

Signals

THE ISICR/ICS NEWSLETTER

IN THIS ISSUE:

Welcome New Members	p2
A Tribute to Ferdinando Dianzani	p8
Award Winners	p10
Paper of Interest	p18

SEPTEMBER 2012 | VOLUME 1 | NO. 1



A note from ISICR President, **Charles Samuel**

Dear Colleagues,

I look forward to seeing you September 11-14 in Geneva at our Annual Meeting. When the 2012 meeting was initially proposed by Cem Gabay and Amanda Proudfoot, and endorsed by the Meetings Committee, it was to be held as the 10th Joint Meeting of the International Society for Interferon and Cytokine Research and the International Cytokine Society. It is now early July as I write this note, and if all happens as anticipated, when we convene in Geneva it may be as the first meeting of the Cytokine and Interferon Society (CIS). In which case, this newsletter issue will represent the first issue of *Signals* under the umbrella of CIS.

The possibility of a merger between ISICR and ICS arose nearly six years ago driven by the increasing overlap of interests between the ISICR and ICS memberships. Leon Platanius and David Wallach more recently then guided discussions and negotiations, working together with their respective ISICR Board of Directors and the ICS Council, and with the help of Howard Young (ISICR) and Nancy Ruddle (ICS), to develop a transition plan and set of ByLaws for a merged new society to be known as the Cytokine and

Interferon Society. This process culminated in a vote early this year by the two society memberships on the merger initiative. The results were clear. About 89 and 95% respectively of the votes cast by ISICR and ICS members were for the merger. If the remaining subsequent steps of the merger process and legal aspects are straightforward as anticipated, the merger may be finalized by the time we convene in Geneva.

The ISICR Board of Directors and the ICS Council agreed that the merger should take place in a manner that recognizes the aspirations and cultures of both ISICR and ICS and captures the strengths of both founding societies as we come together to form our new Society. David Wallach and I have worked together during the past year to achieve this outcome, and I look forward to continuing this effort with Luke O'Neill during the upcoming year as we move further along the transition plan. Among the important next steps will be the election of new CIS society officers in 2013. Some of you have asked about the process. During the current year 2012, the ISICR and ICS each will need to elect three members that will constitute a Nominations Committee...*continued on pg 3*

Future Meetings

2013 Meetings

JULY 7-10, 2013
International TNF
Québec City, Canada

Cytokines 2013
Sept. 29-Oct. 3, 2013
San Francisco, CA

Newsletter Editors

Howard Young
younghow@mail.nih.gov
Seng-Lai (Thomas) Tan
Marta Catalfamo
Annette Khaled
Hiroki Yoshida



ISICR
International Society for Interferon
& Cytokine Research

WELCOME

NEW ISICR MEMBERS

Ferial Aslani

Justus Liebig Univ Giessen
Giessen, Hessen Germany

Kiran Bhaskar

Cleveland Clinic Foundation
Cleveland, OH

Mehdi Bourouba

Univ H. Boumendiene
Algiers, Algeria

Annie Bruns

Northwestern Univ
Evanston, IL

Taylor Cohen

Columbia Univ
New York, NY

W. Matthew Dickerson

BioScale
Lexington, MA

Faten El Asmi

CNRS FRE3235
Paris, TX France

Lili Gu

Inst of Immunology Natl
Univ of Ireland
Co.Kildare, Co.Kildare
Ireland

Krishna Gundabolu

Albert Einstein College of
Medicine
Bronx, NY

Eda Holl

Duke Univ
Durham, NC

Laura Icardi

VIB-Ghent Univ
Ghent, Belgium

Tali Lang

Justus Liebig Univ Giessen
Giessen, Germany

Rute Nascimento

Instituto Gulbenkian de
Ciencia
Oeiras, Portugal

Jose Vicente Perez Giron

Heinrich Pette Institut
Hamburg, Hamburg
Germany

John Pong

Univ of Hong Kong
Hong Kong, Hong Kong

Giorgio Raimondi

Univ of Pittsburgh School of
Medicine
Pittsburgh, PA

Vijay Rathinam

UMASS Medical School
Worcester, MA

Anna Lisa Remoli

Istituto Superiore di Sanita
Rome, Italy

Flore Rozenberg

Hospital Cochin-APHP
Paris, France

Grigory Ryshakov

Univ of Oxford
London, United Kingdom

Junmei Wang

MD Anderson Cancer
Center
Houston, TX

NEW ICS MEMBERS

Werner Absenger

Saybrook University
San Francisco, CA

Anna Boyajyan

Institute of Molecular
Biology
Republic of Armenia

Catherine Bruyns

Université libre de Bruxelles
Brussels, Belgium

Nitin Chouthai

Wayne State University
School of Medicine
Detroit, MI

Taylor Cohen

Columbia University
New York, NY

W. Matthew Dickerson

Bioscale
Lexington, MA

Richard H. Duerr

University of Pittsburgh
Pittsburgh, PA

Denise Fitzgerald

Queens University
Belfast, Northern Ireland

Abhishek Garg

University of Pittsburgh
Pittsburgh, PA

Benjamin Gordon

University of South Carolina
Charleston, SC

Mark Hogarth

Burnet Institute
Melbourne, Australia

Ian Humphreys

Cardiff University
Wales, UK

James Chun-bong Li

Hong Kong University
Hong Kong, China

Erik Lubberts

Erasmus Centre for
bioinformatics
Rotterdam, The Netherlands

E. Angela Murphy

University of South Carolina
School of Medicine
Charleston, SC

Alison Giles Murphy

Trinity College
Dublin, Ireland

Majed Odeh

Bnai Zion Medical Center
Haifa, Israel

Kate O'Keefe

Trinity College
Dublin, Ireland

Chandraskhar Pasare

University of Texas
Southwestern
Dallas, TX

Datta K.Sandip

National Institute of Allergy
and Infectious diseases
Bethesda, MD

Yuliang Wang

Tianjin First Central Hospital
Nankai District, China

Nicole Ward

Case Western University
Cleveland, OH

Shuang Wei

University of Michigan
AnnArbor, MI

Mieszko Wilke

Trinity College
Dublin, Ireland

A note from ISICR President, **Charles Samuel** *continued from cover*

which will play an important role in the selection of candidates for our future officers. To help assure an orderly transition, during the formative period of the new society it was agreed that the current officers of ISICR and ICS will remain in position and act and work together prior to election of the new officers. The plan is for the new President to assume leadership in 2014, along with new committees.

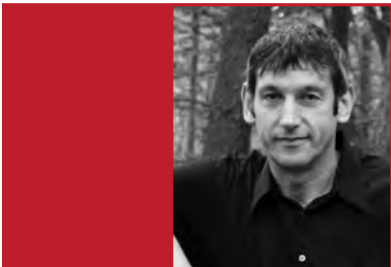
We have witnessed tremendous progress in the cytokine field since the seminal discovery of interferon as the first cytokine by Isaacs and Lindenmann and by Nagano and Kojima. The decision to merge and form CIS is a crucial milestone in the history of both ISICR and ICS. As many of the ISICR members are aware, ISICR evolved from ISIR, the International Society for Interferon Research founded by Bill Stewart in 1983. I was a Charter Member of ISIR. I hold a special place in my scientific heart for interferon, just as each of us as a Founding Member of CIS likely hold a special attachment to our favorite cytokine or cytokines that we have studied during our careers. One of the activities that we will continue to enjoy together as society members is the Annual Meeting. Learning of the newest exciting scientific advances across the broad range of

cytokines, together with our culture of friendships, has been and will continue to be an important benefit of society membership and aspect of the annual meeting.

Our desire is that the new merged Cytokine and Interferon Society will become a vibrant organization, one that grows in membership number and assumes a position of further scientific strength. We are excited about future opportunities in both the basic and clinical science arenas. While some challenges presently exist globally that impact not only research funding but also employment opportunities across the academic, government and private sector science areas, we hope for a combination of reasons that the climate will soon improve. With talented new investigators entering the cytokine and interferon fields, coming from different backgrounds and bringing with them new experimental tools and cross disciplinary approaches, we look forward to a future of continued exciting discoveries.

With best wishes,
Chuck Samuel
President, ISICR

New Member MINIBIOs *Contributed by Thomas Tan*



Werner Absenger, MS
Saybrook University
San Francisco, CA

Werner is a research scientist and Mind-Body Medicine (MBM) skills groups facilitator interested in using state-of-the-art imaging techniques and immunological assays, qualitative and mixed methods research to investigate MBM modalities. As a MBM research scientist, he takes special interest in the study of the modulatory effects Clinical Hypnosis, Guided Imagery and MBM skills groups have on psychoneuroimmunology and the expression of tumorigenic cytokines in cancer patients. As a MBM skills group facilitator, Werner specializes in conducting MBM skills groups for persons affected by cancer, whether they are the patient or the loved one/caretaker of a person suffering from cancer. A MBM skills group can provide persons affected by cancer a sense of control over their journey, connecting mind, body and spirit. This allows for a fundamental shift in perspective that could allow persons affected by cancer to heal, rather than to focus solely on curing the disease.

New Member MINIBIOs *continued*



Dr. Kiran Bhaskar

Assistant Professor
University of New Mexico
Albuquerque, NM

Dr. Kiran Bhaskar did his Ph.D. training at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India. After completing his doctoral studies, Dr. Bhaskar's postdoctoral training began in Dr. Gloria Lee's laboratory at the University of Iowa, USA, where he studied the molecular mechanisms of neurodegenerative disease, specifically understanding the role of tyrosine phosphorylation of tau protein in the pathogenesis of Alzheimer's disease (AD). Dr. Bhaskar then joined as a Research Associate in the laboratory of Dr. Bruce Lamb at the Cleveland Clinic Foundation, where he demonstrated that oligomeric Abeta peptide induces neuronal cell cycle events, which is one of the pathological hallmarks of AD. Subsequently, he continued to work on the role of tau protein in AD and recently demonstrated that neuroinflammation, cell-autonomous to microglia, accelerates tau hyperphosphorylation, aggregation and behavioral impairment in a mouse model of tauopathy (hTau). Notably, the effects of microglial activation on tau pathology were enhanced when mice were deficient for the microglial-specific fractalkine receptor, CX3CR1. His team also demonstrated that interleukin-1 (IL1) released by reactive microglia induces tau phosphorylation in primary neurons via activating neuronal IL1 receptor (IL1R) and p38 mitogen activated protein kinase (p38 MAPK) pathway. In recent months (as of summer 2012), Dr. Bhaskar has been successful in obtaining several research grants from private foundations (AA, AHAF and CurePSP) as well as US-NIH (R21) to continue his studies on understanding the role of neuroinflammation in AD-related pathologies. He recently accepted a tenure-track Assistant Professor faculty position at the University of New Mexico, Albuquerque NM, USA.



Mehdi Bourouba, Ph.D.

Associate Professor
Faculty of Biological Sciences
University Sciences and Technology H. Boumediene
(USTHB)
Algiers, Algeria

Dr. Bourouba received his PhD training at the University of Karlsruhe, Germany, where he worked on the role of T cell activation in inflammatory bowel disease. He held post-doctoral positions at the Institut Gustave Roussy-INSERM and Paris-7 University-CNRS, France, where he respectively worked on understanding the role of the tumor suppressor PML in HIV-1 induced cell death and the role of the PML-RAR oncogene in tumor stem cell development. Since 2009, he holds an Associate Professor position at USTHB (University of Sciences and Technology H Boumediene, Algiers). In 2011, he was invited to participate in the first Arab-American Frontiers of Science, Engineering, and Medicine symposium, Kuwait. In 2012 he was the recipient of the American National Academy of Science award and joined Boston University (BU) to work on the invasive dynamic properties of nasopharyngeal carcinoma in Prof. Zaman's laboratory. Dr. Bourouba has recently found evidence of differential molecular processes that drive nasopharyngeal carcinoma progression in Maghrebi juvenile and elderly patients and the role of nitric oxide in NPC development. His current projects at USTHB focus on the relationship between inflammation and tumorigenesis and on biomarker discovery to predict nasopharyngeal carcinoma development in Algerian patients. Dr. Bourouba is actively involved in the development of PhD programs in tumor biology and virology at USTHB.

