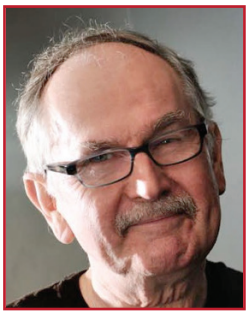
Signals

THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY NEWSLETTER

OCTOBER 2015 | VOLUME 3 | NO. 2

IN THIS ISSUE:



REFLECTIONS Richard Flavell

As I near the end of my two-year term as the first president of ICIS, I would like to reflect upon my experience to the membership of this young society.

After a protracted gestation, our new society was born early in 2013 by the merger of ICS and ISICR. Of course, this merger reflected the universal realization of the commonalities between the interferons and cytokines both in their evolution and their function. The complementary strengths of these two founder societies have resulted in an even stronger joint society with a focus on a cytokine field which has never been more exciting. Discovery of new molecules, new functions for "old" molecules and new cell populations such as innate lymphoid cells which produce many of the familiar players in host defense and damage control – all of these and much more have filled journals with much exciting material in the past few years.

In this same vein, meetings worldwide have reflected these and many more exciting discoveries. And indeed, the measure of all scientific societies is commonly through the annual conferences which they sponsor. Thus, the ICIS conferences have all been of a world-class level from the initiating meeting at San Francisco in 2013 followed by the Melbourne meeting of 2014. Those spectacular programs anticipate an equally spectacular meeting Co-organized by Peter S Stäheli and Otto Haller in October 2015. This will be held in historic Bamberg in Germany, a beautiful and unspoiled medieval/baroque city in beautiful Bavaria renowned for its architecture and potent beers – a friendly warning to the delegates for the upcoming meeting. As in our prior meetings, we anticipate greeting delegates from all inhabited continents of the world at this exciting event. Work is already far advanced for the 2016 meeting organized by David Artis, John O'Shea and Erika Pearce which is planned to be held in San Francisco in October of that year and promises to be spectacular.

I anticipate a rosy future for ICIS with a robust membership, vibrant science and strong leadership and management. We welcome new members from all over the globe, particularly in the Southern Hemisphere and the expanding community of immunologists and cytokine biologists in Asia. I particularly look forward to welcoming Professor Tadatsugu Taniguchi as my successor in 2016, a scientist who has played such a critical role in interferon and cytokine research ever since the dawn of the molecular era of this field.

Of course there are challenges that we and other societies face. How do we maintain and expand the ICIS membership? Observing the impressive growth of immunology in China, India and other rapidly developing countries, it behooves us to explain why ICIS is the international society that those talented communities should join. This must mean that ICIS caters to the needs of cytokine biologists worldwide. In an era of contraction of scientific funding and understandable concern on the part of scientists at all levels of their careers on the stability and longevity of immunologic science, it is essential that our society address the needs of this community.

continued on page 3

Future Meetings

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

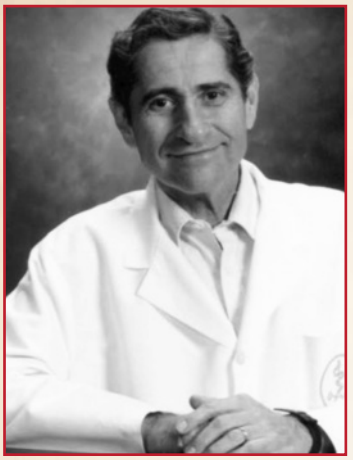
Newsletter Editors

Howard Young
younghow@mail.nih.gov
Marta Catalfamo
Haiying Li

ICIS
International Cytokine & Interferon Society

In Memoriam

Sam Baron
1929 – 2015



Sam Baron

Alick Isaacs and Sam Baron

With the death of Sam Baron, the field of interferon studies lost not only one of its pioneers, but a scientist with a long record of high level achievement. Sam was born in the Bronx and educated in the New York City school system. He received his MD degree from New York University School of Medicine in 1953 and interned at Montefiore Hospital. Instead of following the pathway physicians traditionally took at this point in their development, he initiated his career in microbiology and immunology with a research fellowship at University of Michigan School of Public Health, one of the outstanding centers for research in virology. In 1955 he was appointed as an investigator in the Division of Biological Standards at NIH, which later became the FDA laboratory at NIH. In that positional he helped in vaccine development and started his studies on antimicrobial mechanisms.

It was this interest which led Sam 1960 to take a Sabbatical year in the laboratory of Alick Isaacs at MILL Hill, three years after the Isaacs lab's first report on interferon. This was a highly productive research period, and upon his return to the NIH in 1961, Sam moved to the Laboratory of Viral Diseases at NIAID. With the death of Isaacs in 1966, Sam became leader of the small group of investigators studying interferon at the time. He was repeatedly called upon for advice and to help in organizing meetings. In the late 1960s, he developed the Interferon Scientific Memoranda which printed papers in press, abstracts, and discussions of concepts relevant to interferon research. The NIH distributed the ISMs gratis by mail to interested investigators.

The Baron lab at NIH continued leadership in the biology of interferon throughout the 1960s and early 70s. Several scientists who were to make important contributions to interferon research spent sabbaticals there, including Fernando Dianzani and Alfons Billiau. In 1975, after 20 years at NIH, Sam assumed the chairmanship of the Department of Microbiology and Immunology of the University of Texas Medical Branch in Galveston. He later became the Director of the Immunology Program and Associate Dean for Research Development and Planning at Galveston. Although these appointments had a heavy burden of administrative responsibilities, the Sam's lab continued to put out a large volume of first-rate research. During this period he also edited a textbook on Microbiology and Immunology and served as President of the International Society for Interferon Research.

He stepped down as a Chair in 1997, but continued to carry on his research as a Professor, Emeritus. The Chairmanship he had occupied was named in his honor. He returned to the NIH in 2002 to serve as a Volunteer Scientist at the Center for Cancer Research and in 2004 until 2015, to a position in the Cytokine Biology Section of his old institute, NIAID.

Sam Baron was to the end of his life an outstanding scientist, a challenging mentor, and an inspiring leader. He had a vision for his field that was far-seeing. He influenced the careers investigators with whom he interacted. He will certainly be missed by the many who knew him.

by Robert Friedman

REFLECTIONS *continued from page 1*

The greatest challenge for incoming leadership of the society is the sheer newness of ICIS and therefore the absence of standardized operating procedures for managing its operations. As a result, people organizing conferences find they have to establish procedures each year de novo rather than follow a tried and true formula. We are changing this, and hopefully by the end of this year, we will have standardized procedures for most of our important activities which will make the lives of all of our hard-working officials much, much easier.

What would make ICIS more attractive to you as members? We would like to hear from you members and in doing so make ICIS even more relevant to your science and work. To do this, we will put in place better mechanisms for communication from the membership to the leadership of ICIS. We do look forward to hearing your views and implementing the best of your suggestions.

Finally, I would like to add my sincere thanks to those hard-working and generous members of the various committees of our society, without which it simply would not function. A listing of all these members is shown on the website, and my thanks go out to all of them. And last, but definitely not least, I extend my personal thanks to Howard Young for his continuing and tireless efforts in generating this newsletter and to Caroline Lieber and Priscilla Musco of my office for their enormous help and support of my work as ICIS president.

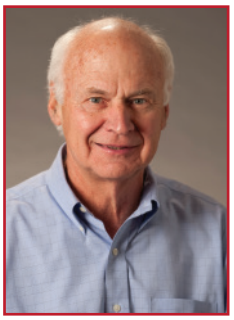
THE HISTORY OF SCIENTIFIC DISCOVERY: A MEMOIR BY JAN VILCEK

"Jan Vilcek's book tells an astonishing story of two intertwined journeys—one scientific, the other personal. The arc of the personal journey is remarkable: a childhood in Bratislava torn apart by Nazism and then overshadowed by Communism and an escape to a new continent. The scientific journey is just as vast—from explorations in immunology and microbiology to the discovery of some of the most remarkable medicines of our times. In both journeys, we encounter the essential ingredients of adventure: the urgency of exploration, flashes of inspiration, false leads, sudden successes, the importance of serendipity, the tortuous ups-and-downs of failures and struggles—but above all, that powerful animus to explore and discover new worlds. I could not put it down."

—Siddhartha Mukherjee, MD, author of *The Emperor of All Maladies*

A Note from the Founding Co-Presidents on the Formation of ICIS

Luke O'Neill
Professor
Trinity College
Dublin, Ireland



Chuck Samuel
C. A. Storke Professor
University of California
Santa Barbara, USA

'Come together...right now...' This year we celebrate the third anniversary of the coming together of the International Cytokine Society and the International Society for Interferon and Cytokine Research, to form the International Cytokine and Interferon Society (ICIS). Never, in the fields of Immunology and biology more broadly, had so much effort gone into fusing two Societies, for the good of our members and the future generations of scientists interested in interferons and cytokines.

The ICS had been founded in 1993, at the annual conference held in Kobe, Japan, the goal being to bring together scientists interested in cytokines to discuss latest findings as well as potential clinical impact. The founding members were pioneers in the area of cytokines, discovering and charactering such heavy-hitting cytokines as IL-1, TNF, IL-2 and IL-6.

> "KEEP ON GOING AND THE CHANCES ARE YOU WILL STUMBLE ON SOMETHING, PERHAPS WHEN YOU ARE LEAST EXPECTING IT. I NEVER HEARD OF ANYONE STUMBLING ON SOMETHING SITTING DOWN."
>
> — CHARLES KETTERING

ISICR had a longer history, being founded a decade earlier by Bill Stewart as the International Society for Interferon Research (ISIR) that first met as a society in 1983 in Rotterdam, The Netherlands. ISIR had an initial focus on the Type I interferons IFN-α and IFN-β, the first cytokines discovered by Isaacs and Lindenmann and by Nagano and Kojima. As additional cytokines were discovered including Type II IFN-γ, the interferon society ISIR evolved to become ISICR. It then made sense over the years for ICS and ISICR to have joint meetings, as clearly there were so many overlaps, be it interferons and many interleukins activating similar signaling pathways, some interleukins clearly losing their way as interferons (a good example being IL-10) and the overall basic biology being shared by this fascinating family of soluble factors made by immune and inflammatory cells. Discussions began between Presidents of both Societies, notably Alberto Mantovani and David Wallach for ICS, and Otto Haller and Leon Platanias for ISICR, culminating in Luke O'Neill for ICS and Chuck Samuel for ISICR brokering the final deal that created ICS. A suitable anthem for these discussions was 'Come Together' by the Beatles, although Chuck didn't have hair down to his knee, and Luke was never heard to say *'one and one and one is three'*, except when he was talking about IL-1 family members. Spirited discussions over the name ICIS were resolved when both parties recognized the very important legacy of interferons, where ISICR was in many ways a model society, supporting members as a family with grants and awards, and with the passion and commitment of committee members over the years. We felt we could live with the tautology of ICIS as a name, reflecting that legacy. Luke and Chuck then served as co-presidents of ICIS that met for the first time as a merged new society in San Francisco. We were delighted when Richard Flavell became the first sole President of ICIS and could not have wished for a better exemplar of all that is outstanding about cytokine and interferon research. Having had very successful meetings in San Francisco in 2013 and then Melbourne in 2014, we can look forward to the 2015 Annual Meeting in Bamberg and a Society that continues to attract the brightest and best working in the field of cytokines and interferons. Given the legacy of the two founding Societies, the tremendous science that was done, and the huge clinical impact of targeting cytokines in diseases such as rheumatoid arthritis, multiple sclerosis, psoriasis and inflammatory bowel disease, we can all be justifiably proud of what has been achieved to date. We look forward to a vibrant ICIS and bright future of more discoveries and medicines, in the relentless pursuit of making a difference and perhaps a re-writing of the Beatles' lyric- *'Hold you in his armchair you can cure his disease'.*

Dear Members,
ICIS is now present on Twitter as well!

