

Signals

THE INTERNATIONAL CYTOKINE AND INTERFERON SOCIETY NEWSLETTER

IN THIS ISSUE:

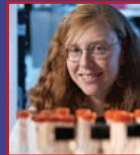
| | |
|---------------------|-----|
| Welcome New Members | p2 |
| ICIS Awards 2013 | p4 |
| In Memoriam | p13 |
| Happy Birthday | p32 |

SEPTEMBER 2013 | VOLUME 1 | NO. 2

2014 ICIS OFFICERS ELECTION RESULTS



President:
Richard Flavell
Yale University



Secretary:
Sarah Gaffen
University of Pittsburgh



Treasurer:
Karen Mossman
McMaster University

Future Meetings

2014 Meetings

Interleukin-6: Biology-
Pathophysiology-Therapy
May 14-17, 2014
Kiel, Germany

Cytokines2014
Oct. 26-29, 2014
Melbourne, Australia

Newsletter Editors

Howard Young
younghow@mail.nih.gov

Marta Catalfamo

Annette Khaled

ICIS
International Cytokine &
Interferon Society

WELCOME

NEW ICIS MEMBERS

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

Iannis Adamopoulos

Shriners Hosp
Sacramento, CA

Afsar Ahmed

Monash Inst of Med Research
Clayton, Victoria Australia

Dirk Baumjohan

Univ of California-San
Francisco
San Francisco, CA

Mandar Bawadekar

Univ of Piemonte Orientale
Novara, NO Italy

Partha Biswas

Univ of Pittsburgh
Pittsburgh, PA

Wojciech Blogowski

Pomeranian Medical Univ
Szczecin
Szczecin, Poland

Susan Carpenter

Univ of Massachusetts Medical
School
Worcester, MA

Rachel Caspi

NEI/NIH
Bethesda, MD

Cierra Casson

Univ of Pennsylvania
Philadelphia, PA

Sandra Clarke

Univ of Ontario Inst of Technol
Whitby, ON Canada

Heather Cohen

Univ of Maryland
College Park, MD

Taryn Cranford

Univ of South Carolina
Charlestown, SC

Angela Crawley

Ottawa Hosp Rsch Inst
Ottawa, ON Canada

Lue Dai

NCI/NIH/SAIC-Frederick
Frederick, MD

Vinh Dao

Univ of Texas Hlth Science Ctr-
San Antonio
San Antonio, TX

Jiehui Deng

Beckman Research Inst
Duarte, CA

Ning Du

NHLBI/NIH
Bethesda, MD

Kam Tai Dermawan

Cleveland Clinic Lerner
Research Institute
Cleveland, OH

Mayumi Fajita

Univ of Colorado School of
Medicine
Aurora, CO

Katja Finsterbusch

Helmholtz Ctr for Infection
Rsch
Braunschweig, Germany

Sandhya Ganesan

Univ of Massachusetts Medical
School
Worester, MA

Sarah Gonzales-van Horn

Univ of Texas Southwestern
Med Ctr
Dallas, TX

Murugaiyan Gopal

Brigham & Womens Hosp
Boston, MA

Daniel Green

NIAID/NIH
Bethesda, MD

Julia Green-Johnson

Univ of Ontario Inst of
Technology
Oshawa, ON

Elona Gusho

Cleveland Clinic
Cleveland, OH

Moritz Haneklaus

Trinity College Dublin
Dublin, Ireland

Miranda Hanson

NCI/NIH
Frederick, MD

Xiao He

Univ of Utah
Salt Lake City, UT

Julia Heinrich

Twincore
Hanover, Germany

Rana Herro

La Jolla Institute for Allergy and
Immunology
La Jolla, CA

Chew Choy Hoong

Univ Tunku Abdul Rahman
Kampar, Malaysia

Vivianty Hou

Fox Chase Cancer Ctr
Philadelphia, PA

Alan Hsu

Univ of Newcastle
Newcastle, NSW Australia

Meng-Ping Hsu

Univ of Sydney
Sydney, NSW Australia

Katie Hudson

Univ of Oklahoma Hlth Science
Ctr
Oklahoma City, OK

Zulfiqar Hussain

Albert Einstein College of