**Annie Bruns**

Graduate student
Northwestern University
Evanston, Illinois

Annie Bruns is a graduate student in the lab of Dr. Curt Horvath at Northwestern University in Evanston, Illinois. She is a recipient of the NIH Cellular and Molecular Basis of Disease Training Grant, and enjoys participating in scientific outreach programs. Her research focuses on the pattern recognition receptor proteins RIG-I, MDA5, and LGP2, collectively referred to as the RIG-I-like receptors (RLRs). These are cytoplasmic DExD/H box proteins that specifically recognize foreign RNA species as a molecular feature discriminating the pathogen from the host. This recognition initiates signaling pathways resulting in the production of antiviral cytokines and establishment of an antiviral state. Her project combines standard biochemical approaches with a single molecule imaging technique in which fluorescently labeled RNAs are tethered to a slide and incubated with purified RLR proteins. Binding, unbinding, and RNA translocation can be monitored via protein-induced fluorescence enhancement. She is particularly interested in determining the role of ATP hydrolysis in foreign RNA recognition by the RLRs.

Matt Dickerson, PhD

Sr. Scientist, Assay Development
BioScale

Matt Dickerson has more than 10 years of experience in the development and optimization of biological assays. He is currently one of the chief architects at BioScale for the design and development of assays utilizing the AMMP technology for bioanalytical, preclinical and clinical development. His work includes assays for cytokines, inflammatory biomarkers, phosphoproteins, heterodimers, kidney injury markers, Chinese Hamster Ovary HCP, Protein A, His-tag fusion proteins and other cell-based assays. Prior to BioScale, Matt was a senior scientist at ILEX Oncology where he focused on the production and development of antibodies for potential therapeutic development and he had similar positions at both Wyeth and Biotransplant. He has also developed cell-based screening assay for potential cancer therapeutics which included Tumistatin and Mucin-1. Matt received his BS in biology at Mary Washington College and PhD in pharmacology at Northeastern University. He has been an invited speaker at major industry conferences and has multiple publications in peer-reviewed journals.

**Benjamin T. Gordon, MS**

PhD. Candidate in Applied Physiology
University of South Carolina, USA

Ben Gordon received a B.S. degree from the University of Miami in Biology and an M.S. degree from the University of South Carolina in Applied Physiology. He is currently working on his Ph.D. in Applied Physiology at the University of South Carolina. He is an investigator in the Psychoneuroimmunology and Nutrition Lab directed by Dr. Mark Davis at the University of South Carolina. His research focuses primarily on exercise and nutrition immunology, with a specific emphasis on inflammatory mediators and their role in various models of brain inflammation.



Giorgio Raimondi, MSc, PhD

Assistant Professor of Surgery and Immunology
Starzl Transplantation Institute
University of Pittsburgh School of Medicine
Pittsburgh, USA

Dr Raimondi received his training (including PhD) at the University of Milano-Bicocca, Italy, where he started forming his expertise on regulation of the activity of the immune system, with particular regard to mechanisms of induction and maintenance of T cell tolerance. Dr. Raimondi's research goal is to define therapeutic treatments that would promote endogenous tolerogenic mechanisms to treat disparate pathologies that require immune-modulation, such as transplant rejection and autoimmune diseases. To this end his lab focuses on characterizing the physiological mechanisms used to regulate the suppressive activity of a population of lymphocytes called regulatory T cells (Treg). In particular, his team is working to: i, identify the soluble mediators that are released as part of an inflammatory response (e.g. in response to a transplant) that reduce Treg activity; ii, clarify the intracellular molecular mechanisms that such mediators use to alter Treg function; iii, determine ways of targeting these modulatory processes in vivo and promote immune-regulation. To study these aspects, Dr. Raimondi's research adopts multiple mouse models including organ transplant models and autoimmunity models. Additionally, the clinical translation of his earlier discoveries is being investigated in non-human primate models of organ transplantation. Dr Raimondi has received prizes and support from multiple societies including The Transplantation Society, the American Society of Transplantation, the American Association of Immunologists, the American Heart Association, and the American Diabetes Association.

Member in the News



Keiko Ozato Wins Japanese Medal

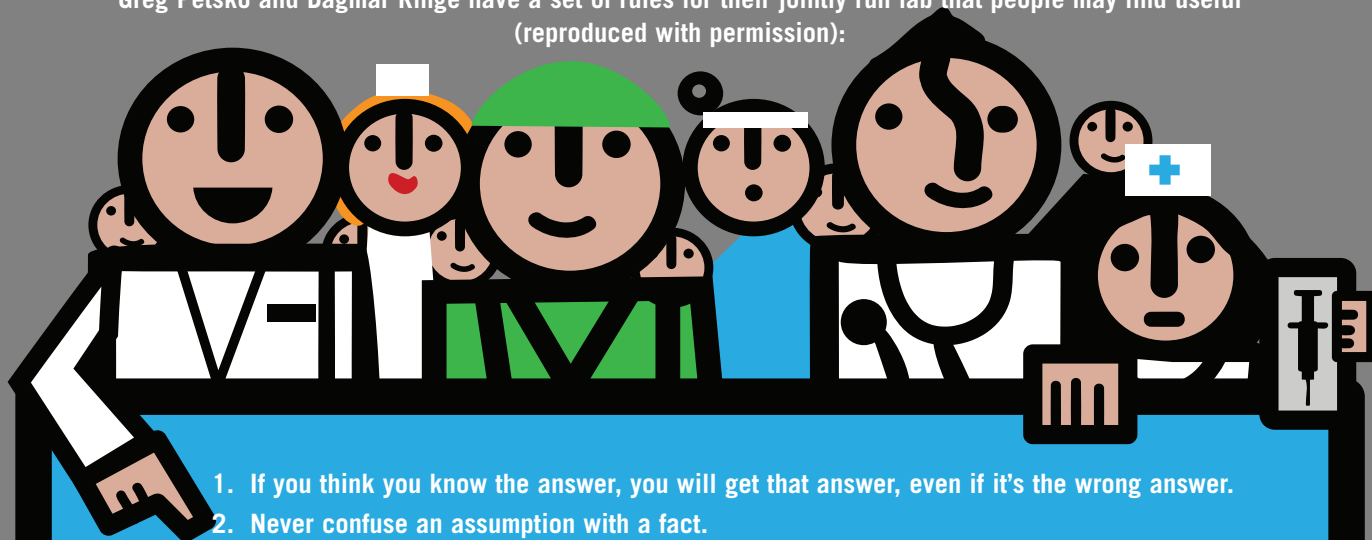
Photo: From Left to Right: Igor Dawid, Keiko Ozato and Ambassador Ichiro Fujisaki (Japanese Ambassador to the United States)

Keiko Ozato, chief of NICHD's Section on Molecular Genetics of Immunity, received the Order of the Sacred Treasure, Gold Rays with Neck Ribbon, from the Japanese government. The Order of the Sacred Treasure is a Japanese Order, established in 1888 by Emperor Meiji as the Order of Meiji. It is awarded in eight classes (from 8th to 1st, in ascending order of importance); Ozato's award is the 3rd class. The award recognizes Ozato's contribution to science and scientific interactions between Japan and the USA, particularly at the NIH. Ozato has been the chair of the NIH Japan Society for the Promotion of Science (JSPS) Fellowship Committee from its inception in 1996, and she has helped young Japanese scientists conduct high-caliber research under supervision of NIH intramural PIs. The fellowship, financed largely by the Japan-based JSPS, has benefitted many intramural

laboratories and has enhanced the scientific productivity of the NIH and Japan. Ozato's own laboratory is interested in chromatin-regulated gene expression with an emphasis on innate immunity. Her lab focuses on two nuclear regulatory factors, Brd4 and IRF-8. An expert in interferon research, Ozato has published more than 350 research papers in scientific journals. As a mentor, Ozato helped train 27 Japanese researchers, among other researchers; many of these researchers, upon returning to Japan, have become leaders in their own research fields. Shortly after the great Tohoku earthquake in 2011, Ozato, along with several other NIH scientists, assembled senior-level NIH employees of Japanese citizenship or descent and friends of Japan to organize a relief effort targeted at biomedical researchers in the earthquake-stricken area of Japan.

RULES FOR THE LAB

Greg Petsko and Dagmar Ringe have a set of rules for their jointly run lab that people may find useful (reproduced with permission):



1. If you think you know the answer, you will get that answer, even if it's the wrong answer.
2. Never confuse an assumption with a fact.
3. One good experiment is worth a thousand expert opinions.
4. The strong shall take from the weak, but the smart shall take from the strong.
5. Take nothing on faith. Things are frequently not what they seem to be or what people tell you they are. Check everything.
6. Excellence is the result of preparation, planning, imagination and tenacity. Neglect any one of these and the result is mediocrity.
7. It's often not that hard to handle a crisis, because usually your course of action is obvious. It's how you deal with day-to-day living that really proves what you're made of.
8. Adversity doesn't build character – it reveals it.
9. You are what you do.
10. Luck is the residue of design.
11. The odds of success are never improved by excessive caution.
12. Never let your sense of morality prevent you from doing what's right.
13. When you fully understand the simpler alternative, it usually will turn out to be as complicated as the complex alternative. Occam's razor is usually a poor reason for making a selection, especially in biology.
14. Only a fool is never afraid, but never let fear make the decisions for you. Do right, and risk the consequences.
15. It's nice to be first, but it's better to be right.
16. Create an environment where people can learn and have fun learning, and the work will take care of itself. The results are just the report card.
17. Be your own toughest referee. Whenever you get a result that you expected or that you think you understand, always ask, "How might nature be trying to fool me?"
18. Be generous to your coworkers, your colleagues and your collaborators. Give more credit rather than less, and err on the side of inclusiveness. It won't cost you a thing, and it will gain you a lot.
19. Underpromise and overdeliver.
20. Fame is a bubble, popularity an accident, and money takes wings. The one thing that endures is character.

A Tribute to

Ferdinando Dianzani

1932 - 2012

by Antonina Dolei, Department of Biomedical Sciences, University of Sassari, Sassari, Italy



Ferdinando Dianzani, ISICR Honorary Member and ISICR President in 1990-91, passed away in Rome, last April 12th 2012, after a short fight against cancer. He was Professor Emeritus of Virology at La Sapienza University of Rome, Italy, and Adjunct Professor of Microbiology & Immunology, at the University of Texas Medical Branch of Galveston, TX, USA. Almost all his scientific/professional life has been linked to interferon.

He was born in Grosseto, Tuscany, in 1932, and the link with his land held steady forever. At high school he met Giuliana, his lovely wife and life's companion. Dianzani attended the Medical School in Siena, Italy, where he graduated in 1959; then he attended the Specialization School (a kind of Ph.D. school) of Hygiene, in Naples, specializing as Hygienist in 1963.

In Italy, the earliest published studies on interferon date back to 1961 (1), by S. Addis, an obscure Microbiologist of Sassari, but the effective seeds sprouted in Siena, where a pivotal symposium on interferon was organized in June 1967, by Prof. Geo Rita, Director of the local Institute of Microbiology (2). Rita seeded interferon in two minds in Siena: Velio Bocci, now Professor Emeritus of Physiology at the University of Siena, who spent decades studying interferon pharmacokinetics (first paper on interferon: 3), and Ferdinando Dianzani, whose interests were the mechanism of action of interferon and its clinical applications (first paper on interferon: 4). Soon thereafter, Dianzani met Sam Baron, at NIH, and established with him a lifelong, deeply rooted,

friendship and scientific collaboration. In 1970, Dianzani became full Professor of Microbiology at the University of Turin, Italy, where further seeds of interferon sprouted, that originated Guido Forni, and Santo Landolfo, now, respectively, full Professors of Pathology and of Microbiology, in the same University. From 1976 to 1981, Dianzani worked in Baron's Lab, at the University of Texas Medical Branch, Galveston, TX, as Adjunct Professor of Microbiology, showing the unexpectedly rapid activation of the interferon system (5).

