nibsc.org) code 86/500.

2. *New standards*

- The WHO Reference Reagent for IL-29 was approved by the WHO ECBS October in 2012 and is now available from the NIBSC (www.nibsc.org) code: 10/176
- The 1st WHO International Standard for pegylated G-CSF was approved by the WHO ECBS in October 2013 and is now available from the NIBSC (www.nibsc.org) code: 12/136.

3. *Standards in Development*

- Establishment of an international collaborative study for the development of the 1st WHO IS for the TNF-alpha sRII receptor-Fc fusion protein (Etanercept) was discussed. The detailed planning is complete and the study will start before the end of the year with the participation of 15 laboratories including those of two committee members.
- A similar study for the first infliximab IS was also discussed and is planned for June 2015. Those wishing to take part in the study please contact Meenu.Wadhwa@nibsc.org

II. Establishment of Standardized Assays and Reference Preparations for Human Anti-drug Antibodies

Repeated treatment of patients with recombinant analogues of cytokines such as interferon-beta or growth factors such as erythropoietin can lead to the production of antibodies against the product which can adversely affect the efficacy of treatment in some patients. There is a need for both international standards and standardized assays in order to standardize immunogenicity data obtained in clinical studies using different drug products.

1. *Ongoing initiatives:*

- The first such standard for antibodies to EPO has been prepared by one of the Committee members Steve Swanson at Amgen, the international collaborative study involving 18 labs has been completed and the data will be reviewed by the WHO in October 2015.
- A manuscript describing the establishment of a standardized assay for the detection of neutralizing antibodies against IFN-beta involving three members of the Committee has recently been published (Wadhwa M, et al., J. Interferon & Cytokine Res. 33:660-671, 2013).

2. *New initiatives:*

- Jorgen Dahlstrom, Molecular Partners Switzerland, presented a report on the need for drug-specific antibody standards of the IgE isotype in addition to the current WHO standard for total IgE. It was decided that Jorgen Dahlstrom would investigate the sourcing of suitable material as well as the development of methodologies to assess the potency of such material.
- Michael Tovey, INSERM France, presented an update on the initiatives under way to establish a common standardized assay for neutralizing antibodies (NAbs) against TNFα antagonists. An international collaborative study will be established in order to compare the performance of suitable assay platforms.

III. Initiatives to promote the use of cytokine standards

The Committee discussed initiatives to promote the use of cytokine standards by the publication in leading immunology journals of an editorial outlining the role of the ICIS Standards Committee, the WHO, and the NIBSC in the establishment of international cytokine standards and reference preparations together with a list of reagents available from the NIBSC, similar to that previously published in Cytokine, JICR, and JLB.

Respectfully submitted,
Michael Tovey
Chair, ICIS Standards Committee

ICIS Financial Report

The financial status of the ICIS remains healthy, although the Finance Committee and Council continue to investigate novel sources of revenue for the Society. Many societies have three major sources of revenue: (1) Annual Dues, (2) Annual Meeting and (3) Society Journal. In recent years, both the annual and mid-year meetings have been successful both scientifically and financially. The Membership and Publication committees remain active in considering new opportunities for revenue from dues and journals, respectively. Novel opportunities with corporate sponsorships are also being investigated.

The following are highlights from 2014. A finalized 2014 Financial Report from FASEB should be available shortly.

2013 Year End Assets $324K

2014 Income

Dues $22K

Annual Meeting $39K

Mid-year meeting $30K

2014 Expenses

Administration Fees $73K

2014 Net Income $18K

2014 Year End Assets $342K

Many thanks to the members of the Finance Committee (Bob Friedman, Tom Hamilton, Amanda Proudfoot and Kathy Zoon) for their input and efforts.

Karen Mossman (Treasurer, Finance Committee Chair)