Medicine
Bronx, NY

Lei Jin

Albany Medical College
Albany, NY

Chase Johnson

NIAID/NIH
Bethesda, MD

Lara Kallal

Brown Univ
Providence, RI

WELCOME

NEW ICIS MEMBERS *continued*

Sheila Marie Keating

Blood Systems Research
Institute
San Francisco, CA

Chandra Kroll

Oklahoma Univ Health
Science Ctr
Oklahoma City, OK

Pawan Kumar

Univ of Pittsburgh
Pittsburg, PA

David Langlais

McGill Univ
Montreal, QC Canada

Larisa Labzin

Univ of Bonn
Bonn, Germany

Hoyong Lim

Univ of Texas at Houston
Houston, TX

Yijie Ma

Univ of Illinois-Chicago
Chicago, IL

Fabienne Mackay

Monash Inst of Med Research
Clayton, Victoria Australia

Shravan Madireddi

La Jolla Institute for Allergy and
Immunology
La Jolla, CA

Tanel Mahlakoiv

Univ of Freiburg
Freiburg, Germany

Katrin Mayer-Barber

NIAID/NIH
Bethesda, MD

Mandy McGeachy

Univ of Pittsburgh
Pittsburgh, PA

Amit Kumar Mehta

La Jolla Institute for Allergy and
Immunology
La Jolla, CA

Amina Metidji

NIAID/NIH
Bethesda, MD

Sharmila Nair

Helmholtz Center for Infection
Research
Braunschweig, Germany

Kalyan Nallaparaju

MD Anderson Cancer Ctr
Houston, TX

Judith Olejnik

Boston Univ
Boston, MA

Amiya Patra

Univ of Wuerzburg
Wuerzburg, Bavaria Germany

Michael Pattison

Univ of Dundee
Dundee, United Kingdom

Erik Peterson

Univ of Minnesota
Minneapolis, MN

Susan Quinn

Trinity College Dublin
Dublin, Ireland

Min Ren

NHLBI/NIH
Bethesda, MD

Estefania Rodriguez-Garcia

Center for Applied Med Rsch
(CIMA)
Pamplona, Navarra Spain

Derek Royer

Univ of Oklahoma Hlth Sci Ctr
Oklahoma City, OK

Fiamma Salerno

Sanquin Blood Research
Amsterdam, Netherlands

Soroush Sarvestani

Monash Inst of Medical Rsch
(MIMR)
Clayton, Melbourne Australia

Ali Abdul Sater

Univ of Toronto
Toronto, Canada

Johannes Schwerk

Helmholtz Ctr for Infection
Rsch
Braunschweig, Germany

Yingli Shang

Hosp for Special Surgery
New York, NY

Padmaja Shastri

Univ Ontario Inst of Tech
Oshawa, ON

Fang Shen

Janssen R&D
Radnor, PA

Hiba Sibaii

National Research Ctr
Cairo, Egypt

Pawan Singal

St. Boniface Hospital
Research Ctr
Winnipeg, Canada

Piotr Siupka

Aarhus Univ
AarhusC, Denmark

Ming-Hsun Tsai

National Taiwan Univ
Taipei, Taiwan

Lauren Vaughn

Univ of South Carolina
Columbia, SC

Edwin Chi Keung Wan

NHLBI/NIH
Bethesda, MD

Yaya Wang

Univ of Minnesota
Minneapolis, MN

Elvira Weber

Univ of Umea
Umea, Sweden

Elia Tait Wojno

Univ of Pennsylvania
Philadelphia, PA

Rui Dan Xie

Univ of Sydney
Camperdown, NSW Australia



**2013 ICIS
AWARD WINNER**
**THE MILSTEIN
AWARDS**

The Milstein Award

The Seymour & Vivian Milstein Award for Excellence in Interferon and Cytokine Research, commonly known as The Milstein Award, represents the pinnacle of scientific achievement in interferon and cytokine research. The Milstein Award is bestowed upon a leading biomedical research scientist(s) who has made outstanding contributions to interferon and cytokine research, either in a basic or applied field.