Meanwhile, G. Rita moved to Rome and founded the Institute of Virology, at La Sapienza University of Rome (1969). When he retired (1981), Dianzani was full Professor of Virology and Director of that Institute in Rome. After the discovery of HIV (HTLV-III at that time), Dianzani's studies on interferon moved naturally towards HIV and AIDS (first paper: 6), and he became actively engaged in the Italian National Health Council and the National Committee against AIDS of the Ministry of Health. His team included Antonina (Ninella) Dolei (Full Professor of Virology at the University of Sassari since 1985), Maria R. Capobianchi (since 2000 Chief of the Laboratory of Virology of National Institute for Infectious Diseases "L. Spallanzani", in Rome), and Guido Antonelli (since 2000 full Professor of Virology at La Sapienza University of Rome). In 1995 Dianzani moved to the new Medical School of the University Campus BioMedico, in Rome, serving also as Faculty Dean, until he retired, in 2007. Since then, he was Scientific Advisor for Clinical Virology of the Spallanzani's Institute, affectionately hosted in Maria's Lab. Dianzani's scientific activity is demonstrated by more than 300 scientific papers, most of them in international journals.

Apart from science, Ferdinando Dianzani was profoundly linked to his motherland Tuscany, particularly to his pleasant

retreat at Porto Ercole, in the municipality of Monte Argentario. In addition, since all the Tuscany is an archeological site, he was a kind of relic hunter, always looking around, searching for any small piece of ancient earthenware; he gathered a remarkable collection of Etruscan finds. He was profoundly devoted to his family: his wife Giuliana, Lorenzo (engineer), and Chicca (Caterina, dermatologist).

His appearance in Florence, at the last ICS/ISICR Meeting, September 2012, revealed a person already ill, but still attentive and watchful. He was happy, since Chicca was expecting a baby, and he would become a grandfather, at last. Luckily, Leonardo Maria arrived soon enough for his grandfather.

1. Addis S. [Phenomenon of viral interference, production of interferon and prednisolone]. *Ig Mod.* 1961 Nov-Dec;54:771-6.
2. The Interferons. A symposium, Siena, Italy, 1967, G. Rita, Ed. Academic Press, 1968.
3. Bocci V, Russi M, Rita G. Recovery and identification of interferon in the rabbit urine. *Experientia.* 1967 Apr 15;23(4):309-10
4. Guerra R, Frezzotti R, Bonanni R, Rita G, Dianzani F. [Possibilities of treatment of human herpetic keratitis with an inducer of the interferon system]. *Atti Accad Fisiocrit Siena Med Fis.* 1968;17(2):1513-7.
5. Dianzani F, Baron S. Unexpectedly rapid action of human interferon in physiological conditions. *Nature.* 1975 Oct 23;257(5528):682-4.
6. Dolei A, Fattorossi A, D'Amelio R, Aiuti F, Dianzani F. Direct and cell-mediated effects of interferon-alpha and -gamma on cells chronically infected with HTLV-III. *J Interferon Res.* 1986 Oct;6(5):543-9.

2012 ISICR
Milstein
AWARD WINNER



DR. JEAN-LAURENT CASANOVA

Rockefeller University

Dr. Jean-Laurent Casanova received his M.D. from the University of Paris Descartes in 1987 and his Ph.D. in immunology from the University of Paris Pierre and Marie Curie in 1992. In 1999 he was appointed a professor of pediatrics at Necker, where, with Dr. Abel, he cofounded and co-directed the Laboratory of Human Genetics of Infectious Diseases. He was appointed professor at Rockefeller in 2008.

Dr. Casanova studies the human genetic determinism of pediatric infectious diseases. He is interested in identifying monogenic “holes” in the immune defense of otherwise healthy children, who are susceptible to specific infectious diseases, work that has profound implications for and has resulted in a paradigm shift in clinical medicine and fundamental immunology. His team has deciphered the molecular genetic basis of various pediatric infectious diseases, including mycobacterial diseases (mutations in *IFNGR1*, *IFNGR2*, *STAT1*, *IL12B*, *IL12RB1*, *NEMO*, *IRF8*, *CYBB*), invasive pneumococcal disease (*NEMO*, *IKBA*, *IRAK4*, *MYD88*), herpes simplex encephalitis (*UNC93B1*, *TLR3*, *TRAF3*, *TRIF*), and chronic mucocutaneous candidiasis (*IL17F*, *IL17RA*, *STAT1*).

Dr. Casanova was an international research scholar with the Howard Hughes Medical Institute from 2005 to 2008 and is a member of the European Molecular Biology Organization and the American Society for Clinical Investigation. Dr. Casanova was the recipient of the Professor Lucien Dautrebande Pathophysiology Foundation Prize from the Belgian Royal Academy of Medicine in 2004, the Richard Lounsbery Award from the French and American Academies of Sciences in 2008, the Oswald Avery Award from the Infectious Disease Society of America in 2009, the E. Mead Johnson Award from the Society for Pediatric Research in 2010 and the InBev Baillet-Latour Health Prize from the Baillet-Latour Foundation in Belgium in 2011.

For more information please visit:

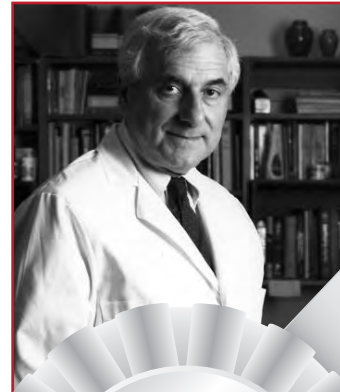
<http://www.rockefeller.edu/research/faculty/abstract.php?id=323>.



**2012 ISICR
Honorary
Membership
AWARD WINNER**

Michael Tovey, Ph.D.

Michael G. Tovey is a British citizen with a B.Sc., and Ph.D from the University of London. He is the author of more than 200 articles on interferon, cytokines, and biotechnology. He is a member of the Board of the Institut Andre Lwoff, President of the Scientific Board of the Institut de Cancérologie et Immuno-Génétique, and he is Vice-President of the Association ICIG. He is a member of the Scientific Council of the INSERM Unit of Applied Oncogenesis. He is a past member of the scientific council of the Faculty of Medicine of the University of Paris XI and the jury that discerns the rights to direct research in the University, and past member of the INSERM Molecular Biology commission and its directorate. In 1984 Michael Tovey was Fogarty Visiting Professor at Rockefeller University in New York, and in 2005 Fogarty Visiting Professor at the US National Cancer Institute in Frederick. He is editor of "Detection and Quantification of Antibodies to Biopharmaceuticals: Practical and Applied Considerations", and section editor of the Journal of Interferon and Cytokine Research. He is French representative for the ISICR International Council, chair of the ISICR Standards Committee, a member of the ISICR Meetings Committee, and a member of the European Adjuvant Advisory Committee. He was awarded the ESSEC Prize in 1976 and he shared the Antoine Lacassagne Prize with Ion Gresser in 1988.



**2012 ISICR
Distinguished
Service
AWARD WINNER**

Robert Friedman, M.D.

Bob Friedman has been carrying out research on interferons since 1959, when he was a postdoc in Sam Baron's lab at NIH. From 1961-63 he was a pathology resident in the NCI, Laboratory of Pathology. He spent a year in 1963-4 in Alec Isaac's lab at Mill Hill. Returning to NIH, he resumed research on the mechanism of action of interferons in the Laboratory of Pathology, NCI. In 1971-73, he returned to Mill Hill to establish with Ian Kerr a cell-free system to investigate interferon's activity. Again returning to NIH, he became a Laboratory Chief in the NIAID. From 1991 until the present he has been Professor and Chair of the Department of Pathology at the Uniformed Services Medical School in Bethesda. And his research has focused on the anti-tumor activity of interferon. Bob has served as a visiting scientist in labs at Warwick University, Jerusalem, Paris, and Madrid.

In 1994-5 he served as Secretary of the ISICR, and with Paula Pitha organized the 1995 ISICR meeting in Baltimore. He served as ISICR President in 1996-7. During his term of office, Norman Finter and he organized the Interferon Archive, now housed at the Wellcome Foundation in London. Jan Vilcek and Bob received the ISICR Honorary Member award in 2003. Since 2006, Bob has been the ISICR's Treasurer.

ISICR Awards

The Milstein Young Investigator Awards

Taylor Cohen
Columbia Univ., New York, NY

Babal Jha
Cleveland Clinic Foundation, Cleveland, OH

Clare Slaney
Peter MacCallum Cancer Ctr, East Melbourne, Australia

The Christina Fleischmann Award to Young Women Investigators

Stacy Horner
Univ of Washington, Seattle, WA

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

Graduate Awardee:

Laura Icardi
University of Ghent, Belgium

Post-graduate Awardee:

Aaron Irving
Monash Univ., Melbourne, Australia

ICS Awards

The Ed Leonard Prize for Chemotaxis/Chemokine Research

Benedetta Savino
Istituto Clinico Humanitas Milan, Italy

The ICS Young Investigator awards (3 awards)

Magali Irla
University of Geneva Medical School, Geneva, Switzerland

Kiran Bhaskar
University of New Mexico, Albuquerque, NM

Emmanuel Thomas
University of Miami Miller School of Medicine, Miami, FL

The Postdoctoral Investigator awards (4 awards)

Nicola Ivan Lore
San Raffaele Scientific Institute, Milan, Italy

Aradhana Rani
King's College London, London, United Kingdom

Karim Brandt
University of Geneva, Genève, Switzerland

Sebastien Jaillon
Istituto Clinico Humanitas Milan, Italy

The Outstanding Scholar Awards (4 awards)

Abhishek Garg
University of Pittsburgh, Pittsburgh, PA

Laura Icardi –
University of Ghent, Belgium

Tiziana Renzi
Istituto Clinico Humanitas Milan, Italy

Kazuya Masuda
Osaka University, Suita, Japan

ISICR/ICS Joint Award-The Journal of Biological Chemistry/Herbert Tabor Young Investigator Award

Vijay Rathinam
Univ. of Massachusetts Medical Center, Worcester, MA

The logo is a shield-shaped emblem with a red-to-orange gradient and a sunburst pattern. It is flanked by two golden ribbon-like banners. The text 'ICS Lifetime Membership AWARD' is centered in white, bold, sans-serif font.

ICS Lifetime Membership AWARD



ANTHONY CERAMI, PhD

Dr. Anthony Cerami is the founder and Chairman of the Board of Warren Pharmaceuticals, and the Founder, Chairman of the Board and CEO of Araim Pharmaceuticals.

Dr. Cerami has had a successful career applying detailed biochemical insights into understanding the pathogenesis of disease, and translating these discoveries into novel therapeutic products which have wide clinical utility.

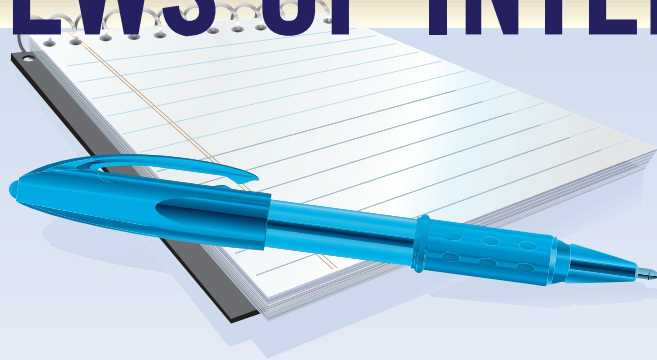
He received his PhD from the Rockefeller University and completed a postdoctoral fellowship at Harvard Medical School, and has received three honorary Doctorates. Dr. Cerami was the Dean of Graduate and Post Graduate Studies at Rockefeller University. He established what is now the Feinstein Institute for Medical Research.

Dr. Cerami is the recipient of a number of prestigious awards, including the Luft Award in Diabetes and the Banting Medal for Scientific Achievement, awarded by the American Diabetes Association in recognition of his lifelong

work on diabetes. He is a member of the National Academy of Sciences, Fellow of the American Academy of Arts and Sciences and Member of the Institute of Medicine of the National Academy of Sciences. He is also an Honorary Member of the American Society for Clinical Investigation and Fellow of the American Academy of Microbiology.