October 11-14, 2015

CYTOKINES

Bamberg, Germany

www.cytokines2015.com

ICIS

Annual Meeting of the
International Cytokine & Interferon Society

ICIS International Cytokine & Interferon Society

Confirmed Plenary Speakers

David Artis Weill Cornell Medical College - *New York, USA*

Yanick Crow University of Manchester - *Manchester, UK*

Takashi Fujita Kyoto University - *Kyoto, Japan*

Raphaela Goldbach-Mansky NIH/NHIAMS - *Bethesda, USA*

Sun Hur Harvard University - *Boston, USA*

Akiko Iwasaki Yale University - *New Haven, USA*

Harmit Malik FHCRC - *Seattle, USA*

Michael Malim King's College - *London, UK*

Caetano Reis e Sousa London Research Institute - *London, UK*

Stefan Rose-John University of Kiel - *Kiel, Germany*

Alan Sher NIH/NIAID - *Bethesda, USA*

Topics include

- **Pathogen recognition**
  Glen Barber (Miami)
- **Cytokines in cancer development and antitumor immunity**
  Tadatsugu Taniguchi (Tokyo), Bob Korneluk (Ottawa)
- **IFN-λ in innate and adaptive immunity**
  Rune Hartman (Aarhus), Markus Heim (Basel)
- **Anti-cytokine therapy of inflammatory human diseases**
  Markus Neurath (Erlangen), Cem Gabay (Geneva)
- **Role of cytokines in skin and mucosal immunity**
  Wenjun Ouyang (South San Francisco), Andreas Diefenbach (Mainz)
- **From basic cytokine research to translational approaches**
  Hergen Spits (Amsterdam), Daniel Cua (San Francisco)
- **Cytokines in pathogen-induced tissue damage and repair**
  Andreas Wack (London), Susanne Herold (Giessen)
- **Sensing in innate immunity and pathogen countermeasures**
  Friedemann Weber (Marburg), Curth Horvath (Evanston)
- **Cytokine-induced proteins mediating pathogen defense**
  Klaus Pfeffer (Düsseldorf)
- **Cytokine and CNS disease**
  Ari Waisman (Mainz), Etty (Tika) Benveniste (Birmingham, Alabama)
- **Cytokines in antifungal and antibacterial immunity**
  Sarah Gaffen (Pittsburgh), Katrin Mayer-Barber (Bethesda)
- **Systems biology in cytokine research**
  Lothar Hennighausen (Bethesda), Andreas Pichlmair (Munich)

Abstract Submission Deadline: July 03, 2015

CONVENERS
Peter Staeheli
Otto Haller
Institute of Virology
University Medical Center Freiburg

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CONGRESS VENUE
KKH – Konzert- und Kongresshalle Bamberg

www.cytokines2015.com

Meeting of Interest

INTERNATIONAL SYMPOSIUM ON INFLAMMATION STRATEGIES FOR PREVENTION

UNIVERSITY OF CENTRAL FLORIDA
College of Medicine

The UCF College of Medicine aspires to bringing together the world's leading researchers, clinicians and thought leaders to understand the nature of inflammation and inflammatory diseases, and particularly the prevention of chronic diseases associated with inflammation. The first major thrust of our efforts to explore this critical area of health and disease will be an International Symposium on Inflammation-Strategies for Prevention that will bring together some of the world's leading scholars, researchers and clinicians who are studying inflammation. The major goal of the conference is to address the issue of whether prevention of inflammation would attenuate chronic inflammatory stress and delay/prevent the onset of chronic diseases. A wide range of topics, including arthritis, atherosclerosis, obesity, Crohn's, cancer, neuro-degenerative diseases, and many others will be discussed. One of the special features of this conference is the inclusion of Ayurvedic principles in the prevention of inflammatory diseases.

We invite you to the conference and to present your new research data for highly interactive scientific communications.

The symposium will be held during October 15-17, 2015 at the University of Central Florida College of Medicine in the Medical City at Lake Nona, Florida. Located 10 minutes from the Orlando International Airport, the College of Medicine sits on 75 acres in Lake Nona's Medical City, one of America's fastest-growing areas and home to internationally recognized research institutes such as the Sanford Burnham, Nemours Children's Hospital and Orlando Veterans Medical Center. Lake Nona is also situated approximately 30 minutes from downtown Orlando and 35 minutes from Walt Disney World, Universal Studios and SeaWorld.

CONFERENCE DATES: October 15-17, 2015
VENUE: UCF, COLLEGE OF MEDICINE, LAKE NONA, ORLANDO, FL 32827

Please follow the link for additional information: http://med.ucf.edu/inflammation-conference

Contact:
Dr. Sampath Parthasarathy,
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REMEMBER TO **JOIN** THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY OR **RENEW** YOUR MEMBERSHIP FOR 2013 OR BEYOND (3 YEAR, 5 YEAR, LIFETIME (AGE 55+) AND STUDENT MEMBERSHIPS ARE AVAILABLE)

Signals

ICIS

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