You can follow us and get instant updates on the new activities, meetings, deadlines and many other aspects of our society.

Our name is CytokinesInterferons and you can write to us using @Cytok_Interf address.

Remember to retweet and feel free to comment and partake in discussions. #cool #newupdates #ICISonTwitter #science #IFN

2015 ICIS
THE SEYMOUR AND VIVIAN MILSTEIN AWARD
for Excellence in Interferon and Cytokine Research

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.

ALBERTO MANTOVANI

Scientific Director, Istituto Clinico Humanitas, President, Fondazione Humanitas per la Ricerca and Full Professor of General Pathology, School of Medicine, Humanitas University.

Main contributions

Tumor biology. Demonstration in the late '70s of the protumor function of tumor-associated macrophages (TAM, an acronym now generally used and coined by him in the '70s) linking inflammation and cancer (reviewed in Balkwill and Mantovani, Lancet, 2001). TAM as a prototypic M2-like population (Mantovani et al., Nature 2008; Balkwill et al., Cancer Cell 2005). First molecular linking of a genetic event (RET/PTC rearrangement) causing cancer in humans to the construction of an inflammatory microenvironment (Borrello et al., PNAS 2005). Proof of principle that targeting tumor promoting macrophages has therapeutic value in humans (Germano et al, Cancer Cell 2013). Demonstration that PTX3 is an extrinsic oncosuppressor regulating complement and macrophage driven tumor promoting inflammation (Bonavita et al Cell 2015). Alberto Mantovani is recognized among his peers as a forerunner in the '70s and a "founding father" of the renaissance of the inflammation-cancer connection.

Chemokines. Original description and role in TAM recruitment of a unique monocyte attractant, Monocyte Chemotactic Protein-1 (CCL2), as tumor-derived chemotactic factor (Bottazzi et al, Science 1983). Characterization of chemokines and role in pathophysiology, including dendritic cell and polarized T cell migration. Induction of chemokine production by IL-6 in endothelial cells via trans-signaling, a key component of chronic inflammation and cancer (Romano et al, Immunity 1997). Characterization of D6 as a decoy receptor for inflammatory CC chemokines (Mantovani et al, Nature Rev. Immunol 2006).

Role of chemokines in carcinogenesis (for a recent contribution Bonavita et al Cell 2015). Role of the chemokines vMIPs in attracting Th2 cells and role of D6 (ACKR2) in Kaposi's sarcoma.

IL-1/Toll-like receptors (TLR). Endothelial cell activation by IL-1 and cytokines (Rossi et al., Science 1985; Bussolino et al, Nature 1989; Romano et al, Immunity 1997). Identification of the type II receptor as a decoy receptor, a novel concept in biology (Colotta et al, Science 1993); the discovery of a decoy receptor represented a paradigm shift after the original definition of the concept of "receptor" by Langley at the end of the 19th century; decoy receptors are now recognized as a general, evolutionary conserved strategy to tune cytokines, chemokines and growth factors. Cloning of an intracellular isoform of the IL-1 receptor antagonist (Muzio et al., J. Exp. Med. 1995). First demonstration of MyD88 as the adaptor of mammalian Toll-Like Receptors (TLR) and identification of downstream transducers (Muzio et al., J. Exp. Med. 1998). Cloning and characterization of TIR8/SIGIRR, (IL-1R8) a negative regulator of IL-1 receptor and TLR signalling (Garlanda, et al, Immunity 2013). Role in carcinogenesis.

Humoral innate immunity: cloning (cDNA and genomic, mouse and human), structural and functional characterization of the first long pentraxin PTX3 as an IL-1 inducible gene (Garlanda et al, Nature 2002; Jeannin et al, Immunity 2005; Jaillon et al. J. Exp Med 2007 ; Deban et al, Nature Immunol. 2010; Jaillon et al. Immunity 2014; Bonavita et al. Cell 2015); structural immunobiology; role as a paradigm for humoral innate immunity; role as an extrinsic oncosuppresor in murine and human tumors regulating complement and macrophage driven tumor promoting inflammation; diagnostic and therapeutic translation (Cunha et al New England J. Med. 2014; ongoing).

Contribution to Public Awareness of Science

Alberto Mantovani has been actively involved in the fostering of science and scientific policy in Italy at various levels, with a focus on Immunology, Vaccines, Public Health, and Biomedicine, taking public stands on several issues including quackery whenever appropriate. He regularly contributes to the most authoritative Italian daily newspapers (eg Corriere della Sera; Il Sole 24 Ore) and magazines (Espresso and Panorama). He wrote a book (I Guardiani della Vita, Dalai Editore, 2011) on Immunology and Health targeted to lay public and contributed to scientific (eg SuperQuark; TGR Leonardo; Radiotre Scienza) and general radio and television programs. To promote science awareness and policy he cofounded the association " Gruppo2003" of Italian highly cited scientists (www.gruppo2003.it) and together with astrophysicist Tommaso Maccacaro founded the website www.scienzainrete.it.

Impact

For several years now, bibliometric analyses have indicated that he is the most quoted italian scientist. He has over 69.00 citations. A recent ranking indicates that he is the most quoted Italian scientist working in Italy (www.topitalianscientists.org/Top_italian_scientists_VIA-Academy.aspx;) and one of the 10 most quoted immunologists worldwide (H-index ISI 117; Scopus 134; Google Scholar 154) www.tisreports.com/products/19-Top_scientists_in_the_world___the_Via_academy_compilation.aspx

2015 ICIS AWARD WINNER

HONORARY LIFETIME MEMBERSHIP

Honorary Lifetime Membership Award

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

ELEANOR FISH

Eleanor Fish is a long-standing member of the ICIS, having joined the ISICR in 1982. Since then she has been active on a number of Society Committees, including Nomenclature, Membership and, most recently as co-Chair of the Awards Committee. Eleanor has been on the Organizing Committee of a number of our annual meetings – co-hosting the Toronto and Chicago Meetings - and assisting with the Jerusalem, Cleveland, Cairns, Shanghai, Montreal, Geneva, Vienna and most recently, the Melbourne Meeting in 2014. Eleanor was elected President of ISICR in 2008 and received the Seymour & Vivian Milstein award in 2010. Eleanor has served on the ISICR and ICS councils.

Eleanor received her undergraduate B.Sc. degree in Biological Chemistry from the University of Manchester, England, and her Master of Philosophy in Virology from King's College, University of London, England. She received her Ph.D. in Cell Biology from the Institute of Medical Science at the University of Toronto, Canada. She is currently Professor in the Department of Immunology at the University of Toronto, is a Senior Scientists in the Toronto General Research Institute, Toronto and Director of the Arthritis & Autoimmunity Research Centre at the University Health Network, Toronto. She is Associate Chair of International Initiatives & Collaborations in the Department of Immunology at the University of Toronto. She is an Adjunct Scientist at Women's College Hospital, Toronto and Visiting Professor in the Department of Immunology at Moi University, Kenya.

Eleanor is the Tier 1 Canada Research Chair in Women's Health & Immunobiology, a McLaughlin Scholar and was elected as a Fellow to the American Academy of Microbiologists. In 2012, she received the Canadian Society for Immunology Investigator Award, in recognition of her excellence in research throughout her career and her mentorship and in 2015 the Canadian Society for Immunology Cinader Award. The Cinader award is the premier scientific award provided by the CSI. The prize is awarded to an Immunologist working in Canada who is an exceptional researcher and also has something extra. Her nomination cites not only her outstanding research contributions but the depth and breadth of her contributions to the community through training, leadership, collaboration and international activities.

She is currently on the editorial boards for the *Journal of Interferon and Cytokine Research, Viruses*, and *Arthritis & Rheumatology*. Her work has been published in many scientific journals, including the *Journal of Immunology, Experimental Hematology, Circulation, Blood, Nature, PNAS, JAMA, Journal of Experimental Medicine, Journal of Virology, Journal of Leukocyte Biology, Nature Immunology, Trends in Immunology, Journal of IFN and Cytokine Research and the Journal of Biological Chemistry.*

A focus of Eleanor's research is the investigation of host-pathogen interactions at the cellular and molecular level, specifically in the context of viruses and interferons. During the 2003 outbreak of SARS in Toronto, she initiated studies to investigate the therapeutic potential of interferon in SARS patients. Encouraging results have directed her group's efforts toward examining interferon activity against a number of emerging infectious diseases, such as avian H5N1 and pandemic H1N1 influenza viruses. Most recently, her studies have focused on investigating the therapeutic effectiveness of interferon treatment for Ebola virus disease, with a clinical trial ongoing in Guinea. Eleanor is a member of a WHO Working Group to evaluate the therapeutic effectiveness of different vaccine and antiviral interventions against Ebola virus. Another focus of her work relates to understanding the immune mechanisms that drive autoimmunity, related to rheumatoid arthritis and multiple sclerosis. Most recently, Eleanor has initiated research studies in breast cancer, within the context of understanding how chemokine-driven alterations to metabolism influence the growth and metastasis of breast tumors.

Another facet related to Eleanor's research activities involves global outreach, specifically to resource poor regions. For many years, as Visiting Professor, she has been involved in curriculum development and mentoring both Faculty and students in the Department of Immunology at Moi University in Kenya. This extends now to the ongoing development of basic science courses with relevance for trainee MDs, nurses and dentists. She has made these courses available to different institutions across Kenya. In addition, she has established an international initiative – Beyond Science Initiative - that sees undergraduate and graduate students from the University of Toronto communicating with students around the globe as mentors as well as activists in the area of social justice; To foster partnerships among the next generation of global scientific leaders who will appreciate cultural sensitivities and global responsibilities.