Dr. Cerami has been the inventor or co-inventor of over 150 issued U.S. patents and hundreds of foreign counterparts, including the anti-TNF monoclonal antibody that has been approved by the FDA for the treatment of Chron's disease and Rheumatoid arthritis. Dr. Cerami is also the inventor of the hemoglobin A1c test that is used by diabetics worldwide. He is the author or co-author of over 500 scientific publications.

REVIEWS OF INTEREST



Aricò E, Belardelli F. **Interferon- α as Antiviral and Antitumor Vaccine Adjuvants: Mechanisms of Action and Response Signature.** *J Interferon Cytokine Res.* 2012 Jun;32(6):235-47.

Casanova JL, Holland SM, Notarangelo LD. **Inborn errors of human JAKs and STATs.** *Immunity.* 2012 Apr 20;36(4):515-28.

Dooley J, Liston A. **Molecular control over thymic involution: from cytokines and microRNA to aging and adipose tissue.** *Eur J Immunol.* 2012 May;42(5):1073-9.

Espinosa V, Rivera A. **Cytokines and the regulation of fungus-specific CD4 T cell differentiation.** *Cytokine.* 2012 Apr;58(1):100-6.

Heim M. **Interferons and hepatitis C virus.** *Swiss Med Wkly.* 2012 May 9;142:0.

Hofmann SR, Rösen-Wolff A, Tsokos GC, Hedrich CM. **Biological properties and regulation of IL-10 related cytokines and their contribution to autoimmune disease and tissue injury.** *Clin Immunol.* 2012 May;143(2):116-27.

Lichtman EI, Helfgott SM, Kriegel MA. **Emerging therapies for systemic lupus erythematosus - Focus on targeting interferon-alpha.** *Clin Immunol.* 2012 Jun;143(3):210-21.

Liew FY. **IL-33: a Janus cytokine.** *Ann Rheum Dis.* 2012 Apr;71 Suppl 2:i101-4.

Mortier A, Van Damme J, Proost P. **Overview of the mechanisms regulating chemokine activity and availability.** *Immunol. Lett.* 2012 July 145:1-2, 2-9.

O'Reilly S, Ciechomska M, Cant R, Hügler T, van Laar JM. **Interleukin-6, its role in fibrosing conditions.** *Cytokine Growth Factor Rev.* 2012 Jun;23(3):99-107.

Rubino SJ, Geddes K, Girardin SE. **Innate IL-17 and IL-22 responses to enteric bacterial pathogens.** *Trends Immunol.* 2012 Mar;33(3):112-8.

Summers deLuca L, Gommerman JL. **Fine-tuning of dendritic cell biology by the TNF superfamily.** *Nat Rev Immunol.* 2012 Apr 10;12(5):339-51.

Tan C, Gery I. **The unique features of Th9 cells and their products.** *Crit Rev Immunol.* 2012;32(1):1-10.

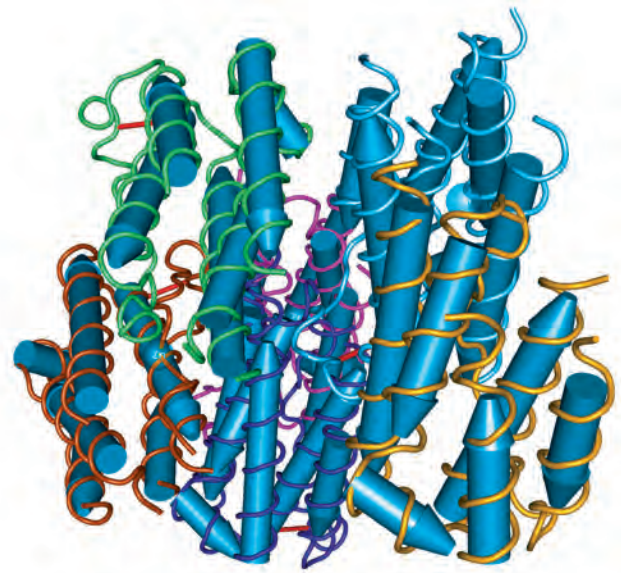
Tete S, Tripodi D, Rosati M, Conti F, Maccauro G, Saggini A, Cianchetti E, Caraffa A, Antinolfi P, Toniato E, Castellani ML, Conti P, Theoharides TC. **IL-37 (IL-1F7) the newest anti-inflammatory cytokine which suppresses immune responses and inflammation.** *Int J Immunopathol Pharmacol.* 2012 Jan-Mar;25(1):31-8.

Uyttenhove C, Van Snick J. **Anti-cytokine auto-vaccinations as tools for the analysis of cytokine function in vivo.** *Cytokine Growth Factor Rev.* 2012 Feb;23(1-2):1-6.

Wu CC, Sytwu HK, Lin YF. **Cytokines in diabetic nephropathy.** *Adv Clin Chem.* 2012;56:55-74.

A HISTORICAL PERSPECTIVE ON THE DISCOVERY AND CHARACTERIZATION OF INTERFERON-GAMMA

Jon Green, M.D. Ph.D.



Editor's Note: Dr. Green was a student in the laboratory of Sidney Kibrick at a point in time when cytokines were called factors and the role of lymphocytes in interferon production was being defined. He examined interferon production induced by non-viral antigens and characterized antigen-induced interferon as one of his projects.

Wheelock's paper in 1965 (1) was certainly the beginning, however it needs to be explained in the context of the four year hiatus between its publication in 1965 and confirmation in our 1969 Science paper (2). His paper is the model of scientific probity, taking pains to describe an activity that broadly conformed to the definition of an interferon as "interferon-like" based on its sole distinguishing characteristic of the loss of activity at pH 2.0. Attempts by others to repeat his observations using PHA and other mitogens were not uniformly successful. Other publications described mitogen-induced antiviral activity that was stable at pH 2.0. To my knowledge Wheelock did not present or publish any additional information to bolster his observation of pH lability.

The standard practice of the day was to directly acidify samples with dilute HCl, hold them at a low temp - neutralize them with NaOH and examine their antiviral activity. In contrast I dialyzed individual samples against a range of pH buffers. Antiviral activity was lost at pH 2 and 3, but preserved when dialyzed against buffers between pH 4.0 and 10. I am not sure if this corresponded to Wheelock's methods, but the results confirmed his original observations. By that time, opinion was against his finding of an "unusual" pH lability. When we were writing the manuscript, Sid Kibrick was disinclined to get into a political debating match and insisted that we not emphasize the finding of relative pH stability. Nevertheless, our observations were the first to confirm Wheelock's defining characteristic of what was to become IFN-gamma. A few years later we published the technical details of characterizing "immune interferon" in Barry Bloom and Phil Glade's "In Vitro Methods In Cell Mediated Immunity". We postulated that sera present in cell culture media are buffered to an extent that partially neutralizes exogenously added HCl and that a low pH is not maintained. Based on pH lability, the interferon induced by PPD, tetanus and diphtheria toxoids is gamma interferon.

Looking at the Wheelock article in Science, a modern single table Science article today is improbable if not impossible. At the risk of over simplification, those were different times. Other realities prevailed, and despite the pressures we all felt to publish, the relatively slow pace of research was dictated by the many limitations of cell separations and interferon bioassays that used primary cell cultures and took days to complete. Our interferon assays were done in glass tubes, and viral CPE was scored subjectively based on often blurry images through curved glass walls.

In 1965 I also found that PHA induced antiviral activity (Wheelock still would have published first) and switched my attention to antigens after reading his paper. It took a long time to show that antigens take longer to induce interferon than mitogens. In keeping with the leisurely nature of the times (I would not discount the possibility that we were slower than most) all of the information published in Science in June 1969 was presented at the Federation Proceedings in 1968. Perhaps we were not concerned with the expropriation of our data by others since the majority opinion held that Wheelock's observations of the acid lability of mitogen-induced interferon were not reproducible.

I think it is fair to say that both Wheelock's article and ours have been eclipsed by time. Both were heavily cited in their day, and I believe that Sam Baron cites them in his retrospective of Alex Isaacs on the 50th anniversary of the discovery of that other interferon.

Ref.

1. Wheelock EF. Interferon-Like Virus-Inhibitor Induced in Human Leukocytes by Phytohemagglutinin. Science. 1965 Jul 16;149(3681):310-1.
2. Green JA, Cooperband SR, Kibrick S. Immune specific induction of interferon production in cultures of human blood lymphocytes. Science. 1969 Jun 20;164(3886):1415-7.



Paper of Interest

Interferon- β Therapy Against EAE Is Effective Only When Development of the Disease Depends on the NLRP3 Inflammasome. *Sci Signal.* 2012 May 22;5(225):ra38.

Comments from the Senior Author, Mari Shinohara
Questions from Annette Khaled and Howard Young

Makoto Inoue¹, Kristi L. Williams², Timothy Oliver^{3*}, Peter Vandenebee^{4,5}, Jayant V. Rajan^{6,7}, Edward A. Miao⁸, and Mari L. Shinohara^{1,9}

¹ Department of Immunology, Duke University Medical Center, Durham, NC 27710, USA.

² Departments of Medicine and Cardiology, Duke University Medical Center, Durham, NC 27710, USA.

³ Department of Cell Biology, Duke University Medical Center, Durham, NC 27710, USA.

⁴ Department for Molecular Biomedical Research, Vlaams Instituut voor Biotechnologie (VIB), 9052 Ghent (Zwijnaarde), Belgium.

⁵ Department of Biomedical Molecular Biology, Ghent University, 9052 Ghent (Zwijnaarde), Belgium.

⁶ Institute for Systems Biology, Seattle, WA 98103, USA.

⁷ Department of Medicine, University of Washington, Seattle, WA 98195, USA.

⁸ Department of Microbiology and Immunology, University of North Carolina, Chapel Hill, NC 27599, USA.

⁹ Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC 27710, USA.

* Deceased.

Abstract: Interferon- β (IFN- β) is widely used to treat multiple sclerosis (MS), and its efficacy was demonstrated in the setting of experimental autoimmune encephalomyelitis (EAE), an animal model of MS; however, IFN- β is not effective in treating all cases of MS. Here, we demonstrate that signaling by IFNAR (the shared receptor for IFN- α and IFN- β) on macrophages inhibits activation of Rac1 and the generation of reactive oxygen species (ROS) through suppressor of cytokine signaling 1 (SOCS1). The inhibition of Rac1 activation and ROS generation suppressed the activity of the Nod-like receptor (NLR) family, pyrin domain-containing 3 (NLRP3) inflammasome, which resulted in attenuated EAE

pathogenicity. We further found that two subsets of EAE could be defined on the basis of their dependency on the NLRP3 inflammasome and that IFN- β was not an effective therapy when EAE was induced in an NLRP3 inflammasome-independent fashion. Thus, our study demonstrates a previously uncharacterized signaling pathway that is involved in the suppression of EAE by IFN- β and characterizes NLRP3-independent EAE, which cannot be treated with IFN- β .

What started you on this project and how did you come upon your initial hypothesis?

*The initial hypothesis came out only after we spent significant time trying to understand how the NLRP3 inflammasome is involved in EAE development. I was interested in how IFN β controls MS, using an EAE model, the mouse model of MS. Since IFN β is a first-choice drug to treat MS patients. Therefore, when I came to Duke as a new assistant professor, we just simply started to generally characterize IFNAR signaling. Using *Ifnar1*^{-/-} cells, we noticed high levels of IL-1 β in the cells. This suggested that type-1 IFNs could suppress NLRP3 inflammasome activation. Luckily, we had an access to *Asc*^{-/-} and *Nlrp3*^{-/-} mice, which do not have the NLRP3 inflammasome that processes IL-1 β maturation. While we worked on EAE in these mice, we also noticed the KO mice could be either resistant or susceptible to EAE, depending on the intensity of immunization (particularly the amount of heat-killed *Mtb* contained in CFA). Here, we first noticed that the NLRP3 inflammasome is not always necessary for EAE development. Since we knew that IFN β suppressed NLRP3 inflammasome activity, we wondered whether NLRP3-independent EAE did not respond to IFN β treatment; and that was exactly the case. We thought that this was an important mechanism to fully understand, because one-third of MS patients do not respond to IFN β therapy. Such patients go through severe side-effects and only determine that IFN β therapy is not for them later on (and the costs of this medication cannot be ignored as well).*

So why does this mechanism exist in the first place? Why would the immune system suppress itself after infection?