PAUL HERTZOG, PH.D.

**Centre Director
Centre for Innate Immunity and Infectious Diseases
NHMRC Senior Principal Research Fellow
Monash Institute of Medical Research**

Professor Paul Hertzog is an Australian who was educated at the University of Melbourne where he obtained his PhD in Biochemical Pathology studying the molecular basis of liver disease. He then undertook postdoc positions in cancer research, firstly in the USA at the Eppley Institute of Cancer Research in Omaha; then at the University of York in the UK. The latter period included a brief training program in monoclonal antibody production and use at the Basel Institute of Immunology, a technology that has both fuelled his interest in immunology and provided a technology to underpin his research moves. He moved back to Australia in the early 1980's to continue his research in cancer, its mechanisms and diagnosis and the effects of the recently cloned interferons. In the Biochemistry Department and the Centre for Molecular Biology and Medicine, he became interested in the molecular mechanisms of interferon action in host defence against not only cancers, but also infectious diseases. In 1991 he moved to the medical campus of Monash University in Clayton to a newly established Institute (now Monash Institute of Medical Research) to join Ismail Kola who was establishing gene targeting technology to generate knockout mice – a technology the promised, and indeed delivered on the ability to

characterise molecular function of a gene product in vivo in the whole animal, rather than in test tubes or cells. They utilised gene targeting technology to generate murine models to study the role of interferons, the immune response, features of Down syndrome, the ETS family of transcription factors, oxidative stress, newly discovered cytokines in collaboration with Smith Kline Beechem and Millenium. In subsequent years Paul's research interests have broadened to include the role of interferons in the context of innate immune signaling via pattern recognition receptors, the role of type I interferon receptors in signaling, negative regulation by SOCS proteins, characterization of our newly discovered interferon epsilon and a systems biology approach to the innate immune response. Paul has served on national and international grant review panels, editorial boards and committees of the ISICR. He convened the 2003 ISICR meeting in Cairns, Australia and will co-convene the 2014 ICIS meeting in Melbourne. He is founder of the Victorian Infection and Immunity Consortium, its' Industry Alliance Program and co-convenes the Lorne Infection and Immunity annual conference.

Dr. Hertzog is recognized for the discovery of IFN-epsilon.



**2013 ICIS
AWARD WINNER**
**THE MILSTEIN
AWARDS**



XIAOXIA LI, PH.D.

**Department of Immunology
Cleveland Clinic Foundation**

Dr. Xiaoxia Li received her Bachelor degree from Wuhan University in China and came to the United States for her doctoral training in 1983. She received a Ph.D. in Biochemistry, Molecular and Cell Biology from M.D. Anderson Cancer Center, University of Texas. She did post-doctoral training in Biochemistry and Molecular Biology with Dr. George Stark at the Cleveland Clinic, where she joined the Department of Immunology as Assistant Professor in 2001. She is currently a Full Professor in the in the Lerner Research Institute and Professor of Molecular Medicine at Cleveland Clinic Lerner College of Medicine. Dr. Li has authored over 100 peer-reviewed papers. During the last several years, the discoveries from her laboratory have illustrated many of the intricate and complex pathways that control innate and adaptive immunity. Her lab elucidated important signaling mechanisms governing how IL-1R-TLRs trigger the inflammatory response by coupling NFκB activation with posttranscriptional pathways to induce robust production of cytokines and chemokines. These studies provide significant insight into fundamental mechanisms regulating innate immunity and yield essential information for the selection of potential drug targets. In addition, her laboratory was one of two groups that discovered SIGIRR, a