2015 ICIS Awards

Milstein Young Investigator Award

ICIS members who attend the 2015 ICIS meeting in Bamberg 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.

Dusan Bogunovic
Icahn School of Medicine at Mt Sinai
Department of Microbiology
New York, NY

Daniel J. Gough
Centre for Cancer Research
Hudson Institute of Medical Research
Clayton, Australia

Shuvojit Banerjee
Lerner Research Inst
Cleveland Clinic Foundation
Dept of Cancer Biology
Cleveland, OH

Aoi Akitsu
Tokyo University of Science
Univ of Tokyo Inst of Medical Science
Noda-shi, Chiba
Japan

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.

Heekyong (Rachel) Bae
Laboratory of Experimental Immunology
NCI-Frederick
Frederick, MD

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

The Sidney & Joan 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. 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.

Pestka Graduate Award

Jan Pencik
Ludwig Boltzmann Inst for Cancer Research (LBI-CR)
Vienna, Austria

Pestka Post-Graduate Award

Abhishek Garg
University of Pittsburgh
Pittsburgh, PA

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 Bamberg. 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 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 .

Roza I. Nurieva
MD Anderson Cancer Center
Immunology
Houston, TX

> “DISCOVERY CONSISTS OF SEEING WHAT EVERYBODY HAS SEEN AND THINKING WHAT NOBODY HAS THOUGHT.”
>
> — ALBERT VON SZENT-GYORGYI

NEW ICIS MEMBERS

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

Nilesh Amatya
University of Pittsburgh
USA

Heekyong (Rachel) Bae
National Cancer Institute
USA

Matteo Biolatti
University of Turin
Italy

Robert Blackburn
USA

Dusan Bogunovic
Icahn School of Medicine at Mount Sinai
USA

J. Agustin Cruz
University of Pittsburgh
USA

George Fisher
Barry University
USA

Priya Ganesan
Duquesne University
USA

Sebastian Guenther
University of Maryland School of Medicine
USA

Jian-Da Lin
Rutgers University-New Jersey Medical School
USA

Barbara Maurer
Ludwig Boltzmann Institute for Cancer Research
Austria

Hila Novak Kotzer
Univ of Oxford Kennedy Inst of Rheumatology
United Kingdom

Ashleigh Poh
Walter and Eliza Hall Institute of Medical Research
Australia

Kritika Ramani
University of Pittsburgh
USA

Tiffany Shih
Rutgers University-New Jersey Medical School
USA

Tamara Suprunenko
University of Sydney
Australia

Taylor Syme
University of Sydney
Australia

Ewa Terczynska-Dyla
Aarhus University
Denmark

Eizo Watanabe
Chiba University
Japan

Bettina Wingelhofer
Ludwig Boltzmann Inst for Cancer Research
Austria

Di Yu
Monash University
Australia

Peng Zhou
Duke-Nus Graduate Medical School
Singapore

The ICIS LinkedIn site has over 1100 members. Ideas for making it more useful to the membership are welcome and can be sent to younghow@mail.nih.gov

New Member MINIBIOs

Sebastian Guenther, PhD
Postdoctoral Fellow
Institute of Human Virology
University of Maryland School of Medicine
Baltimore, MD

Dr. Sebastian Guenther is currently a Postdoctoral Fellow at the Institute of Human Virology at the University of Maryland School of Medicine in the group of Eric J. Sundberg. He is studying the molecular basis for cytokine signaling in the Interleukin-1 family. In particular, he is using X-ray crystallography and biophysical and cell-based assays to dissect agonism and antagonism in the IL-33 and IL-36 subfamilies of cytokines. The work will be used to create "super-antagonists" for these cytokines that can potentially be employed as asthma (IL-33) and psoriasis (IL-36) therapeutics. Prior to this position, Sebastian received his doctorate in biochemistry from the Free University in Berlin, Germany in 2011. During his PhD studies at the Max-Delbrück-Center for Molecular Medicine (MDC) in the group of Kirsten Falk and Olaf Rötzschke and at the Leibniz-Institut für Molekulare Pharmakologie (FMP) in the group of Christian Freund, he investigated conformational variants of empty and peptide-loaded MHC class II proteins.

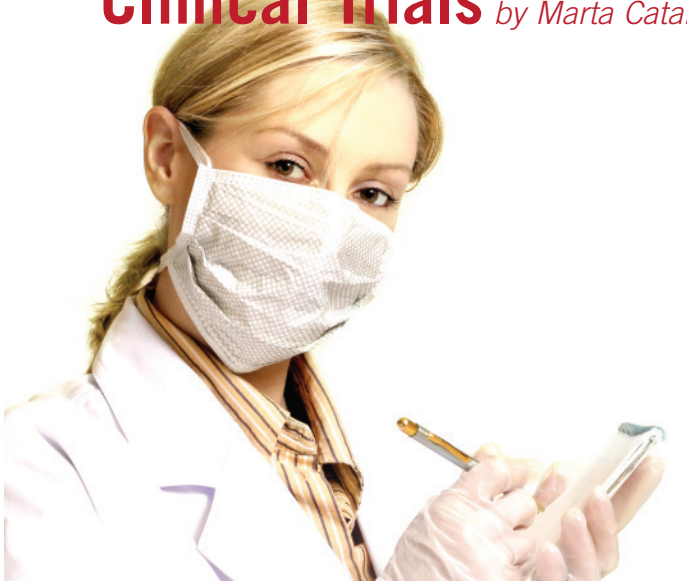
Eizo Watanabe, M.D., Ph.D.
Graduate School of Medicine
Chiba University
Chiba, Japan

Dr. Watanabe received his MD from Chiba University School of Medicine in 1997 and his Ph.D. in from Chiba University School of Medicine in 2004. In 2014 he was appointed Associate Professor, Department of Emergency and Critical Care Medicine, Graduate School of Medicine, Chiba University. His research interests include: genetic predisposition to sepsis and to hypercytokinemia, autophagy-associated cell death in sepsis, gene expression profiling in inflammatory diseases, novel biomarkers and/or mediators in critical illness and artificial organ support for critical illness.

Di Yu, Ph.D.
Head of Laboratory for Molecular Immunomodulation
Department of Biochemistry and Molecular Biology,
Department of Medicine (joint)
Monash University, Melbourne, Victoria, Australia

Dr. Yu completed his PhD with Professors Carola Vinuesa and Chris Goodnow at the Australian National University (Canberra) in 2007 and conducted postdoctoral research with Professor Charles Mackay at the Garvan Institute of Medical Research (Sydney) from 2007-2010. In 2011, he was awarded with the Monash Fellowship to establish the Molecular Immunmodulation Laboratory. In the Molecular Immunomodulation Laboratory, Dr Di Yu and his team are investigating the molecular mechanisms of the adaptive immunity to control the balance of immune responses, with the aim to design new strategies including cytokines-based immunotherapies to modulate the immune system to treat autoimmune disease, infection and cancer.

Clinical Trials *by Marta Catalfamo*



IL1-TRAP, Rilonacept, in Systemic Sclerosis
Principal Investigator: Robert Lafyatis, MD. Boston University Medical Center-Rheum/Arthritis Center. Boston, Massachusetts, United States, 02118
Contact: Jessica Ziemek.
Phone: +1 617-638-5383
jziemek@bu.edu
ClinicalTrials.gov Identifier: NCT01538719

Adaptive Study of IL-2 Dose Frequency on Regulatory T Cells in Type 1 Diabetes (DILfrequency)
Principal Investigator: Frank Waldron-Lynch, MB BChir PhD. Wellcome Trust Clinical Research Facility, Addenbrookes Hospital. Cambridge, Cambridgeshire, United Kingdom, CB2 0QQ
Contact: Frank Waldron-Lynch, MB BChir PhD.
Phone: +44 (0)1223 763213
frank.waldron-lynch@cimr.cam.ac.uk
ClinicalTrials.gov Identifier: NCT02265809

Induction of Regulatory T Cells by Low Dose IL2 in Autoimmune and Inflammatory Diseases (TRANSREG)
Principal Investigator: David KLATZMANN, MD, PhD. Assistance Publique - Hôpitaux de Paris. France.
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ClinicalTrials.gov Identifier: NCT01988506

A Phase I/II Dose Escalation Study of the Tumor-targeting Human L19-IL2 Monoclonal Antibody-cytokine Fusion Protein in Combination With Dacarbazine for Patients With Metastatic Melanoma
Principal Investigator: Claus Garbe, Prof. M.D. University Hospital Tuebingen (Germany)
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ClinicalTrials.gov Identifier: NCT02076646

Biological Activity and Safety of Low Dose IL2 in Relapsing Remitting Multiple Sclerosis (MS-IL2)
Principal Investigator: David Klatzmann, MD, PhD
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ClinicalTrials.gov Identifier: NCT02424396

Combination Therapy of F8IL10 and Methotrexate in Rheumatoid Arthritis Patients
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ClinicalTrials.gov Identifier: NCT02076659

Recombinant Interleukin-15 in Treating Patients With Advanced Melanoma, Kidney Cancer, Non-small Cell Lung Cancer, or Squamous Cell Head and Neck Cancer
Principal Investigator: Jeffrey S. Miller, MD. Cancer Immunotherapy Trials Network, National Cancer Institute (NCI)
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ClinicalTrials.gov Identifier: NCT01727076

Haploidentical Donor Natural Killer Cell Infusion With IL-15 in Acute Myelogenous Leukemia (AML)
Principal Investigator: Jeffrey S Miller, MD. Masonic Cancer Center, University of Minnesota. Minneapolis, Minnesota, United States, 55455
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Phone: + 612-273-2800. tkrepsk1@fairview.org
ClinicalTrials.gov Identifier: NCT01385423

Multiple Ascending Dose Trial of MSB0010841 (Anti-IL17A/F Nanobody) in Psoriasis Subjects

Principal Investigator: Medical Responsible Merck KGaA. Darmstadt, Germany
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ClinicalTrials.gov Identifier: NCT02156466

Genetically Modified T-cells in Treating Patients With Recurrent or Refractory Malignant Glioma

Principal Investigator: Behnam Badie, MD. City of Hope Medical Center. Duarte, California, United States, 91010
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ClinicalTrials.gov Identifier: NCT02208362

Interferon Alpha 2b Intensification in HIV-Positive Individuals on Antiretroviral Therapy