*Prolonged and/or hyper inflammation is harmful to us; therefore, the innate immune system is also equipped with various mechanisms to suppress inflammation after innate immune responses are initiated. A typical example of the failure to suppress excessive inflammation is seen in sepsis, in which people die from their own excessive inflammation, not from the infection itself. Suppression of the NLRP3 inflammasome by type-1 IFNs is probably one of those mechanisms that has evolved to suppress excessive inflammation in order to protect the host. An interesting thing about type-1 IFNs is that type-1 IFNs work as double-barreled molecules, but this also means that the host response mechanisms that include type-1 IFNs are not simple. Type-1 IFNs suppress NLRP3 inflammasome activity and Th17 responses (this was one of my postdoctoral projects). At the same time, type-1 IFNs enhance immunity against viral infections and tumor development (but we do not want to have type-1 IFNs for *Listeria* infection). Based on those findings, an immune suppressive role of type-1 IFNs is obvious only in certain types of infections and autoimmune diseases.*

Is this a built in shut off switch to prevent autoimmunity or is there another reason?

It is probably so, i.e., the IFNAR-NLRP3 axis can prevent an autoimmune response, such as EAE. However, the role of IFNAR-NLRP3 axis may be more complicated in other types of autoimmune diseases, such as lupus. It is known that very low levels of Type-1 IFNs are constitutively produced without infections. A hypothesis for the constitutive Type 1 IFN production is to prepare for possible future infections by “revving-up” the immune system. It will be very interesting to test whether the low and constitutive levels of Type-1 IFNs also play a role to protect hosts from developing autoimmunity.

It would be helpful to elaborate more on why IFN-beta therapy also fails in some patients – does this reveal the underlying complexity of MS?

We hope that our finding – IFN β therapy does not ameliorate NLRP3-independent EAE – applies to MS. If so, it may be possible to identify patients who will not respond to IFN β therapy. Although EAE is a very good model to better understand MS, EAE and MS are not the same disease. It is also possible that human NLRP3 inflammasome may not work in the same manner as the mouse NLRP3 inflammasome. Therefore, we still need more studies in humans. For example, one thing we really need to nail down is what “aggressive immunization” means in human. As I described above, we use aggressive EAE induction regimen to induce a subtype of EAE, which does not need the NLRP3 inflammasome and does not respond to IFN β treatment. However, of course, MS is not induced by such an artificial disease induction regimen. Then, why do some people develop NLRP3-independent and IFN β -resistant MS, if our hypothesis applies to human MS pathology? What are the natural triggers to induce IFN β -resistant MS? These are the questions that we are currently trying to answer as a next step in our research.

Are you going to be screening MS patients and if so, how are you going to do this?

Yes, we have started to collaborate with clinicians to do so. The first thing we need to do is to determine whether NLRP3 activity and the response to IFN β therapy positively correlate. If we could identify molecules that are specifically expressed in NLRP3-independent MS, it will also be possible to study if there is a reverse correlation between the molecules and the response to IFN β therapy.

Finally, I would like to thank National Multiple Sclerosis Society for the funding that has supported this research. The key person who carried out this work is an extremely talented research fellow in my lab, Dr. Makoto Inoue.

THE ISICR SLIDE REPOSITORY

Ever see a slide in a talk that you wish you could use for your own presentation? Well now this may be possible through the ISICR Slide Repository. **All CIS Members** can go in and post slides that they have developed or download slides that others have provided to the membership. ICS members should please contact Howard Young for access to the repository. **OVER 500 SLIDES ARE NOW AVAILABLE!!!!!!** For this member only feature, you need to have your ISICR member number so if you are not sure what that is, please contact the membership office. We urge members to upload general slides that other members can use for lectures, classes, seminars, etc. Slides are not to be changed without permission from the donor and all copyright permissions must be obtained. The repository now has a useful search capability that allows you to find slides on a particular topic. If you have trouble uploading or downloading slides, please contact Howard Young at younghow@mail.nih.gov.



<http://149.156.177.116/cremag/>

Alternate Splicing Prediction Database

<http://t.caspur.it/ASPicDB/>

ASPicDB is a database designed to provide access to reliable annotations of the alternative splicing pattern of human genes, obtained by **ASPic** algorithm (*Castrignano' et al. 2006*), and to the functional annotation of predicted isoforms.

Enhanced query and download facilities allow users to select and extract specific sets of data related to genes, transcripts and introns fulfilling a combination of user-defined criteria. Several tabular and graphical views of the results are presented, providing a comprehensive assessment of the functional implication of alternative splicing in the gene set under investigation. ASPicDB also includes information on tissue-specific splicing patterns of normal and cancer cells, based on available EST data and their library source annotation.



Cytokines & Cells Online Pathfinder Encyclopedia

<http://www.copewithcytokines.org/>

Version 29.0 (Spring/Summer 2012 Edition)

29,000+ entries/pages • 77,250+ cited references • 963,000+ internal hyperlinks

Fully integrated **subdictionaries** on Angiogenesis, Apoptosis, Bacterial Modulins, CD Antigens, Cell lines, Eukaryotic cell types, Chemokines, CytokineTopics, Cytokine Concentrations in Body Fluids, Cytokine Inter-Species Reactivities, Dual identity proteins, Hematology, Innate Immunity Defense Proteins, Metalloproteinases, Protein domains, Regulatory peptide factors, Virokines, Viroceptors, Virulence Factors

cREMaG is a database interface allowing for detection of the over-representation of transcription factor binding sites (TFBS) for a queried set of co-expressed genes. If the genes are co-expressed it is highly probable that they are co-regulated. Analysis of common properties of their promoters could suggest the transcription factors responsible for their coregulation.

GeneGlobe Pathway Central

<https://www.qiagen.com/geneglobe/pathways.aspx>

Over 500 cellular pathways available
Easy-to-read graphical format

New! Downloadable pathway images

New! Downloadable, editable PowerPoint slides

Pathway information and literature references provided

Use one of the search options below to view pathway information for your gene of interest. Comprehensive pathway details enable study of the role of the gene of interest and planning of future experiments.

By function • By organism • Alphabetically Search

- Apoptosis
- Cell Adhesion
- Cell Cycle Regulation
- Cell Motility
- Cell Signaling
- Cell Survival
- Chemokines
- Cytokines
- Developmental Biology
- Diseases
- DNA Maintenance
- Growth Factors
- Hematopoiesis
- Hormones
- Immunology
- Kinases
- Metabolic
- Neuroscience
- Neurosciences
- Pathogens
- RNA Pathways
- Signaling Through G-Proteins
- Stress Activated
- Transcription Regulation

Immune Modeling Community Portal

<http://www.imcportal.org/>

Welcome to the Immune Modeling Community Web Portal. This website features news and resources relevant to investigators interested in immune response modeling for infectious disease research.

The purpose of the website is to facilitate collaboration and exchange information (including data, models, publications, events, funding opportunities) among researchers interested in using, developing and validating mathematical models of the immune response to infectious diseases.

Pathogen Portal

<http://www.pathogenportal.org/portal/portal/PathPort/Home>

Pathogen Portal's Infectious Disease Triangle perspective supports an integrative understanding of human disease through the study of multiple levels of interactions between a susceptible Host, an infectious Pathogen, and a conducive (to disease) Environment. Originating from plant pathology, this ecological approach is increasingly relevant to health sciences. Because some diseases include invertebrate Vectors as part of their ecology, the Disease Triangle broadly considers Environment to include Vectors.

Pathway Commons

<http://www.pathwaycommons.org/pc/home.do>

Pathway Commons is a convenient point of access to biological pathway information collected from public pathway databases, which you can browse or search.

- **Biologists** can browse and search Pathway Commons pathways.
- **Computational biologists** can download all pathways in BioPAX format for global analysis.
- **Software developers** can build software on top of Pathway Commons using our web service API. You can also download and install the cPath software to create a local mirror of Pathway Commons.

All data is freely available, under the license terms of each contributing database.

The PSI:BiologY-Materials Repository

<http://psimr.asu.edu/>

The PSI:BiologY-Materials Repository (PSI:BiologY-MR) stores, maintains and distributes protein expression plasmids and vectors created by the PSI centers. As of February 2012, we have over 53,000 PSI plasmids and 85 empty vectors available for request with additional PSI plasmids processed and added to DNASU monthly.



1. Breast Cancer 1000 (BC1000): A collection of clones containing 1000 human genes related to breast cancer
2. Yeast - All of the open reading frames (ORFs) of *S. cerevisiae* in the Gateway Entry vectors
3. >5,500 *S. cerevisiae* ORFs in two yeast expression vectors pBY011 and ZM552
4. A collection of the 5,600 genes encoded by *P. aeruginosa*
5. Complete genome collections for *Bacillus anthracis*, *Francisella tularensis*, *Vibrio cholerae* and *Yersinia pestis*
6. A set of >500 human kinases both in the Creator Entry Vector and two mammalian retroviral vectors (pJP1520 and pJP1563)
7. A set of 14,000 clones of human genes in the Gateway Entry vector
8. Over 10,000 human genes in a cell free expression vector.
9. set of over 1,000 human transcription factors in a lentiviral vector

Rodent Respect

<http://www.rodentrespect.com/>

A screenshot of the Rodent Respect website. The header features the title "RODENT RESPECT" and a quote: "Roughly 97% of all lab animals are mice and rats. Regardless of whether one views them as pets or pests, rodents are mankind's most constant companions on the road toward a healthier future. They are the unsung heroes of scientific progress. This project is dedicated to them." Below the quote is a navigation menu with items: LAB, GALLERY, WORLD, LIBRARY, Curiosity CABINET, READING FILE, and CONTACT. A central section titled "SCIENTISTS TALK ABOUT RODENTS" includes "INTERVIEWS", "ETHICS", "LINKS", and "BLOG". On the right, there are buttons for "FURNISH A LAB OR OTHERS" and "DEMAND YOUR RODENT RESPECT BUTTONS!". A "DOWNLOAD POSTER" button is also present. A small illustration of a white mouse is in the top right corner.

Simgene

www.simgene.com

A Portal to Free Molecular Biology and Bioinformatics Tools

SimGene.com hosts the most comprehensive range of free and open access molecular biology and bioinformatics tools. We develop and maintain resources to serve the needs of scientists world-wide. The site is intended to provide a platform to assist scientists in their pursuit to further science. The website offers free access to popular online bioinformatics tools contributed by research organizations and personal websites that aid research in life sciences. No registration is required here.

Any comments and suggestions that can help us improve our complimentary services to the research community are welcome. This would help us ensure that the online tools are serving their best to individual research requirements and are maintained and developed at the leading edge of science.



Continued

The MIT/ICBP siRNA Database

<http://web.mit.edu/sirna/>

With the increasing number of experimentally verified siRNAs and shRNAs created and used by members of the MIT community, it has become desirable to have a comprehensive, easily accessible database to store and distribute information on tested siRNAs and shRNAs. The MIT/ICBP siRNA Database is an effort to catalog these experimentally validated reagents and make that information available to other researchers, both within and outside the MIT community.

Currently the database has validated siRNA and shRNA sequences against over 100 genes from three sources.

1. Sequences designed and tested by MIT researchers
2. Sequences designed by Qiagen; tested by Natasha Caplen's group at the NCI Sequences designed by Greg Hannon and Steve Elledge; tested by the ICBP and CGAP programs at the NCI

VecScreen

<http://www.ncbi.nlm.nih.gov/VecScreen/VecScreen.html>

VecScreen is a system for quickly identifying segments of a nucleic acid sequence that may be of vector origin. NCBI developed VecScreen to combat the problem of vector contamination in public sequence databases. This Web page is designed to help researchers identify and remove any segments of vector origin before sequence analysis or submission.

ATTENDING THE ANNUAL SCIENTIFIC MEETING: **The Trainee Perspective**

The ISICR offers student/fellow memberships for only \$30 USD for a 3 year membership. By becoming a member, students and fellows have the opportunity to apply for a number of ISICR awards, including the Milstein Travel Awards. If students/fellows in your labs or neighboring labs are not members, urge them to join and become active in the society.

They are our future.