member of the TLR family that provides negative regulatory function. This finding was extended to show that SIGIRR modulates intestinal inflammation/tumorigenesis by maintaining the microbial tolerance of the colonic epithelium and limiting the development of pathogenic Th17 cells. The study of SIGIRR provides a novel mechanism by which the mucosal surface responds to commensal flora and participates in innate and adaptive immune responses. Finally, Dr Li's laboratory was one of the groups that identified Act1 as a necessary signaling component in the IL-17 pathway. Using this she has made important contributions to understanding the molecular and cellular mechanisms that regulate the functions of IL-17 in vivo. For example, a variant of Act1 (D10N) has been linked to psoriasis susceptibility in humans and Dr. Li's laboratory has demonstrated that this molecular form is defective in its interaction with the molecular chaperone Hsp90, resulting in a global loss of function of Act1. This work thus demonstrates the molecular basis for the contribution of Act1 (D10N) in psoriasis and psoriatic arthritis.

Dr. Li is recognized for her discovery of novel genes implicated in immune signaling pathways.

**2013 ICIS
AWARD WINNER**
**THE MILSTEIN
AWARDS**



LEONIDAS PLATANIAS, M.D.

**Deputy Director of the Robert H. Lurie Comprehensive Cancer Center
Professor of Medicine
Lurie Family Professor of Oncology
Feinberg School of Medicine of Northwestern University.**

Dr. Platanias is originally from Athens, Greece and moved to the United States in 1984, after graduating from the University of Patras medical school. He initially worked at the National Institutes of Health (NIH) as a postdoctoral fellow in the Clinical Hematology Branch, researching the mechanisms of regulation of normal hematopoiesis bone marrow failure by cytokines. He completed his residency in Internal Medicine at the State University of New York, Downstate Medical Center in Brooklyn, New York, from 1986 until 1989. In 1989, he moved to Chicago as a clinical and research fellow in Hematology-Oncology at the University of Chicago. He worked there until 1992, and at that time he was introduced to the field of interferon and cytokine signaling. He established his own laboratory working on cytokine signaling pathways in malignant cells in 1992 at Loyola University Chicago. From 1996 until 2002 he was at the University of Illinois in Chicago (UIC), initially as Associate Professor and subsequently as Professor and Chief of the Division of Hematology-Oncology. In 2002 he became Deputy Director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University in Chicago and

Professor of Medicine and Lurie Family Professor of Oncology at the Feinberg School of Medicine of Northwestern University. Dr. Platanias's laboratory was the first to describe the activation of several non-Stat signaling cascades that play critical roles in the generation of IFN-responses, including pathways involving the Vav proto-oncogene and Crk-proteins; the p38 Map kinase pathway and the mTOR signaling cascade. Another aspect of his work is the therapeutic targeting of signaling cascades that promote leukemogenesis in chronic myeloid leukemia (CML) and acute myeloid leukemia (AML) and over the years has identified several signaling pathways and effectors that are deregulated in leukemic cells. Dr. Platanias has served and/or chaired several study sections and committees at NIH, the Department of Veterans Affairs and the Department of Defense. He has served as President of the International Society of Interferon and Cytokine Research (ISICR) from 2010-2011.

Dr. Plantanias is recognized for his fundamental contributions to defining signaling pathways in the IFN system.



**2013 ICIS
AWARD WINNER**
**HONORARY LIFETIME
MEMBERSHIP
AWARD**

Honorary Lifetime Membership Award

The Honorary Lifetime Membership Award is made to individuals who have made substantive contributions to the interferon/cytokine field over much of their careers, either in basic, clinical or applied research. Honorary members are the treasures of the society and provide us with an historical perspective and valued research tradition.



WARREN J. LEONARD, M.D.