Principal Investigator: Frank Maldarelli, M.D. National Cancer Institute. National Institutes of Health Clinical Center, 9000 Rockville Pike . Bethesda, Maryland, United States, 20892 (NCI)
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ClinicalTrials.gov Identifier: NCT01295515

A Study in Asthma Patients to Evaluate Efficacy, Safety and Tolerability of 14 Days Once Daily Inhaled Interferon Beta-1a After the Onset of Symptoms of an Upper Respiratory Tract Infection (INEXAS)

Principal Investigator: Per Gustafson, MD PhD. AstraZeneca, R&D mölndal
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information.center@astrazeneca.com
ClinicalTrials.gov Identifier: NCT02491684

The Effects of Interferon-gamma on Sepsis-induced Immunoparalysis

Principal Investigator: Peter Pickkers, MD, PhD. Radboud University Nijmegen Medical Centre. Nijmegen, Netherlands
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ClinicalTrials.gov Identifier: NCT01649921

Study of TGF-β Receptor Inhibitor LY2157299 and Enzalutamide in Metastatic Castration-resistant Prostate Cancer

Principal Investigator: Channing Paller, MD. Sidney Kimmel Comprehensive Cancer Center. Johns Hopkins. 401 N Broadway, Baltimore, MD 21231
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Phone: 410-955-8239
cpaller1@jhmi.edu
ClinicalTrials.gov Identifier: NCT02452008

Anti TNFα Improves Endothelial Dysfunction in IBD Patients

Principal Investigator: Zittan Eran, M.D. Carmel Medical Center - Haifa -Israel
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eranzittan@gmail.com
ClinicalTrials.gov Identifier: NCT01881464

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WWW

Disease Ontology

http://www.disease-ontology.org/

The Disease Ontology has been developed as a standardized ontology for human disease with the purpose of providing the biomedical community with consistent, reusable and sustainable descriptions of human disease terms, phenotype characteristics and related medical vocabulary disease concepts through collaborative efforts of researchers at Northwestern University, Center for Genetic Medicine and the University of Maryland School of Medicine, Institute for Genome Sciences. The Disease Ontology semantically integrates disease and medical vocabularies through extensive cross mapping of DO terms to MeSH, ICD, NCI's thesaurus, SNOMED and OMIM.

Eukaryotic Promoter Database

http://epd.vital-it.ch/

The Eukaryotic Promoter Database is an annotated non-redundant collection of eukaryotic POL II promoters, for which the transcription start site has been determined experimentally. Access to promoter sequences is provided by pointers to positions in nucleotide sequence entries. The annotation part of an entry includes description of the initiation site mapping data, cross-references to other databases, and bibliographic references. EPD is structured in a way that facilitates dynamic extraction of biologically meaningful promoter subsets for comparative sequence analysis. This database contains 4806 promoters from several species.

EPDnew is a new collection of experimentally validated promoters in human, mouse, D. melanogaster and zebrafish genomes. Evidence comes from TSS-mapping from high-throughput expreriments such as CAGE and Oligocapping. ChIP-seq experiments on H2AZ, H3K4me3, Pol-II and DNA methylation are also taken into account during the analysis. The resulting database contains 23360 promoters for the human (H. sapiens) collection, 21239 promoters for the mouse (M. musculus) collection, 15073 promoters for the D. melanogaster collection, 10728 promoters for the zebrafish (D. rerio) collection, 7120 promoters for the worm (C. elegans) collection and 10229 promoters for the A. thaliana collection.

GENE

http://www.ncbi.nlm.nih.gov/gene

Gene supplies gene-specific connections in the nexus of map, sequence, expression, structure, function, citation, and homology data. Unique identifiers are assigned to genes with defining sequences, genes with known map positions, and genes inferred from phenotypic information. These gene identifiers are used throughout NCBI's databases and tracked through updates of annotation. Gene includes genomes represented by NCBI Reference Sequences (or RefSeqs) and is integrated for indexing and query and retrieval from NCBI's Entrez and E-Utilities systems. Gene comprises sequences from thousands of distinct taxonomic identifiers, ranging from viruses to bacteria to eukaryotes. It represents chromosomes, organelles, plasmids, viruses, transcripts, and millions of proteins.

Immune Epitope Database

http://www.iedb.org

The IEDB is a free resource, funded by a contract from the National Institute of Allergy and Infectious Diseases. It offers easy searching of experimental data characterizing antibody and T cell epitopes studied in humans, non-human primates, and other animal species. Epitopes involved in infectious disease, allergy, autoimmunity, and transplant are included. The IEDB also hosts tools to assist in the prediction and analysis of B cell and T cell epitopes.

lncRNAdb v2.0: expanding the reference database for functional long noncoding RNAs

http://www.lncrnadb.org/

The lncRNAdb - Database that provides comprehensive annotations of eukaryotic long non-coding RNAs (lncRNAs). Entries are manually curated from referenced literature. Each entry contains references information about the RNA including:

- nucleotide sequences
- genomic context
- gene expression data derived from the Illumina Body Atlas
- structural information
- subcellular localization
- conservation
- function with referenced literature.

LncRNA2Target

http://www.lncrna2target.org

Long noncoding RNAs (lncRNAs) have been emerged as critical regulators of gene expression at epigenetic, transcriptional and post-transcriptional level, yet what genes are regulated by lncRNAs remains to be characterized. To assess the effects of a specific lncRNA on gene expression, increasing researchers profiled the genome-wide or individual gene expression level changes after knocking down or overexpressing the lncRNA. However, no online repository is currently available to collect these differentially expressed genes regulated by lncRNAs.

To make it convenient for researchers to know what genes are regulated by a lncRNA or which lncRNAs regulate a given gene of interest, we develop this database to provide a comprehensive resource of differentially expressed genes after lncRNA knockdown or overexpression.

In our database system, target genes of a lncRNA are defined as the differentially expressed genes after knocking down or overexpressing the lncRNA. By reviewing all published lncRNA papers, we manually curated the differentially expressed target genes confirmed by qRT-PCR or western blot, and identified all the differential target genes from the microarray or RNA-seq data.

Currently, users can

- obtain the target genes regulated by a lncRNA by searching the lncRNA gene ID or symbol
- obtain the regulatory lncRNAs of a specific target gene by searching the target gene ID or symbol.
- download all manually curated lncRNA-target association data.
- submit information on new lncRNA knockdown and overexpression experiments to the LncRNA2Target database

Mouse Tumor Biology (MTB) Database

http://tumor.informatics.jax.org

The Mouse Tumor Biology (MTB) Database supports the use of the mouse as a model system of hereditary cancer by providing electronic access to:

- Information on endogenous spontaneous and induced tumors in mice, including tumor frequency & latency data,
- Information on genetically defined mice (inbred, hybrid, mutant, and genetically engineered strains of mice) in which tumors arise,
- Information on genetic factors associated with tumor susceptibility in mice and somatic genetic-mutations observed in the tumors,
- Tumor pathology reports and images,
- References, supporting MTB data
- Links to other online resources for cancer

Pathogen-Host Database

http://www.phi-base.org/

PHI-base is a web-accessible database that catalogues experimentally verified pathogenicity, virulence and effector genes from fungal, Oomycete and bacterial pathogens, which infect animal, plant, fungal and insect hosts. PHI-base is therfore an invaluable resource in the discovery of genes in medically and agronomically important pathogens, which may be potential targets for chemical intervention. In collaboration with the FRAC team, PHI-base also includes antifungal compounds and their target genes.

Each entry in PHI-base is curated by domain experts and is supported by strong experimental evidence (gene disruption experiments, STM etc), as well as literature references in which the original experiments are described. Each gene in PHI-base is presented with its nucleotide and deduced amino acid sequence, as well as a detailed description of the predicted protein's function during the host infection process. To facilitate data interoperability, we have annotated genes using controlled vocabularies and links to external sources (Gene Ontology terms, EC Numbers, NCBI taxonomy, EMBL, PubMed and FRAC).

> “WE SHOULD NOT WORRY IF STUDENTS DON’T KNOW EVERYTHING, BUT ONLY IF THEY KNOW EVERYTHING BADLY.”
>
> — PETER KAPITSA

RNAMiner

http://calla.rnet.missouri.edu/rnaminer/

A bioinformatics protocol for mining large RNAseq transcriptomics data

Superfamily

http://supfam.org/SUPERFAMILY/

SUPERFAMILY is a database of structural and functional annotation for all proteins and genomes. The SUPERFAMILY annotation is based on a collection of hidden Markov models, which represent structural protein domains at the SCOP superfamily level. A superfamily groups together domains which have an evolutionary relationship. The annotation is produced by scanning protein sequences from over 2,478 completely sequenced genomes against the hidden Markov models.

For each protein you can:
- Submit sequences for SCOP classification
- View domain organisation, sequence alignments and protein sequence details

For each genome you can:
- Examine superfamily assignments, phylogenetic trees, domain organisation lists and networks
- Check for over- and under-represented superfamilies within a genome

For each superfamily you can:
- Inspect SCOP classification, functional annotation, Gene Ontology annotation, InterPro abstract and genome assignments
- Explore taxonomic distribution of a superfamily across the tree of life

All annotation, models and the database dump are freely available for download to everyone.

UniPROBE

http://thebrain.bwh.harvard.edu/uniprobe/

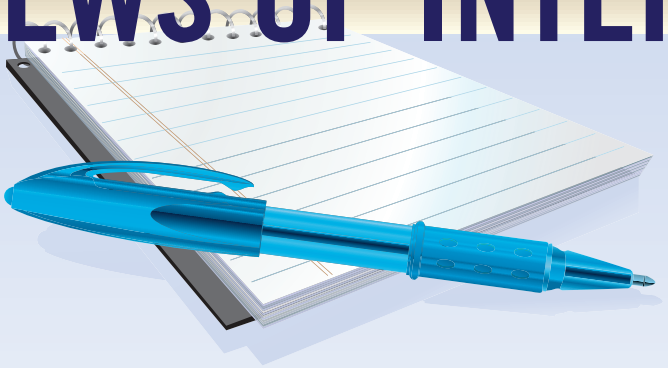
The UniPROBE (Universal PBM Resource for Oligonucleotide Binding Evaluation) database hosts data generated by universal protein binding microarray (PBM) technology on the in vitro DNA binding specificities of proteins. This initial release of the UniPROBE database provides a centralized resource for accessing comprehensive data on the preferences of proteins for all possible sequence variants ('words') of length k ('k-mers'), as well as position weight matrix (PWM) and graphical sequence logo representations of the k-mer data. In total, the database currently hosts DNA binding data for 519 nonredundant proteins and complexes from a diverse collection of organisms, including the prokaryote Vibrio harveyi, the eukaryotic malarial parasite Plasmodium falciparum, the parasitic Apicomplexan Cryptosporidium parvum, the yeast Saccharomyces cerevisiae, the worm Caenorhabditis elegans, mouse, and human. The database's web tools (on the right) include a text-based search, a function for assessing motif similarity between user-entered data and database PWMs, and a function for locating putative binding sites along user-entered nucleotide sequences.