- **Darrin Gao (MSc student):** Attending the 2011 ISICR annual conference in Florence, Italy, was truly an eye-opening experience for me. Not only was I able to have the opportunity to listen to talks from world-renowned scientists, but I was also thoroughly impressed by the depth of international cytokine research through the poster sessions. In addition, the meeting provided an excellent stage for potential collaborations with colleagues from around the world, normally difficult to achieve.
- **Erin Rogers (medical student):** I enjoyed the annual international meeting because it allowed me to see new research outside of the four walls of the lab. The research was often new, innovative and inspiring. It allowed me to return to the lab with a fresh perspective on subjects that I had been road blocked on, and gave me a greater perspective on the career that I could have down the line.
- **Jae Kwang Yoo (Research Associate):** During my Ph.D. training I had opportunities to attend both international and domestic scientific meetings. Among those meetings, I have no hesitation in saying that the ISICR annual meetings were the most memorable and enjoyable ones. During these meetings, I had the privilege to meet internationally recognized scientists in my research field and also communicate with them to improve my research significantly, which eventually enhanced my enthusiasm for scientific research. Finally, the travel awards given to me made this possible and helped me tremendously to further develop my scientific career in medical science research.
- **Leesa Pennell (PhD student):** As a trainee, attending the annual ISICR meetings has enabled me to interact with scientists both in my field and in other fields about the experiments I conduct, my methodologies, and I have learned about various techniques that I feel have improved my research. I've had the opportunity to give talks at a few of the meetings and got great feedback from world class

scientists who I otherwise would not have been able to speak to. Finally, the Milstein Travel Awards have made it so that young scientists like myself can participate in such an excellent annual meeting.

- **Carole Galligan (Research Associate):** Attending the ISICR meeting has been a very positive experience for me. The scientific caliber of the meeting is excellent and affords one the opportunity to keep current with new discoveries/concept from world-renowned researchers in the field. Meeting new colleagues has been invaluable for obtaining new perspectives on my research. Overall, the meeting is an excellent experience and the very generous travel awards make it realistic for trainees to attend.
- **Daniel Burke (PhD student):** I have been fortunate to attend the ISICR annual meetings that I have over the span of my graduate studies. Having been to smaller local meetings (Canadian Society of Immunology) and enormous international conferences (ASV & ICI), I can say that the gathering of ISICR members has struck a great balance! These meetings have been large enough to attract a number of researchers with similar focus, yet are able to maintain a sense of community. Every time I return from one of these meetings I have a renewed excitement for continuing research and a notebook full of ideas to draw from.
- **Craig Hawkshaw (MSc student):** Attending the ISICR annual meetings has allowed me to step back from the lab bench and gain insights into the other side of the scientific community through networking and building connections. The world-class talks not only inspire through demonstration of novel ideas and techniques but also

inspire the scientist to take the cutting edge to their own project. Attending an ISICR meeting shows you how close and amiable the community can be and stresses the importance of friendships in developing bright new scientists. Without the support from ISICR travel awards it simply would not be possible for students, such as myself, to have access to the knowledge and relationships these meetings provide.

- **Ben Wang (MSc student):** The annual ISICR meeting has given me the opportunity to present my work to an international community of researchers. Each meeting is highlighted by world-class talks and engaging workshops that have presented new perspectives and enhanced my enthusiasm for research. I have been fortunate to attend these meetings with generous support from the ISICR student travel award and look forward to future meetings!
- **Olivia Chan (Scientific writer):** Each year, the Society never fails to provide a robust learning and training opportunity about the principles of scientific research and the clinical applicability of basic research. The ISICR conferences consistently define what is new and important in the field of cytokine research therefore facilitating the transfer of cytokine research from the bench to the clinic and back again. Trainees that attend the ISICR conferences rarely leave without feeling stimulated, encouraged and highly enthusiastic about research, since the conference often provide a fresh perspective on their own work and challenges them to be innovative. The ability to tap into this unique network of researchers and to experience such an empowering experience could not have been possible without the support of the Travel Awards and the support of generous supervisors.

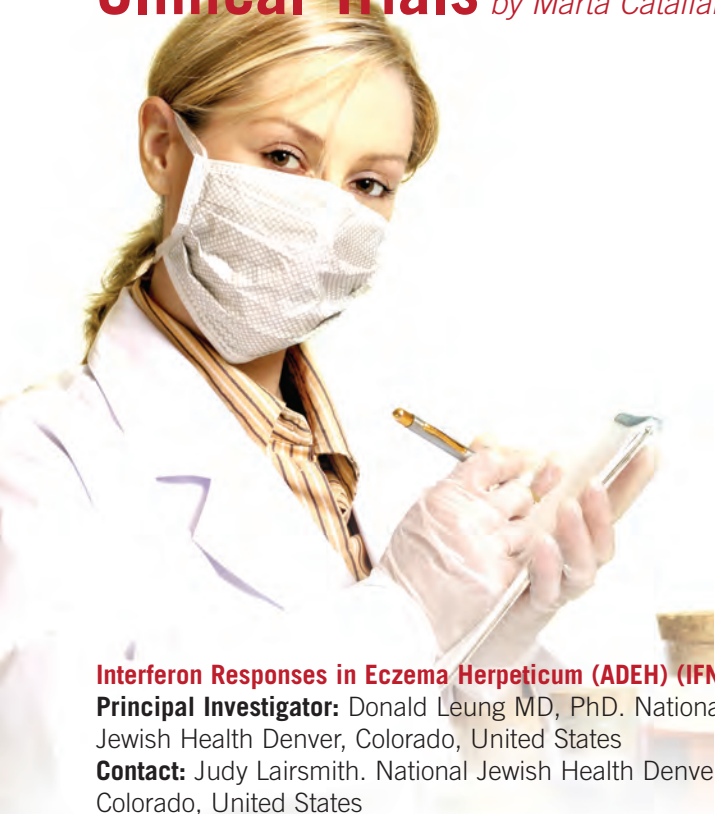
A NOTE OF CAUTION

Reconstituting National Institute for Biological Standards and Control (NIBSC) chemokines

Hoadley, ME; Scarth, S ; Hopkins, SJ. *Cytokine* 58:2, 162-164, 2012

Abstract: We observed significant discrepancies between immunoassay results when using different internally prepared reference preparations for interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1) from the National Institute for Biological Standards and Control (NIBSC). To evaluate the reasons for this we prepared the chemokines using diluents that incorporated protein at different steps. This showed that even brief addition of water to these preparations, in the absence of additional protein, resulted in loss of immunoreactivity in assays. The data obtained emphasize the importance of adding protein at an early stage of preparation to avoid loss of material and potential loss of activity. (C) 2012 Elsevier Ltd. All rights reserved.

Clinical Trials *by Marta Catalfamo*



Interferon Responses in Eczema Herpeticum (ADEH) (IFN)

Principal Investigator: Donald Leung MD, PhD. National Jewish Health Denver, Colorado, United States

Contact: Judy Lairsmith. National Jewish Health Denver, Colorado, United States
lairsmithj@NJHealth.org

ClinicalTrials.gov Identifier: NCT01429311

A Phase I/II Clinical Trial With Interferon Alfa 5 in Treatment-Experienced Patients With Genotype-1 Chronic Hepatitis C

Principal Investigator: Jesús Prieto, MD, PhD Clínica Universidad de Navarra. Spain.

Contact: Javier Camara, PhD. Digna Biotech S.L.
jcamara@dignabiotech.com

ClinicalTrials.gov Identifier: NCT01121731

The Effects of Immunostimulation With GM-CSF or IFN- γ on Immunoparalysis Following Human Endotoxemia

Principal Investigator: Peter Pickkers, Prof, MD, PhD. Radboud University Nijmegen Medical Centre, The Netherlands

Contact: Radboud University Nijmegen Medical Centre Nijmegen, Gelderland, Netherlands, 6500 HB

ClinicalTrials.gov Identifier: NCT01374711

PEG-IFN Plus Ribavirin Combination Therapy for Older Patients

Principal Investigator: Jun Hayashi, Department of General Medicine, Kyushu University Hospital Fukuoka, Japan

Contact: Jun Hayashi. Department of General Medicine, Kyushu University Hospital Fukuoka, Japan,
hayashij@genmedpr.med.kyushu-u.ac.jp

ClinicalTrials.gov Identifier: NCT00956982

Pegylated Interferon Alfa-2a Plus Low Dose Ribavirin for Treatment-Naïve Dialysis Patients With Chronic Hepatitis C

Principal Investigator: Chen-Hua Liu, MD Department of Internal Medicine, National Taiwan University Hospital

Contact: Chen-Hua Liu, MD. National Taiwan University Hospital

jacque_liu@mail2000.com.tw

ClinicalTrials.gov Identifier: NCT00491244

Evaluating the Safety and the Biological Effects of Intratumoral Interferon Gamma and a Peptide-Based Vaccine in Patients With Melanoma (Mel 51)

Principal Investigator: Craig L. Slingluff, M.D. University of Virginia. United States

Contact: Sasha White, BS. University of Virginia. United States
snw2z@hscmail.mcc.virginia.edu

ClinicalTrials.gov Identifier: NCT00977145

Aerosol IL-2 for Pulmonary Metastases

Principal Investigator: Aung Naing, MD. UT MD Anderson Cancer Center. Houston, Texas.

Contact: Aung Naing, MD. UT MD Anderson Cancer Center. Houston, Texas, United States. 713-563-0181

ClinicalTrials.gov Identifier: NCT01590069

Evolution of Interleukin 7, Fat Mass and Metabolic Profile Before and After Transplantation (IL-7tran)

Principal Investigator: Marie Christine VANTYGHEM, PhD. Lille University Hospital. France.

Contact: Marie Christine VANTYGHEM, PhD. Lille University Hospital. France.

mc-vantyghe@chru-lille.fr

ClinicalTrials.gov Identifier: NCT01414660

Safety and Efficacy Study of Immunotherapy With Rituximab and Interleukin-2 in Patients With Non-Hodgkin's Lymphoma

Principal Investigator: Matthew Carabasi, MD. Thomas Jefferson University. Philadelphia, Pennsylvania, United States

Contact: Matthew Carabasi, MD. Thomas Jefferson University. Philadelphia, Pennsylvania, United States.

215-955-8874.

ClinicalTrials.gov Identifier: NCT00994643

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

Contact: Timothy Krepski Masonic Cancer Center, University of Minnesota Minneapolis, Minnesota, United States.

tkrepsk1@fairview.org

ClinicalTrials.gov Identifier: NCT01385423

IL-11 in Adults With Von Willebrand Disease Undergoing Surgery

Principal Investigator: Margaret V Ragni, MD, MPH. Hemophilia Center of Western PA

Contact: Margaret V Ragni, MD, MPH. Hemophilia Center of Western PA, Pittsburgh, Pennsylvania, United States. ragni@dom.pitt.edu

ClinicalTrials.gov Identifier: NCT00524225

An Open Label Dose Escalation Safety Study of Convection-Enhanced Delivery of IL13-PE38QQR in Patients With Progressive Pediatric Diffuse Infiltrating Brainstem Glioma and Supratentorial High-grade Glioma

Principal Investigator: Russell R Lonser, M.D. National Institute of Neurological Disorders and Stroke (NINDS)

Contact: Gretchen C Scott, R.N. National Institutes of Health Clinical Center, 9000 Rockville Pike, Bethesda, Maryland, United States. scottgc@mail.nih.gov

ClinicalTrials.gov Identifier: NCT00880061

CYTOKINES (sī'tə-kīn'): One Word, Many Definitions

WebMD

"Any of numerous hormonelike, low-molecular-weight proteins, secreted by various cell types, which regulate the intensity and duration of immune response and mediate cell-to-cell communication."

Medicinenet.com

"A small protein released by cells that has a specific effect on the interactions between cells, on communications between cells or on the behavior of cells."

Freedictionary.com

"A generic term for nonantibody proteins released by one cell population on contact with specific antigen, which act as intercellular mediators, as in the generation of an immune response."

Mosby's Medical Dictionary

"One of a large group of low-molecular-weight proteins secreted by various cell types and involved in cell-to-cell communication, coordinating antibody and T cell immune interactions, and amplifying immune reactivity. Cytokines include colony-stimulating factors, interferons, interleukins, and lymphokines, which are secreted by lymphocytes."