NIH Distinguished Investigator
Laboratory of Molecular Immunology
National Heart, Lung, and Blood Institute

Warren Leonard received his A.B. in mathematics, magna cum laude and Phi Beta Kappa, from Princeton University in 1973 and his M.D. from Stanford University in 1977. After completing residency training in medicine at Barnes Hospital and a year of research in biochemistry at Washington University, Dr. Leonard came to the NIH as a postdoctoral fellow in the Metabolism Branch, National Cancer Institute in 1981. He began directing his own laboratory in the Cell Biology and Metabolism Branch, National Institute of Child Health and Human Development in 1985 and then joined the NHLBI in 1992. Dr. Leonard is the recipient of many honors and awards, including the American Federation for Clinical Research Foundation Outstanding Investigator Award, Food and Drug Administration Center for Biologics Evaluation and Research Outstanding Service Award, and American Association of Immunologists (AAI)-Huang Foundation Meritorious Career Award. Dr. Leonard has authored or coauthored more than 300 articles and book chapters and holds 19 patents. He is currently on the editorial board of Cytokine and is an Associate

Editor of International Immunology, an Associate Editor and former Co-Editor of Immunity, and a contributing member of the Faculty of 1000. Additionally, he is a Fellow of the American Association for the Advancement of Science and member of the American Society for Clinical Investigation and the Association of American Physicians. He is a Past-President of the International Cytokine Society, a member of the American Association of Immunologists, American Association for the Advancement of Science, and a member of the Board and former Vice President of the Foundation for Advanced Education in the Sciences.

Critical to proper development and orchestration of the cells that comprise the immune system are a number of intercellular signaling molecules, collectively known as cytokines, which act through multimeric receptors. Dr. Leonard's laboratory focuses on the biology, signaling, and molecular regulation of a key family of these cytokines, the interleukins, with studies ranging from basic molecular mechanisms to human disease.

**2013 ICIS
AWARD WINNER**
**HONORARY LIFETIME
MEMBERSHIP
AWARD**



OTTO HALLER, M.D.

**Professor
Former Director of the Department of Virology
University of Freiburg**

Dr. Haller did some early experimental work as a medical student in the laboratory of Jean Lindenmann (co-discoverer of interferon) at the Institute of Medical Microbiology of the University of Zürich in Switzerland. He was then accepted as a doctoral student, and, while working with Dr. Lindenmann, he became interested in genetically determined inborn resistance and host defense mechanisms against viruses and cancer cells. Later, he decided to study the newly described Natural Killer (NK) cells with Hans Wigzell at the Department of Immunology in Uppsala as a postdoctoral fellow and also worked in close collaboration with Rolf Kiessling at the Karolinska Institute in Stockholm, Sweden. This early work was recognized by the Research Award of the Swiss Society for Microbiology and the Swiss Cancer Prize in 1977. After additional postdoctoral years at the Department of Immunology and Virology in Zürich and at the Rockefeller University in New York, he became an Associate Professor of virology at the University of Zürich and eventually moved to Germany to head the Department of Virology at the University of Freiburg. Although he became involved with clinical and diagnostic virology as well as teaching, he devoted most of his time to the understanding of innate immune responses and how viruses subvert the interferon system. His major contribution is the identification and characterization of Mx proteins as large GTPases involved in host defense against a range of different RNA and DNA viruses. Mx proteins are effector molecules of the interferon-induced antiviral state and belong to the most highly inducible and potent antiviral restriction factors characterized to date.