ViRBase: a resource for virus-host ncRNA-associated interactions

http://www.rna-society.org/virbase

Increasing evidence reveals that diverse non-coding RNAs (ncRNAs) play critically important roles in viral infection. Viruses can use diverse ncRNAs to manipulate both cellular and viral gene expression to establish a host environment conducive to completion of the viral life cycle. Many host cellular ncRNAs can also directly or indirectly influence viral replication and even target virus genomes. ViRBase (http://www.rna-society.org/ViRBase) aims to provide the scientific community with a resource for efficient browsing and visualization of virus-host ncRNA-associated interactions and interaction networks in viral infection. The current version of ViRBase documents more than 12000 viral and cellular ncRNA-associated interactions involving more than 460 non-redundant ncRNAs and 4400 protein-coding genes from between more than 60 viruses and 20 hosts. Users can query, browse and manipulate these virus-host ncRNA-associated interactions. ViRBase will be of help in uncovering the generic organizing principles of cellular virus-host ncRNA-associated interaction networks in viral infection.

REVIEWS OF INTEREST



Cross-regulation between cytokine and microRNA pathways in T cells
Amado, T; Schmolka, N; Metwally, H; Silva-Santos, B; Gomes, AQ *European J Immunology* 45 (6):1584-1595; 2015

Antibody-independent functions of B cells: a focus on cytokines
Shen, P; Fillatreau, S *Nature Reviews Immunology* 15, 441–451; 2015

Type I interferons in anticancer immunity
Zitvogel, L; Galluzzi, L; Kepp, O; Smyth, MJ; Kroemer, G *Nature Reviews Immunology* 15, 405–414; 2015

New dog and new tricks: evolving roles for IL-33 in type 2 immunity
Lott, JM; Sumpter, TL; Turnquist, HR *J Leukocyte Biol*, 97 (6):1037-1048; 2015

STAT3-Activating Cytokines: A Therapeutic Opportunity for Inflammatory Bowel Disease? Nguyen, PM; Putoczki, TL; Ernst, M *J Interferon & Cytokine Res* 35, (5) 340-350; 2015.

Epigenetic control of interferon-gamma expression in CD8 T cells de Araújo-Souza, PS; Hanschke, SC; Viola, JP. *J Immunol Res*. 2015:849573. doi: 10.1155/2015/849573. Epub 2015

The STING pathway and the T cell-inflamed tumor microenvironment.
Woo, SR; Corrales, L; Gajewski, TF *Trends Immunol.* 36 (4):250-256, 2015

Role of type I interferon in inducing a protective immune response: perspectives for clinical applications.
Rizza, P; Moretti, F; Capone, I; Belardelli, F *Cytokine Growth Factor Rev.* 26 (2):195-201, 2015

TNF and its receptors in the CNS: The essential, the desirable and the deleterious effects.
Probert; L *Neuroscience*. Jun 24. pii: S0306-4522(15)00579-5, 2015

Proallergic cytokines and group 2 innate lymphoid cells in allergic nasal diseases.
Matsushita, K; Kato, Y; Akasaki, S; Yoshimoto, T *Allergol Int.* 64 (3):235-240, 2015

GM-CSF: An immune modulatory cytokine that can suppress autoimmunity
Bhattacharya, P; Thiruppathi, M; Elshabrawy, HA; Alharshawi, K; Kumar, P; Prabhakar, BS *Cytokine*. Jun 22. pii: S1043-4666(15)00218-5, 2015

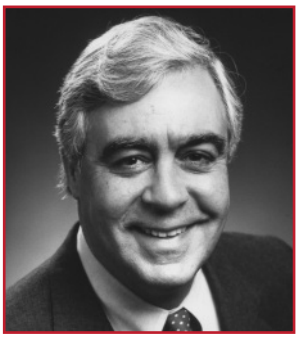
Transcription of Interleukin-8: How Altered Regulation Can Affect Cystic Fibrosis Lung Disease.
Jundi, K; Greene, CM. *Biomolecules*. 5 (3):1386-1398, 2015

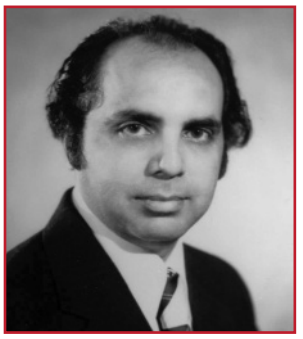
Monogenic autoinflammatory diseases: Cytokinopathies Moghaddas F; Masters, SL *Cytokine*, 74(2):237-246; 2015

IFNA2: The prototypic human alpha interferon Paul F; Pellegrini S; Uze, G *Gene*, 567(2):132-137; 2015

Interleukin-35: Expanding Its Job Profile Sawant DV; Hamilton K; Vignali DAA *J. Interferon & Cytokine Res.*, 35(7): 499-512; 2015

CRYSTALLIZATION OF INTERFERONS IN SPACE





Charles E. Bugg, PhD **Tattanahalli L. Nagabhushan, PhD**

(**Editor Note:** Drs. Bugg and Nagabhushan were recipients of the 1994 Milstein Award)

Some 25 years ago, the protein crystallography group at the University of Alabama at Birmingham(UAB) and the interferon/cytokine research group at Schering Plough Research enjoyed a productive collaboration that led to some of the early information about the three dimensional structures of interferons and cytokines. An interesting component of this collaboration was the role that space experiments played in the crystallization of these proteins.

In 1985 UAB had initiated a joint research program with NASA's Marshall Space Flight Center, which is located fairly close to UAB in northern Alabama and is one of the major centers for microgravity research. Marshall was also managing the Space Shuttle program. The Shuttle was flying on a regular schedule at the time and was available for microgravity research. In 1985 NASA was in the midst of designing the Space Station, and much of this work was being coordinated at Marshall. NASA was actively in the process of trying to identify high priority scientific projects that could take proper advantage of this expensive facility. Alabama Senator Howell Heflin, who was from north Alabama and was a major supporter of the Space Station project, contacted the Director of the Marshall Space Flight Center and the President of UAB and urged them to get their two institutions together to identify projects in Alabama that might be competitive for funding from the Space Station science budget. The protein crystallography group ended up on a committee from UAB to meet with the Huntsville scientists to see if they could identify common interests. At that meeting there were presentations about crystal growth experiments that had been performed years earlier in space, with very interesting results. These experiments involved optical measurements of disruptive convection caused by solution density changes during crystal growth, which was pronounced on Earth but was essentially eliminated in microgravity, resulting in enhanced quality of crystals grown in space. Crystal growth of electronic materials and metals had been identified as a priority area for microgravity research by the Marshall scientists.

The protein crystallography group presented some of the research programs at UAB and explained the challenges that everyone in this field was facing in efforts to grow high quality protein crystals for structural studies. It quickly became obvious to the NASA scientists that protein crystal growth might be an incredibly important area for experiments in microgravity and for parallel NASA-sponsored research programs on Earth. It was clear that protein crystal growth had about every component they were looking for, including past evidence of microgravity effects on crystal growth, a key problem that plagued important crystallographic structural studies in biology, and potential commercial applications for structure-based drug design in the pharmaceutical industry. Anything that might enhance the internal order of protein crystals, which tend to be poorly ordered, would be of immense scientific, and potentially commercial, value, since high resolution structural details obtained from crystallography are greatly affected by the internal order of the crystals used. It was not clear how the effects observed in microgravity growth of inorganic materials might relate to growth of macromolecular crystals, but there was enthusiastic agreement that this was an area that should be investigated.

The Birmingham crystallography group immediately began working closely with scientists and engineers from the Marshall Space Flight Center to design suitable protein crystal growth experiments that might be performed initially on the Space Shuttle and later on the Space Station. Vapor diffusion was selected as the first method to be explored since it was the technique most widely used for crystallization of proteins, and it allowed experiments to be performed using very small protein samples. Since it was the method of choice in protein crystallography, most of the data on quality of Earth grown crystals had been obtained using crystals grown by vapor diffusion, and crystallization conditions for many proteins were well developed using this method.

Working with scientists and engineers from Marshall, the UAB group quickly designed a simple vapor diffusion crystallization apparatus that might be suitable for use on the Shuttle. This apparatus was composed of a series of cavities in an aluminum plate. A syringe containing the sample of protein solution was positioned at one end of the cavity, which also contained an absorbent material soaked in the precipitant solution. The cavities in the aluminum plate were covered by clear sheets of plastic on each side of the plate, so that the operations and crystal growth could be observed and photographed. The protein solutions were prepared and loaded in the syringes at the launch site as close to the time of launch as possible, and the absorbent material was soaked with the solutions of precipitating agents prior to transferring the apparatus to the Shuttle. Once in orbit droplets of the protein solutions were extruded onto the tips of the syringes. The crystallization process was then initiated by vapor equilibration between the precipitating agents and the droplets of protein solution. The protein solutions, along with microgravity grown crystals, would then be withdrawn back into the syringes for return to Earth at the end of the Shuttle flight.

The first Space Shuttle experiments were conducted in April, 1985 using a prototype vapor diffusion apparatus. The apparatus was improved and then used for protein crystallization experiments on one additional Shuttle flight in 1986, prior to the Challenger accident. Following the Challenger disaster, the space shuttle program was suspended while an extensive investigation of the cause of the crash could be determined and corrected. This down period provided time to develop an advanced vapor diffusion crystallization apparatus for much improved control of crystallization processes. This advanced system was included on the first post- Challenger shuttle flight STS-26, which launched in September 1988 (Figure 1).

Several crystal growth experiments with gamma interferon were included, and produced crystals that appeared to be more highly ordered than any produced previously on earth [1] (Figure2). Data from these crystals were used in the high resolution refinement of the gamma interferon crystal structure [2], which was the first structure determined for interferons or cytokines.