McGraw-Hill Concise Dictionary of Modern Medicine

"Biological response modifier Any of a number of small 5–20 kD polypeptide signaling proteins of the immune system, which are produced by immune cells and have specific effects on cell-cell interaction, communication and behavior of other cells."

Wikipedia

"Cytokines (Greek *cyto-*, cell; and *-kinos*, movement) are small cell-signaling protein molecules that are secreted by numerous cells and are a category of signaling molecules used extensively in intercellular communication."

Biology Online

"Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types rather than by specialised glands. They generally act locally in a paracrine or autocrine rather than endocrine manner."

World English dictionary

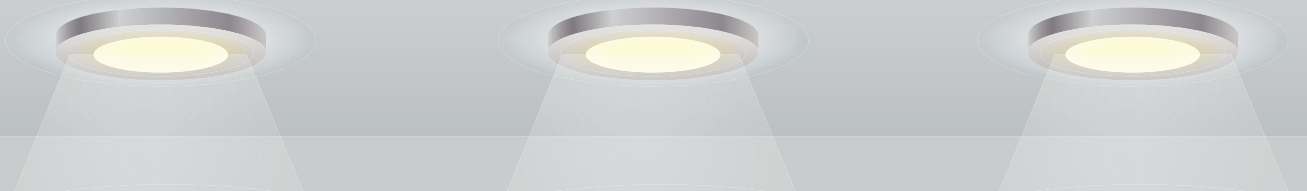
"Any of various proteins, secreted by cells, that carry signals to neighbouring cells."

Merriam Webster dictionary

"Any of a class of immunoregulatory proteins (as interleukin, tumor necrosis factor, and interferon) that are secreted by cells especially of the immune system"

Cytokine Research Portal

"Cytokines are signaling peptides that consist of water-soluble proteins and glycoproteins with a mass of 8 to 30 kDa. Cytokines are released by many different types of cells and are important in innate and adaptive [[immune response]]. They also play an important role in many diseases. Cytokines bind to specific cell-surface receptors producing intracellular signaling cascades that can up- or downregulate genes, transcription factors, and even other cytokines and cytokine receptors. The effect of a given cytokine is dependent upon the abundance of the cytokine, the presence or abundance of complementary cell surface receptors, and downstream signals that are activated by receptor binding. Overstimulation of cytokines can trigger a so-called cytokine storm which is a potentially fatal condition."



CYTOKINES AND METABOLISM – SPOTLIGHT ON TECHNOLOGY **Annette Khaled**

The study of cell metabolism is old story that has been invigorated by new technology. Starting with the classic observations of Otto Warburg in 1927 [1] on the non-oxidative breakdown of glucose in tumor cells, leading to the investigations of glucose metabolism in proliferating T cells in the late 1970's and early 1980's [2,3] to the current day, measuring cellular bioenergetics has been performed with the similar investigative tools (i.e. radioactive glucose analogs and cumbersome and complex probe-based equipment). Given that growth conditions can exert rapid changes on a cell's metabolic activity, the inability to measure both glycolysis and respiration in the same sample with high sensitivity has been a major obstacle. New technology released by Seahorse Biosciences addresses this problem in an innovative way.

The Seahorse XF Analyzers open a window into the two major energy pathways in cells: oxygen consumption rate (OCR) or mitochondrial respiration and extracellular acidification rate (ECAR) or glycolysis. In a 24 or 96-well format, a sensor cartridge, with probes and delivery ports for compounds, is lowered into a well containing cells, creating a transient microchamber. Within the transient microchamber system, the sensor probes contain fluorophores sensitive to oxygen (O_2) and protons (H^+), enabling simultaneous, real-time kinetics measurements of metabolic activity within an area of approximately 200 microns. Because the system requires less than $1-5 \times 10^4$ cells and can directly assay live cells responding to stimulation, the ability to assess cytokine-driven metabolic signals in lymphocytes is achievable.

Three recent publications elegantly demonstrate how the new Seahorse technology advances discovery in the interplay between growth factors and metabolism. It is known that T cells undergo a metabolic switch to glycolysis when stimulated to proliferate [4]. A key question was, however, does metabolism play role in establishing long-term memory cells after antigen-stimulation. This was answered in part, in a compelling publication by van der Windt et al. Investigators showed that CD8 memory T cells had a significant mitochondrial respiratory capacity, and that interleukin-15, a key cytokine in memory cell homeostasis, was an essential regulator of oxidative metabolism [5]. The research group from the Siegel lab investigated the role of reactive oxygen species (ROS) in inflammatory cytokine signaling. They used metabolic measurements to show that the electron transport chain was the major source of ROS that drove inflammatory cytokine synthesis and the hyperproduction of cytokines that occurred in patients suffering from TNFR-1-associated periodic syndrome (TRAPS) [6]. Returning to the study of metabolism in tumor biology, the research group from the Spies lab found that engagement of the natural killer group 2 member D (NKG2D) lymphocyte receptor, typically expressed on NK

cells and CD8 T cells, on tumor cells increased bioenergetics metabolism, suggesting a relationship between the immunoreceptor and tumor growth factor receptors [7]. These three studies typify how revealing the intricacies of cellular metabolism advance the field of cytokine and growth factor research, leading to a better understanding of the diseases that results when cytokine signaling pathways go awry.

Reference List

1. Warburg O, Wind F, Negelein E (1927) THE METABOLISM OF TUMORS IN THE BODY. *J Gen Physiol* 8: 519-530.
2. Hume DA, Radik JL, Ferber E, Weidemann MJ (1978) Aerobic glycolysis and lymphocyte transformation. *Biochem J* 174: 703-709.
3. Hume DA, Weidemann MJ (1979) Role and regulation of glucose metabolism in proliferating cells. *J Natl Cancer Inst* 62: 3-8.
4. Krauss S, Brand MD, Buttgeriet F (2001) Signaling takes a breath--new quantitative perspectives on bioenergetics and signal transduction. *Immunity* 15: 497-502.
5. van der Windt GJ, Everts B, Chang CH, Curtis JD, Freitas TC, Amiel E, Pearce EJ, Pearce EL (2012) Mitochondrial respiratory capacity is a critical regulator of CD8+ T cell memory development. *Immunity* 36: 68-78.
6. Bulua AC, Simon A, Maddipati R, Pelletier M, Park H, Kim KY, Sack MN, Kastner DL, Siegel RM (2011) Mitochondrial reactive oxygen species promote production of proinflammatory cytokines and are elevated in TNFR1-associated periodic syndrome (TRAPS). *J Exp Med* 208: 519-533.
7. Benitez AC, Dai Z, Mann HH, Reeves RS, Margineantu DH, Gooley TA, Groh V, Spies T (2011) Expression, signaling proficiency, and stimulatory function of the NKG2D lymphocyte receptor in human cancer cells. *Proc Natl Acad Sci U S A* 108: 4081-4086.



The NIH Intramural Research Program is Recruiting Tenure-Track “Earl Stadtman Investigators”



The National Institutes of Health, the U.S. government’s premier biomedical and behavioral research enterprise, is pleased to announce its fourth annual call for “NIH Earl Stadtman Investigators.” Scientific discoveries from our intramural laboratories, with their extensive infrastructure and critical mass of expertise, have a crucial role in both maintaining America’s research excellence and advancing medical treatments and cures. Come join the team whose hallmarks are stable funding, intellectual freedom, shared resources, and access to a broad range of scientific expertise. We seek creative and independent thinkers eager to take on high-risk, high impact research in tenure-track positions.

A variety of basic and translational/clinical positions are available, with areas of active recruitment including (but not limited to): Biostatistics/Bioinformatics; Chromatin Biology/Epigenetics; DNA Replication, Repair and Recombination; Molecular Epidemiology and Population Genetics; Molecular Immunology; Molecular Pharmacology and Toxicology; Neuroscience; Population Science; Stem Cells/iPS Cells; Structural Biology and Systems Biology; and Virology.

Who we are: Among our approximately 1,200 principal investigators and 4,000 trainees are world-renowned experts in basic, translational and clinical research. Our strength is our diversity in pursuit of a common goal, to alleviate human suffering from disease. Similar to academia, we offer our scientists the opportunity to mentor outstanding trainees at all levels (e.g., graduate students and postdoctoral fellows) in a research setting.

Whom we seek: For this broad, trans-NIH recruitment effort, we seek talented, early-career scientists with a clear and creative research vision who wish to contribute to the nation’s health.

Qualifications/eligibility: Candidates must have an M.D., Ph.D., D.D.S./D.M.D., D.V.M, D.O., R.N./Ph.D., or equivalent doctoral degree and have an outstanding record of research accomplishments as evidenced by publications in major peer-reviewed journals. Applicants may be in early stages of their research careers or non-tenured early-to-mid career scientists. Appointees may be U.S. citizens, resident aliens, or non-resident aliens with, or eligible to obtain, a valid employment-authorization visa.

How to apply: Applicants must submit a CV, a three-page research plan, a one-page description of their vision for future research and its potential impact, and contact information for three professional references through our online application system at <http://irp.nih.gov/stadtman> between August 1 and

October 1, 2012. You will be asked to designate a primary and secondary scientific area of expertise to aid in assigning your application to the appropriate review committee. Requests for letters of recommendation will be sent to your references when you submit your application. Reference letters will be accepted via upload to the website until 11:59 p.m. EDT October 15, 2012. We cannot accept paper applications.

What to expect: Search committees of subject-matter experts will review and evaluate applicants based on the following criteria: publication record, scientific vision and potential scientific impact of current and proposed research, demonstrated independence, awards and references. The committees will identify the most highly qualified candidates to invite to the NIH for a lecture in November or December 2012, which will be open to the NIH scientific staff, and for subsequent interviews with the search committees. The search committee chairs and NIH Scientific Directors, who lead our intramural programs, will identify finalists to be recruited as Earl Stadtman Investigators. Candidates not selected as Stadtman finalists can still be considered for other open NIH research positions. The entire process from application review to job offer may take several months, depending on the volume of applications.

We call upon individuals who will open our eyes to possibilities we haven’t yet envisioned, to complement our scientific mission and enhance our research efforts. More information about our program is at <http://irp.nih.gov>. The inspiring story of Earl and Thressa Stadtman’s research at the NIH is at <http://history.nih.gov/exhibits/stadtman>. Specific questions regarding this recruitment effort may be directed to Dr. Roland Owens, Assistant Director, NIH Office of Intramural Research, at owensrol@mail.nih.gov. DHHS and NIH are Equal Opportunity Employers.

ALBANY MEDICAL CENTER PRIZE AMERICA'S LARGEST PRIZE IN MEDICINE



Drs. **James Darnell** and **Robert Roeder** Share America's Most Distinguished Prize in Medicine

'Towering Figures' in Cell Research to Share Albany Medical Center Prize

Albany, N.Y., March 28, 2012—Two New York City scientists whose pioneering achievements in understanding how our genes are regulated and expressed have helped medical professionals and researchers improve health and combat diseases are the recipients of the 12th annual Albany Medical Center Prize in Medicine and Biomedical Research.

The two recipients, both from The Rockefeller University, will share the \$500,000 award, the largest in medicine and science in the United States. They are:

- James E. Darnell Jr., M.D., who is considered the “father” of RNA processing and cytokine signaling, and;
- Robert G. Roeder, Ph.D., a pioneer in the field of gene transcription in animal cells.

The scientists will receive the prize on May 11 during a celebration in Albany, N.Y.

According to James J. Barba, president and chief executive officer of Albany Medical Center and chairman of the National Selection Committee, “Understanding how our cells express their genetic information provides insight into all of human health. By helping to define how cells grow, replicate, and become specialized, these two

scientists have allowed countless other scientists and physicians to explore new ways to fight disease including viruses, heart disease, anemia and autoimmune disorders. I commend Drs. Darnell and Roeder for their extraordinary lifetime contributions.”

The Albany Medical Center Prize was established in 2000 by the late Morris “Marty” Silverman to honor scientists whose work has demonstrated significant outcomes that offer medical value of national or international importance. A \$50 million gift commitment from the Marty and Dorothy Silverman Foundation provides for the prize to be awarded annually for 100 years. A total of three Albany Prize recipients have gone on to win the Nobel Prize.

According to Joseph Goldstein, M.D., chair of the Department of Molecular Genetics at the University of Texas Southwestern Medical Center and 2003 Albany Prize winner, “Darnell and Roeder have contributed perhaps as much as any two individuals to the understanding of mammalian gene expression in all of its phases which has progressed from virtually nothing in 1961 to a remarkably detailed understanding today of what is the most complex of all intracellular synthesis functions.”

James E. Darnell Jr., M.D.,

Vincent Astor Professor Emeritus, Head of the Laboratory of Molecular Cell Biology, The Rockefeller University

Darnell was a professor at the Massachusetts Institute of Technology in 1963 when he discovered “RNA processing” in human cells while studying messenger RNA – or mRNA. mRNA carries genetic information from DNA out of the nucleus to a cell’s protein-making machinery located in the cytoplasm where the machinery gets to work with the goal of replicating the cell.

Darnell wondered how the mRNA in each different cell receives only the specialized genetic information it needs from the vast information store in DNA. By identifying very long strings of RNA inside the nucleus as opposed to the shorter strings of information that mRNA was carrying to the cytoplasm, he discovered that a precursor to mRNA was actually first copied from DNA and then “processed” for a cell’s specific purpose.

This pivotal discovery paved the way for the later defining of “RNA splicing,” a fundamental biological function in all nucleated cells by which RNA copies of DNA must be “cut and spliced” to furnish useful information for a specific cell.

“His lab gathered the first evidence that the useful form of most RNAs is fashioned by trimming and modifying the originally synthesized molecule in a pre-determined way,” explained Joan Steitz, Ph.D., the Sterling Professor of Molecular Biophysics and Biochemistry at the Howard Hughes Medical Institute of Yale University. Steitz was a 2008 recipient of the Albany Prize.

Darnell later made critical discoveries in the area known as “cytokine signaling” – the passage of signals from outside a cell to direct copying of RNA from specific DNA sites (genes). This work uncovered an important signaling route named the JAK-STAT pathway.

“The JAK-STAT pathway of signal transduction explains how cytokines (such as interferons, interleukins, and erythropoietin) exert their myriad actions of cells throughout the body, influencing the body’s response to inflammation and hypoxia. Moreover, the JAK-STAT pathway has recently been implicated in malignancy, with several of its components undergoing mutational alteration in cancers such as multiple myeloma and tumors of the head and neck,” said Goldstein.

Work is progressing on the so-called anti-STAT compounds that could potentially cure some types of cancer. And, some of the compounds that stimulate the JAK-STAT pathway are currently used as medical treatments, including erythropoietin, which stimulates the production of red blood cells in people with kidney disease and anemia.

Darnell is the co-author of two textbooks considered essential to educating science students, *General Virology* and *Molecular Cell Biology*. More recently he published *RNA: Life’s Indispensable Molecule*.

Robert G. Roeder, Ph.D.

Arnold O. and Mabel S. Beckman Professor of Biochemistry and Molecular Biology, Head of the Laboratory of Biochemistry and Molecular Biology, The Rockefeller University

The first step in gene expression involves the copying (transcription) of genes (DNA) into RNA, which is then processed and translated into proteins. As a University of Washington graduate student in 1969, Roeder discovered that three enzymes, called RNA polymerases, play this role in animal cells. In the late 1970s, using purified polymerases and synthetic copies of genes (DNA), he was

successful in developing the first cell-free systems to study transcription, a scientific breakthrough that allowed scientists to recreate transcription in a test tube to better study the complex processes by which cells turn genes on and off.

Roeder’s initial work with these systems, leading to a greater understanding of gene regulation, included the identification of polymerase-associated helper factors, called the general transcription machinery, and the definition of the first of many hundreds of gene-specific DNA-binding regulatory proteins, called activators and repressors, that control the rate of transcription and effect major cell fate decisions. His further demonstration that the prior assembly of DNA and histones into chromatin, the natural template in cells, directly represses the general transcription machinery established a predicted general repression mechanism and indicated the existence of other factors that counteract this repression.

“This area of research is central to understanding gene regulation and thus processes such as oncogenesis and development. He was the first to show accurate initiation *in vitro* by these enzymes and thus to develop the biochemical basis for current research in factors regulating transcription,” said Phillip Sharp, professor at the Koch Institute for Integrative Cancer Research at MIT.

In the early 1990s, Roeder and his colleagues discovered another class of transcriptional regulatory proteins, called “coactivators,” that serve as bridges between activators and the general transcription machinery and thereby provide the cell with added control over gene activity. In an important integration of transcription and chromatin studies, Roeder recently has established activation of genes within chromatin dependent upon these co-activators, the general transcription machinery, and various chromatin modifying factors -- offering powerful systems for studying transcriptional regulatory (including epigenetic) mechanisms.

The control of gene expression -- the proper activation or silencing of genes in cells -- is crucial for normal processes such as embryonic development, cell growth and differentiation, and homeostasis; and many diseases, including cancer, arise when gene activity is not tightly controlled. Thus, the gene regulatory studies pioneered by Roeder provide insights into possible therapeutic approaches to maintain or restore proper gene activity.

Roeder’s current interests include an understanding of the function of the tumor suppressor p53 in effecting either growth arrest and DNA repair or killing of potential tumor cells, regulators that effect the differentiation and function of fat cells (with implications for treating diabetes, heart disease and obesity), and leukemic fusion proteins that preclude the differentiation of early blood stem cells and lead to leukemia.

Both scientists have extensively published research and have been cited by countless medical and scientific journals. Although they have been close colleagues for years this is their first joint award. Both are members of the U.S. National Academy of Sciences and both have received numerous other prestigious national and international awards and honors that include the Gairdner Foundation International Award and the Lasker Award. Darnell is a recipient of the National Medal of Science.

For more detailed biographies and downloadable photos of this year’s recipients and more information on the Albany Medical Center Prize in Medicine and Biomedical Research, go to: www.amc.edu/Academic/AlbanyPrize.



Interesting Facts about Transgenic Mice

1. The first transgenic mice were produced in 1974 by Rudolf Jaenisch. This was the same year that Rubik's cube was invented.
2. Fifteen years later in 1989 the first knockout mice were created by Martin Evans, Mario Capecchi, and Oliver Smithies. In that same year the first episodes of the Simpsons were aired.
3. In 2007, a team of researchers in University of Kentucky successfully created a transgenic mouse that was resistant to spontaneous and artificially-induced cancer by inserting a gene that codes the tumor-suppressor protein Par-4.
4. As part of the "Evolved Mouse Project", a team in University of Osaka has generated transgenic mice that are prone to miscopying DNA. As an unexpected result, they have created mice that can tweet like birds in 2010. The goal of the "Evolved Mouse Project" was to shed new light on how languages evolve.

**Best Regards,
Cyagen Biosciences**



Please join us for the 14th International TNF Meeting
Loews Le Concorde, Québec City, Canada • July 7-10, 2013

The TNF Conference holds a biannual meeting focused on the biology of the TNF superfamily of ligands and receptors. This tradition began in 1987 with the cloning of TNF and continued with the ongoing discovery of new ligand and receptor family members. Currently, approximately 300-350 attendees come together from Europe, North America and Asia, with broad representation from academia and the biopharmaceutical industry. Our delegates include international leaders in the field, established academics and trainees.

To register, please go to <http://www.tnf2013.com/>

Take advantage of the early registration fees and student rates! **Bienvenue à Québec!**



SAVE THE DATE

SEPTEMBER 29 – OCTOBER 3, 2013

Cytokines in Health and Disease

September 29 - October 3, 2013

Hyatt Regency Hotel

San Francisco, CA

www.cytokines2013.com

Plans are well underway for the 2013 San Francisco Meeting Cytokines 2013 and the website is now under construction. The “city by the bay” is ready to welcome you with all of its excitement, scenic vistas and tasty California fare.

The organizers for this meeting, Warren Leonard, Sarah Gaffen, Bob Schreiber and Karen Mossman are planning a strong scientific program. Please watch the website for more information on the program.

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.

Visit www.cytokines2013.com often and watch as the web pages develop. Be sure to mark September 29 to October 3, 2013 on your calendar!

See you in San Francisco!



International Society for Interferon
& Cytokine Research

INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH

Dues and Subscriptions Services

9650 Rockville Pike, Bethesda, Maryland 20814-3998 (USA)

Telephone: (301) 634-7250 • Fax: (301) 634-7099

WEBSITE: <http://www.isicr.org> • EMAIL: ISICR@faseb.org

2013 MEMBERSHIP APPLICATION: New Renewal

Name _____
First Middle Last

Department _____

Organization _____

Address _____

City State/Province Zip Country

Note: Street address and zip+4 now required by Postal Service for delivery (US Only)

Telephone _____ Fax _____

E-Mail address: _____

**PLEASE RETURN THIS APPLICATION WITH
YOUR REMITTANCE**

U.S. Currency ONLY (checks to be drawn
on a U.S. Bank)

Make checks payable to: ISICR or International
Society for Interferon and Cytokine Research

For Credit Card payments, see below.

ISICR Federal Tax ID # : 59-2471233

Dues payments entitle a member to receive the annual Directory of Members, Newsletters, annual meeting program, and all meeting announcements.

MEMBERSHIP DUES

ONE-YEAR

TWO-YEAR

THREE YEAR

FIVE YEAR

Regular Member (2013)	<input type="checkbox"/> \$50.00	<input type="checkbox"/> \$90.00	<input type="checkbox"/> \$120.00	<input type="checkbox"/> \$200.00
Emeritus Member (2013)	<input type="checkbox"/> \$20.00	<input type="checkbox"/> \$35.00	<input type="checkbox"/> \$45.00	<input type="checkbox"/> N/A
Student and/or Postdoctoral Fellow Member (2013-2015)	N/A	N/A	<input type="checkbox"/> \$30.00	

(Students/post-docs please complete box on lower portion of form)

Life Member (Must be over 55) \$500.00

JOURNAL OF INTERFERON AND CYTOKINE RESEARCH

2013 Member Rates \$362.00 (USA Online Only) \$362.00 (Foreign Online Only)

TOTAL PAYMENT \$ _____

Online questions, contact the Publisher (Mary Ann Liebert) directly at (914) 740-2100.

To assure proper crediting of dues and processing of Journals, please remit dues promptly.

CREDIT CARD INFORMATION (PLEASE TYPE OR PRINT LEGIBLY)

American Express VISA Master Card Discover

Card Number _____ Name on Card _____

Expiration Date _____ 3 or 4 Digit CVV# _____

Authorized Signature _____

NOTE: Credit Card Charges will be processed by the Federation of American Society for Experimental Biology.

STUDENT/FELLOW MEMBERSHIP (PLEASE TYPE OR PRINT LEGIBLY)

I certify that _____ is a candidate for an advanced degree or a post-doctoral fellow in a field related to Interferon and Cytokine Research

Institution _____ Department _____

(Signature of applicant's major research advisor)

RECOMMENDATIONS FOR MEMBERSHIP

Name _____ Email address _____

Name _____ Email address _____

SPEEDBUMP

by Dave Coverly



Reproduced with permission
www.speedbump.com

REMEMBER TO **JOIN** THE CYTOKINE AND INTERFERON SOCIETY OR **RENEW** YOUR MEMBERSHIP FOR 2012 OR BEYOND (3 YEAR, 5 YEAR, LIFETIME (AGE 55+) AND STUDENT MEMBERSHIPS ARE AVAILABLE)

ISICR Memberships will be applied to the new Cytokine and Interferon Society at no additional cost

Signals

The logo for the International Society for Interferon & Cytokine Research (ISICR). It features the letters 'ISICR' in a bold, sans-serif font. The 'I' is a solid red triangle pointing downwards. The 'S' is filled with a pattern of red and blue diagonal lines. The 'I', 'C', and 'R' are solid blue. The 'I' and 'S' are connected at the top.

International Society for Interferon
& Cytokine Research

9650 Rockville Pike
Bethesda, MD 20814-3998
USA