Protein crystal growth experiments using the vapor diffusion apparatus were performed on a number of Space Shuttle flights following the initial experiments in 1985, and several proteins involved in the UAB/Schering Plough collaboration were included, along with samples from many other collaborators from academia, industry, and government laboratories. In addition, UAB and Schering Plough worked with NASA to explore the potential of using large scale protein crystallization in space as an approach for processing protein products for clinical and commercial applications. Biologically active proteins are extremely potent molecules. There are some serious issues with regards to purity of these proteins and their inherent biological activity. Sometimes, a small amount of a contaminating protein may actually express its biology preferentially and strongly override the biology of the main protein component. Thus purity and protein homogeneity is of major concern in proteins developed as pharmaceutical products. Highly ordered protein crystals should minimize any heterogeneity, and we felt that this aspect of microgravity should be explored. We also felt that the uniformity of crystal morphology and size from bulk crystallization in microgravity might prove useful in formulation of protein delivery systems for clinical and commercial applications.

Working closely with NASA, we designed a system that used temperature change to activate crystallization, which is one of the most common techniques in manufacturing of pharmaceuticals. This also was a fairly straightforward method for scaling up our experiments to accommodate large samples. Temperature change is potentially ideal for optimizing microgravity effects, since temperature driven convection is essentially eliminated in space along with normal crystal growth convection and crystal sedimentation. The system designed for these bulk crystallization experiments was fairly simple, consisting of clear plastic cylinders of various volumes with metal caps that abutted a metal plate that had precise temperature control. The cylinders were loaded with protein solutions prior to launch and were maintained at temperatures where the proteins were soluble. Once in orbit, the temperature of the solution was gradually adjusted by changing the temperature of the metal plate that was in

CRYSTALLIZATION OF INTERFERONS IN SPACE *continued*

contact with the metal cap of the cylinder. This resulted in a temperature gradient across the cylinder, which would have been unstable in the convection driven flows on Earth, but was quite stable in microgravity. The temperature across the solution then gradually equilibrated during the flight, producing an unusually stable environment for gradual nucleation and growth of large quantities of crystalline material. The rate of equilibration could be controlled by varying the rate of temperature change on the temperature control plate, depending upon the length of time that the Shuttle was expected to remain in orbit. This bulk crystallization system was included on four Shuttle flights between 1991 and 1994, using samples of alpha interferon from Schering Plough, in addition to insulin samples from other investigators. The results of these preliminary experiments were encouraging, producing gram quantities of crystals in microgravity that were generally much more uniform than those grown in this system on Earth.

These initial experiments suggested that space might provide an ideal environment to create unique therapeutic protein crystals suitable for sustained release of the drug into circulation from the site of introduction of the drug. Alternatively, crystalline suspensions of the drug may be deposited directly into a tissue when higher concentration of the drug is warranted. Biologically active proteins have short half-lives and often do not reach the site where they are needed. Besides, peak blood levels are often way over the levels needed for efficacy and such unnecessary concentrations might be the reason for their toxic effects. In an experimental model, zinc interferon microcrystals we obtained on Space Shuttle flight STS-78 were injected into cynomolgous monkeys and the interferon blood levels measured over a period of 48 hours. As a control, an equal amount of interferon in solution was administered to monkeys. As seen in the Figure 3, solution interferon was cleared rapidly after quickly reaching a high peak level. In contrast, crystalline zinc interferon was available in an active form for a much longer period of time and at a considerably lower peak level. More research is needed, but our initial results indicate that microgravity processing has potential in designing and optimizing drug delivery systems for a variety of protein therapeutics.

Following the crystallographic analysis that produced the high resolution gamma interferon structure [2], the UAB/Schering Plough collaboration resulted in determination of the crystal structures of human granulocyte-macrophage colony stimulating factor (GMCSF) [3], and human interleukin-4 [4]. This work led to the 1994 Milstein Award for Interferon and Cytokine Research given to the two of us as representatives of the UAB and Schering Plough groups. These structural studies had only been possible because of the major contributions from Drs. Steve Ealick, Bill Cook, Mark Walter, and Vijay Senadhi at UAB; and Drs. Paul Trotta, Paul Reichert, G.S. Hammond, and H.V. Le at Schering Plough. The space experiments involved a large number of other investigators and engineers from UAB and NASA, under the leadership of Dr. Larry DeLucas from the UAB crystallography group. Larry actually flew as a Payload Specialist to perform some of our crystal growth experiments on a Spacelab shuttle flight in 1992, and is now coordinating protein crystal growth experiments on the Space Station. At this stage, well over a hundred different proteins from multiple protein crystallographers in academic, government and commercial laboratories have been included in the space crystallization experiments, using a variety of crystallization methods.

References

1. DeLucas, L.J., Smith, C.O., Smith, H.W., Vijay-Kumar, S., Senadhi, S.E., Ealick, S.E., Carter, D.C, Snyder, R.S., Weber, P.C, Salemme, F.R, Ohlendorf, D.H., Einspahr, H.M., Navia, M.A, McKeever, B.M., Nagabhushan, T.L., Nelson, G., McPherson, A., Koszelak, S., Taylor, G., Stammers, D., Powell, K., Darby, G. and Bugg, C.E. Protein Crystal Growth in Microgravity. Science 246: 651-654 (1989).
2. Ealick, S.E., Cook, W.J., Senadhi, V-K., Carson, M., Nagabhushan, T.L., Trotta, P.P. and Bugg, C.E. Three-Dimensional Structure of Recombinant Human Interferon-gamma. Science 251: 698-702 (1992).
3. Walter, M.R, Cook, W.J., Ealick, S.E., Nagabhushan, T.L., Trotta, P.P. and Bugg, C.E. Three-Dimensional Structure of Recombinant Human Granulocyte-Macrophage Colony-Stimulating Factor. J. Mol. Biol. 224: 1075-1085 (1992).
4. Walter, M.R, Cook, W.J., Zhao, B-G., Cameron, R.P., Reichert, P., Nagabhushan, T.L., Trotta, P.P. and Bugg, C.E. Crystal Structure of Recombinant Human Interleukin-4. J. Biol. Chem. 267: 20371-20376 (1992).

Figure 1: Payload specialist Pinky Nelson using the advanced vapor diffusion crystallization apparatus, which was constructed following the Challenger accident. The apparatus was partially automated, and was housed in a special temperature controlled unit that was designed to replace one of the mid-deck lockers on the Space Shuttle. Pinky performed our first experiments with this equipment on Space Shuttle Flight STS-26, which launched on September 29, 1988, and produced crystals of gamma interferon used in the refinement of the high resolution crystal structure.

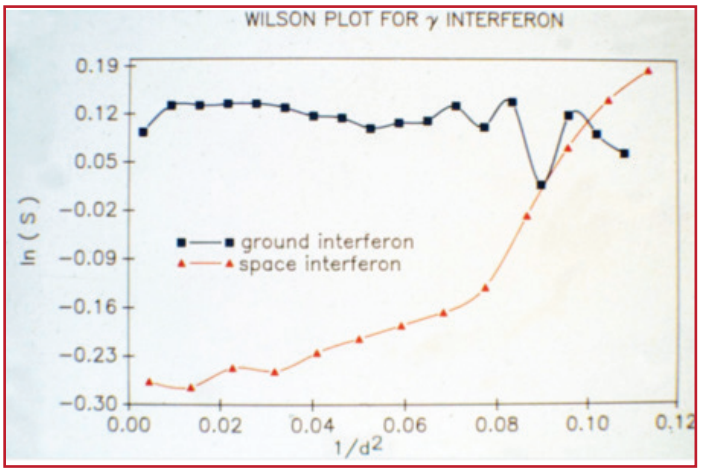


Figure 2. Relative Wilson plots comparing crystals of gamma interferon. The slope of a relative Wilson plot is a measure of differences in order when diffraction data sets from different crystals are compared. The upper plot (black) compares data sets from earth grown crystals. The slope is close to zero, which is to be expected if the order is unchanged. The lower plot (red) compares data from space grown crystals with data from earth grown crystals, and displays a slope indicating that the crystals grown in microgravity are more highly ordered than those grown on earth.

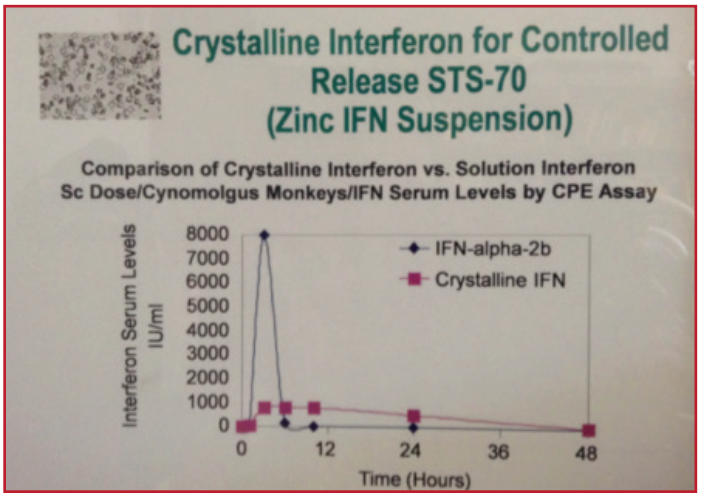


Figure 3: Alpha interferon formulation using crystalline samples from experiments on Space Shuttle flight STS-70.

NEWS FROM AUSTRALIA

The Melbourne-based Hudson is one of Australia's newest medical research institutes, born of the January 2014 merger of the Monash Institute of Medical Research (MIMR) and the Prince Henry Institute (PHI). The merged MIMR-PHI was renamed the Hudson Institute of Medical Research this year to honour the late Professor Bryan Hudson, who was instrumental in the early formation of both organisations.

The merger has given Hudson significant momentum. Several of its research breakthroughs are moving into clinical trials; it is a key player in the $84 million Translational Research Facility, due for completion in October 2015; and it has made several prominent appointments this year. World-renowned Australian scientist Professor Alan Trounson has returned to the Institute after six years as Director of the California Institute of Regenerative Medicine. In his new role as Distinguished Scientist, Professor Trounson is mentoring the development of an active research program in translational therapy, including the development of the Cell Therapy and Regenerative Medicine translational platform.

Dr Ron Firestein, a physician-scientist who focuses on cancer biomarker development in early-stage research and clinical trials, and who most recently worked at Genentech, is joining Hudson to lead its Centre for Cancer Research. **Professor Bryan Williams** is standing down from this role to focus on his duties as Director and Chief Executive Officer of Hudson, retaining his own research group and driving the Institute's next growth phase.

Both Professor Trounson and Dr Firestein join a senior faculty that includes Hudson's Distinguished Scientist, Professor John Funder, a recipient of the Companion of the Order of Australia (AC) award in the 2015 Australia Day Honours for eminent service to medicine; Hudson's Associate Director, Professor Peter Fuller, Head of the Centre for Endocrinology and Metabolism, who was awarded a Member of the General Division of the Order of Australia (AM) in 2015 for his significant service to medicine as an endocrinologist; and Professor Euan Wallace AM, recognised in 2013 for his significant service to medicine, particularly in the areas of obstetrics and gynaecology. The Institute also includes Professor David de Kretser, Professor Henry Burger and Professor Evan Simpson as Fellows of the Australian Academy of Sciences, and Professors **Paul Hertzog**, Stuart Hooper, Lois Salamonson and Justin St John as Centre heads.

'It's an exciting time for Hudson,' says Professor Williams. 'We are recruiting world-class scientists to add to our existing research strengths, and are looking to make several appointments in the next few years. Outstanding scientists are attracted to Hudson because they recognise the calibre of its research, the facilities available to them, our links with Monash University, and our share of National Health and Medical Research Council (NHMRC) grants.'

Hudson has 452 full-time employees and PhD students, and another 50 affiliated researchers. A distinguishing feature is Hudson's diverse research focus. It has core strengths in cancer research, endocrinology and genetic diseases, innate immunity and infectious diseases, women's and men's reproductive health, and baby health through the Ritchie Centre. Merger gives newly named Hudson Institute of

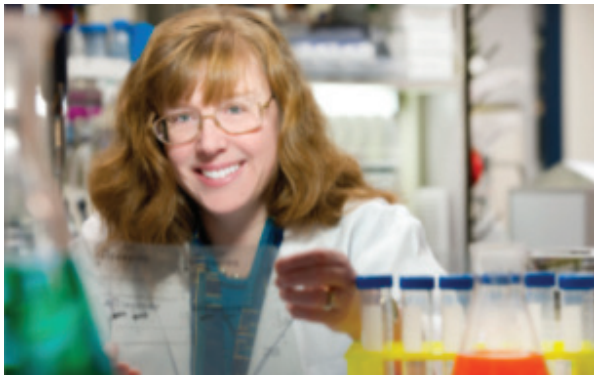
Medical Research significant momentum. Hudson's research program is broader than that of many medical research institutes – a strategy that allows for greater multidisciplinary research discoveries and collaborations. 'The diversity of Hudson's research is one of its great strengths,' says Williams. 'There's always a danger in being too prescriptive about where and what to research. Our scientists need the freedom to explore new areas, and the scope to go in different directions with their research, if Hudson is to achieve breakthrough innovations and solve complex problems.'

Hudson also benefits from its relationships with Monash University, Australia's largest university and one of its top ranked; and Monash Health, Victoria's largest integrated health service, which is a prominent, university-affiliated international research and teaching facility. Hudson at the centre of exciting new research precinct Hudson's forerunners, MIMR and PHI, had a combined history of discovery and innovation stretching back 75 years. The merger was a natural progression of what had been a long and fruitful research partnership, co-location, and recognition that combining the institutes would create greater critical mass and economies of scale. The merger was designed to make Hudson the translational research centrepiece at Clayton's Monash Health Translation Precinct. Working closely with Monash Health and Monash University, Hudson is expediting the translation of research discoveries to benefit patients. The precinct is a partnership between Hudson, Monash Health and Monash University to bring clinicians, researchers and educators together to advance discoveries and improve healthcare through collaboration and innovation. It will be the largest healthcare precinct of its kind in Melbourne's south-east, and a critical new piece of Australia's health-research infrastructure. Construction of the federally funded Translational Research Facility began in February 2014. The six-story building will house 220 Hudson researchers on several floors, have a clinical trials facility, a floor for platform technologies that analyze patient samples, and a floor for biotechnology firms that want to rent space to collaborate at Hudson and share its facilities. 'The building will be a significant step forward in how Hudson and its partners approach multidisciplinary research, and how our scientists collaborate with industry,' says Williams. 'We want industry to be involved earlier in the research process, so that more of our discoveries are translated much faster into products that improve patient outcomes.'

Research highlights continue Hudson scientists continue to make significant discoveries. A team lead by Dr Tony Sadler, Dr Dakang Xu and Professor Williams has provided insights into how inflammation is controlled. They discovered that a factor termed PLZF, originally identified in the development of a rare form of childhood leukaemia, plays a critical role in dampening inflammation by restricting the expression of inflammatory gene products. Research by the same team had identified PLZF protein as a host restriction factor limiting virus infection. Led by Professor Paul Hertzog, researchers are investigating the relationship between some oral contraceptives and an increased susceptibility to sexually transmitted infections, including HIV, based on a new cytokine they discovered called interferon epsilon. Hudson received $1 million from the Bill and Melinda Gates Foundation to continue research on this world-first discovery, which was published in prestigious journal Science and has many implications for future studies into the prevention of diseases of the female reproductive tract, including sexually transmitted infections. 'A number of Hudson's research discoveries sit on the brink of being ready to move into clinical trials,' says Williams. 'The Institute's drug discoveries in innate immune signaling pathways show great promise, and our cell therapy research is now in the clinical phase.'

A promising future

Williams is buoyed by Hudson's progress since the merger – and the increased potential. He wants the Institute to attract more world-class scientists, develop stronger internal processes to translate discoveries, work more closely with industry and have a strong, collaborative culture. 'It's never easy merging organisations. This merger had been talked about for years, and took 18 months to put together when the agreement was reached. There is always uncertainty in any merger, but the institutes' stakeholders recognised there was significant research overlap between the two organisations, and that it no longer made sense to have two medical research institutes in the same research precinct. I'm very pleased with the goodwill from both organisations to come together and move forward as one organisation.' Williams says that the critical mass that comes from the merged organisations is vital if Hudson wants to lift its global standing in medical research. 'Leading institutes typically have at least 500 researchers, a strong focus on research translation, state-of-the-art facilities and a culture of collaboration. Hudson is putting these pieces together; our challenge is to use that foundation to change the landscape of medical research in Australia.'

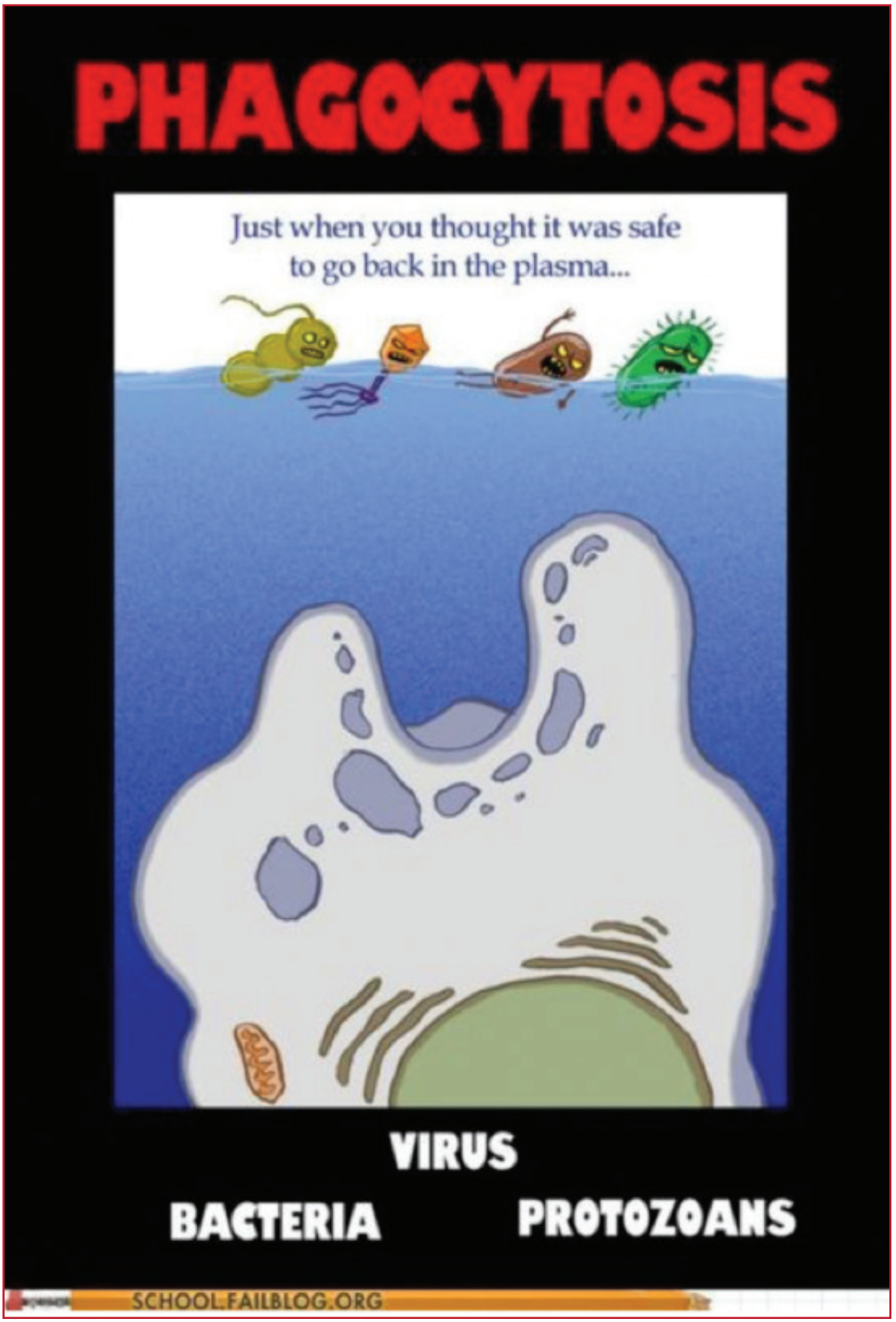


SARAH L. GAFFEN, PH.D

Sarah L. Gaffen, Ph.D. has been appointed the Gerald P. Rodnan Professor of Rheumatology, University of Pittsburgh School of Medicine. This Chair in Rheumatology is endowed by the Rodnan family and through the efforts of Dr. Thomas Medsger. Dr. Rodnan (1927-1983) was one of the first rheumatologists to study scleroderma and the Chair was created to support research in arthritis.

Dr. Gaffen just started a yearlong sabbatical at King's College in London in the laboratory of Dr. Julian Naglik and she invites all ICIS members who might be stopping in London to come by and say hello.

Reproduced courtesy of phdcomics.



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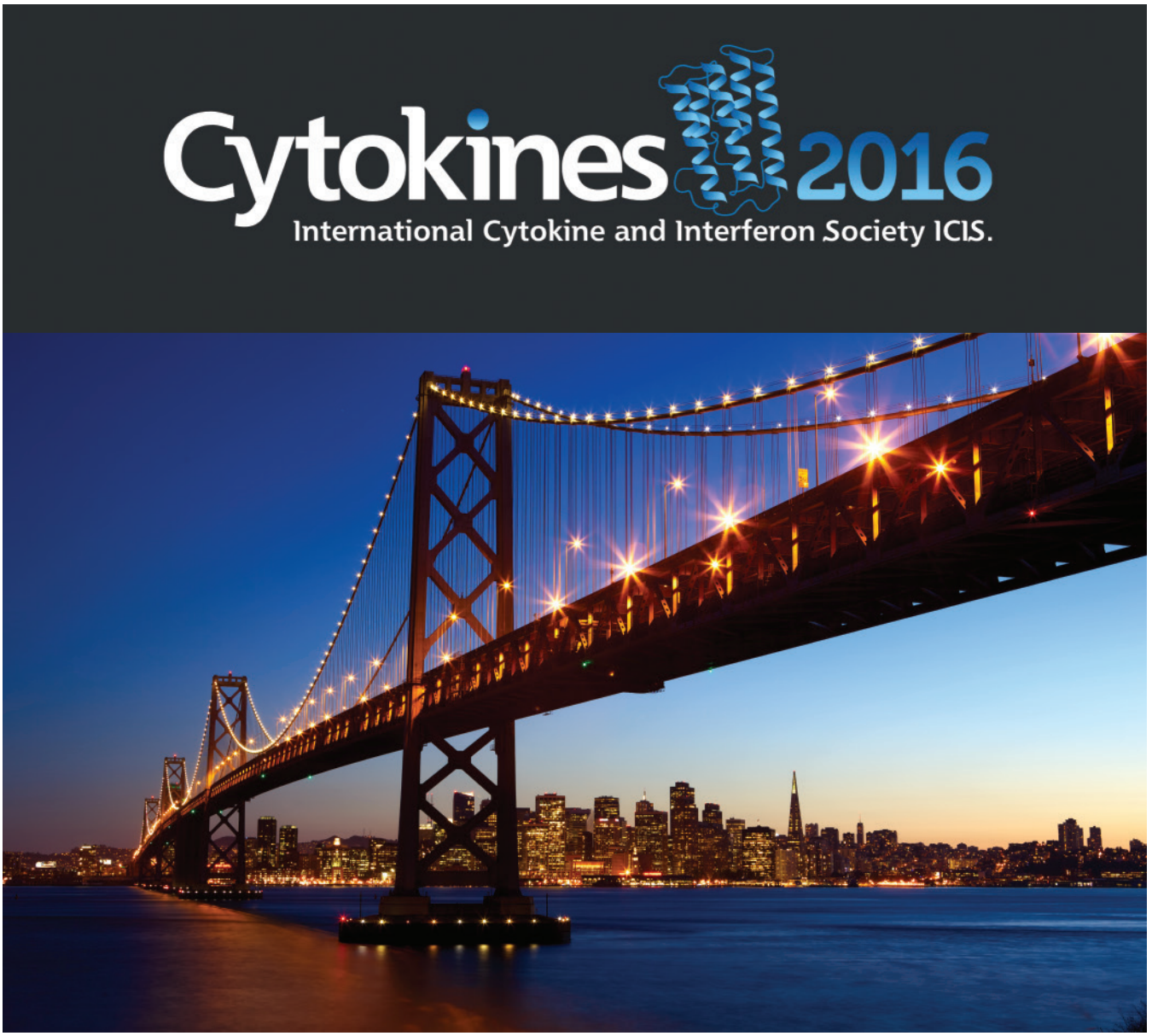


SAVE THE DATE

OCTOBER 16-19, 2016

Hyatt Regency Hotel
San Francisco, CA
www.cytokines2016.com

Cytokines and interferons: master controllers of immunity, inflammation, metabolism and Cancer

Plans are well underway for the Cytokines 2016 meeting that will be held in San Francisco between 16-19 October 2016. The scientific organizing committee for the 2016 meeting includes David Artis (Cornell), Erika Pearce (Max Planck Institute of Immunobiology and Epigenetics) and John O'Shea (NIH). Working with the scientific advisory committee composed of investigators from academia and industry, an outstanding scientific program is planned.

Please mark your calendar for 16-19 October 2016 and watch the website (www.cytokines2016.com) for more information on the program.

The Keynote speaker this year is Dr Yasmine Belkaid from the National Institutes of Health. Dr Belkaid is a world-leader in the areas of cytokine regulation of host defense, inflammation and tissue protection. Her research has spanned areas of immunity to infection, host-microbiota interactions and regulation of effector and regulatory T cell function. Dr Belkaid is an outstanding speaker and an excellent colleague to launch the 2016 meeting.

Each day of the meeting will begin with an exciting plenary session, topics include inflammation and cancer, mechanisms of host defense and regulation of innate and adaptive immunity. Additional major- and mini-symposia will cover topics including microbiota-immune interactions, cytokine regulation of cellular metabolism, epigenetic regulation of cytokine signaling, interferons and host defense, innate immunity, cytokines and metabolic disease, primary immuno-deficiencies, innate lymphoid cell biology and to the clinic – emerging therapies. There will also be multiple venues to promote networking for trainees and junior faculty with established investigators and representatives from biotech, pharma and scientific journals.

Confirmed speakers so far include:

Yasmine Belkaid
Jeff Bluestone
Xuetao Cao
Jean-Laurent Casanova
Jason Cyster
Vishva Dixit
Wendy Garrett
Jorge Henao-Mejia
Kenya Honda
Christopher Hunter
Axel Kallies
Michael Karin
Hiroshi Kiyono
Shigeo Koyasu
Richard Locksley
Diane Mathis
Wenjun Ouyang
Dhavalkumar Patel
Federica Sallusto
Skip Virgin
Laurence Zitvogel

There will also be multiple open speaker slots for selected abstracts.

The conference venue and hotel arrangements are confirmed for the Hyatt Regency Hotel at Embarcadero Center. This is a large atrium hotel with views of the Bay and cityscape. State of the art meeting facilities combine with a relaxing atmosphere to be the perfect meeting venue.

There are many travel awards, prizes and events for trainees and junior faculty. More information about the meeting and the application process for the society awards can be found at www.cytokines2016.com. Remember you must be an ICIS member to be eligible for society awards.

Tell your friends and look for the FREE Smartphone/iPad App, Cytokines2016, coming later this year.

TIPS FOR TALKS

As your session will be heavily attended, we ask that you strongly consider the following to optimize the effectiveness of your presentation and the session.

1. The audience is broad in its background. Avoid jargon and abbreviations that are unique to your specific field.

2. Avoid overly wordy text slides – bullet statements are often best.

3. On data slides, only include information that you actually will discuss. Panels that are not discussed are distracting and are not useful. This often includes much of your control data and such data is better left for a poster.

4. Every data slide should have a descriptive title that summarizes the CONCLUSION of the slide rather than only the type of experiment. Lettering should be large (Titles are often best if 36 point or larger and lettering on figure panels should be at least 12 point and ideally larger)-- many use lettering way too small to be seen well from the back of the room.

5. Conclusions should be concise and probably no more than 4/slide. Again, lettering should be very large (e.g., 22 Point font)

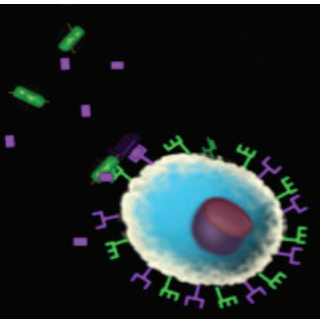
6. Future plans/directions - We recommend a slide with your future plans/directions. This may lead to better questions and collaborations.

7. Color - Your color combinations must be able to project well in a large room that is not completely dark! There is nothing wrong with black & white slides.

8. Include your poster number and time on your last slide, if applicable.

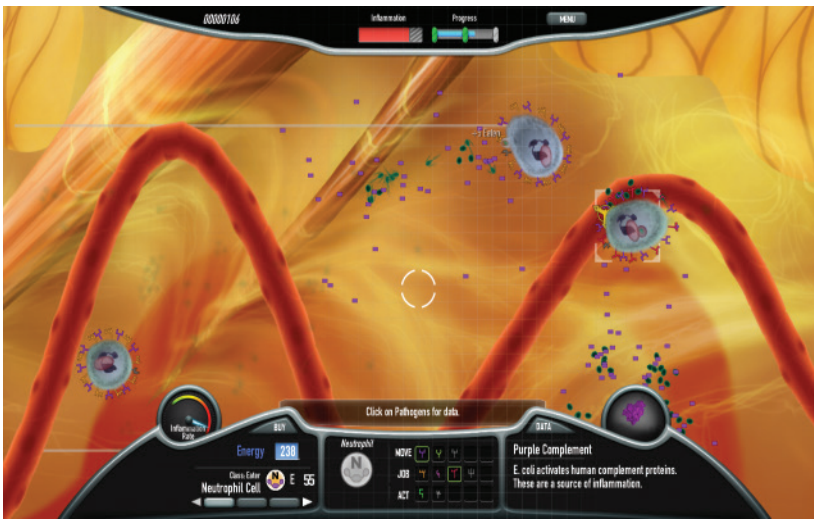
9. Practice - Formally practice in front of colleagues at least several days in advance of the meeting so you have time to alter slides. There is no excuse for having typing/spelling mistakes! Indicating that chocolate will be available at your practice will ensure attendance by many of your invitees.

IMMUNE DEFENSE



ImmuneDefenseGame.com

Molecular Jig Games, LLC shares the goals of the International Cytokine and Interferon Society: we hope to educate the public about the molecular mechanisms of immune system function. We make popular commercial games that take place in the natural world. Our first title is Immune Defense, a strategy game like Starcraft or Plants vs. Zombies, in which players use cytokines, interferons and their receptors to manage the immune cells in a fight against viruses, bacteria and parasites. In Immune Defense, players can arm individual cells with proteins that impart various abilities.



Begun in 2009 as a National Institutes of Health (NIH) funded project, we boiled the core mechanics of molecular cell biology and biochemistry into a game that has been accepted in several juries game festivals. We conducted a controlled study of the effect of our games on 7th through 12th grade students and showed significant increases in learning and confidence with molecular cell biology. We still need your help! Play our free demo at ImmuneDefenseGame.com.

Melanie Stegman, Ph.D.
@MelanieAnnS
Cell: 917-886-6079
Owner, Molecular Jig Games, LLC.
www.MolecularJig.Com

Immune Defense trailer
http://youtu.be/TEUaaHoPLYQ

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REMEMBER TO **JOIN** THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY OR **RENEW** YOUR MEMBERSHIP FOR 2015 OR BEYOND (3 YEAR, 5 YEAR, LIFETIME (AGE 55+) AND STUDENT MEMBERSHIPS ARE AVAILABLE)

Signals

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