Additional projects focused on the biology of influenza and influenza-like viruses as well as the characterization of viral

proteins as interferon antagonists subverting innate immunity. For these achievements, he was awarded the Latsis Prize of the Swiss National Science Foundation, the Aronson Research Award of the Land Berlin and the Milstein Award of ISICR. He served as Dean of the Medical Faculty of the University of Freiburg and as Vice Medical Director of the University Medical Center Freiburg. He was on many Scientific Advisory Boards in and outside Europe and was an elected reviewer of the German Research Foundation (DFG) for Medical Microbiology, Virology, Immunology, and Hygiene for eight years. He is an Editorial Board Member of Virology and was on the Editorial Board of The Journal of Biological Chemistry and The Journal of Virology among others. He contributed chapters on virology to textbooks for students, and the University of Freiburg recognized his commitment in educating students by awarding him the University Award for Excellence in Teaching. Dr. Haller was President of ISICR from 2006-2007 and was actively involved in initiating the merger of ISICR with the ICS. He is a Past-President of the German Society for Virology (GfV) and a Honorary Member of the European Society for Clinical Virology. Dr. Haller retired from his University position on Sept. 30, 2012 but is now active as a Member of the Board of Directors of the University Hospital Zürich, Switzerland, and is the first President of the European Society for Virology, which he helped to shape. Additionally he serves as a Member of the Scientific Advisory Board, Institut Pasteur of Shanghai of the Chinese Academy of Sciences, is a Member of the German Academy of Sciences Leopoldina and is involved in regular teaching activities at the Institut Pasteur in Paris and elsewhere.

2013 ICIS Awards

ICIS Distinguished Service Award:

Philip Milstein

Ed Leonard Prize for Chemotaxis/Chemokine Research:

Acharyya Swarnali

Dept of Cancer Biology and Genetics
Memorial Sloan Kettering Cancer Center
New York, NY

ICIS Young Investigator Award for Cytokine Research:

Mandy J McGeachy

Dept of Medicine
University of Pittsburgh
Pittsburgh, PA

ICIS Postdoctoral Investigator Award:

co- 1st Elia D Tait Wojno

Dept of Microbiology
University of Pennsylvania
Philadelphia, PA

co- 1st Amiya K Patra

Institute for Pathology
University of Wuerzburg
Wuerzburg, Bavaria, Germany

2nd Gareth W Jones

Institute of Infection and Immunity
Cardiff University
Cardiff, Wales, UK

3rd Dirk Baumjohann

Dept of Microbiology and Immunology
University of California, San Francisco
San Francisco, CA

ICIS Outstanding Scholar Award:

1st Jarod A Zepp

Dept of Immunology
Cleveland Clinic Foundation
Cleveland, OH

2nd Stephan Wilmes

Dept of Biology/Chemistry
University of Osnabrueck
Osnabrueck, Lower Saxony, Germany

3rd Heather B Cohen

Dept of Cell Biology and Molecular Genetics
University of Maryland
College Park, Maryland

Sidney & Joan Pestka Post-Graduate Award in Interferon Research

Sponsored by PBL Interferon Source:

Yaya Wang

Department of Medicine
University of Minnesota
Minneapolis, MN

Sidney & Joan Pestka Graduate Award in Interferon Research

Sponsored by PBL Interferon Source:

Angel Morrow

Cytokine Biology Section
NIAID, NIH
Bethesda, MD

Christina Fleischmann Award to Young Women Investigators:

Michaela Gack

Dept of Microbiology and Immunobiology
Harvard Medical School
Boston, MA

The Journal of Biological Chemistry/Herbert Tabor Young Investigator Award:

Ludmila Prokunina-Olsson

Investigator
Laboratory of Translational Genomics
Division of Cancer Epidemiology and Genetics
National Cancer Institute

Milstein Young Investigator Award:

David Langlais

Dept. of Biochemistry
McGill University
Montreal, Canada

Hilario J Ramos

Department of Immunology
University of Washington
Seattle, WA

John W Schoggins

Department of Microbiology
UT Southwestern Medical Center
Dallas, TX

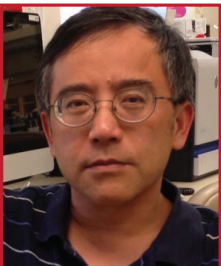
New Member MINIBIOs



Iannis E Adamopoulos, BSc(Hons), M.Phil, D.Phil

Assistant Professor of Medicine
University of California at Davis

Dr. Adamopoulos received his BSc (Hons) degree in Microbiology from the University of Surrey and an MPhil research degree in growth factor cell signaling from University College London, (UCL) in the UK. In 2003 he awarded a DPhil scholarship to study the effect of growth factors and pro-inflammatory cytokines in the progression of arthritis at Wolfson College, University of Oxford. His work identified RANKL-independent osteoclastogenesis pathways in inflammatory arthritis. He continued his research on cytokines and autoimmune diseases at the Merck Research Laboratories (formerly DNAX, Palo alto, USA) in the laboratory of Dr Bowman, where he worked on the IL-23/IL-17 axis and alternative osteoclast differentiation pathways. In 2010 he joined the University of California at Davis, Division of Rheumatology, Allergy and Clinical Immunology where he is currently an Assistant professor. Adamopoulos was recognized in 2011 as an Arthritis National Research Foundation Scholar and a Sontag Foundation Fellow. Dr Adamopoulos and his research team at UC Davis are investigating the effect of cytokines in activating novel molecular pathways of osteoclast activation and bone destruction. This work will help to design treatments and therapeutic strategies for inflammatory arthritis and immune bone loss.



Dr. Xiao He

Research Assistant Professor
University of Utah

Dr. Xiao He obtained his medical education at Chongqing Medical University, China. After finishing his master degree in immunology at Shanghai Medical University, he received his Ph.D. in immunology from the College of Medicine at Drexel University.

His postdoctoral training began in Dr. Matt Thomas' laboratory at Washington University at St. Louis where he studied the role of tyrosine phosphatases in TCR initiated signal transduction. Subsequently, during his second postdoctoral training with Dr. Dietmar Kappes at Fox Chase Cancer Center, he identified the transcription factor, zbtb7b/ThPOK, as a key regulator in CD4 versus CD8 T cell lineage commitment.

He joined the Division of Microbiology and Immunology at the University of Utah's School of Medicine Department of Pathology as a Research Assistant Professor in 2006. He continues to do basic research on T cell development and function and expands his study on disease-centered research, such as type-1 diabetes and other autoimmune diseases.

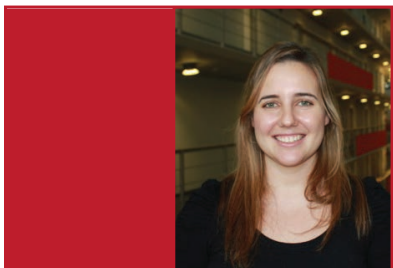
New Member MINIBIOs *continued*



Dr. Sheila Keating

Blood Systems Research Institute
San Francisco, CA

Dr. Sheila Keating received her BA in Biology from the College of the Holy Cross (Worcester, MA), an MSPH in Tropical Medicine from Tulane University (New Orleans, LA), and in 2006, completed her PhD studying immune responses to malaria vaccines from the laboratory of Prof. Adrian Hill at the Weatherall Institute for Molecular Medicine at Oxford University (Oxford, UK). Her postdoctoral research was at the Institute of Child Health in London investigating pneumococcal-specific memory B cell responses in the elderly with Drs. David Goldblatt and Helen Baxendale. Since 2008 she has been head of the Core Immunology Department under the direction of Philip Norris and Michael Busch at the Blood Systems Research Institute, San Francisco. Dr. Keating's research focus is on studying immune responses to vaccines and infectious diseases. This work has provided her with the foundation for investigating soluble biomarkers in a number of different diseases including HIV, HBV and HCV. At BSRI, Dr. Keating and her colleagues are studying cytokines, chemokines, growth factors, cardiac and metabolic markers in the context of chronic HIV infection as part of the Women's Interagency HIV Study (WIHS). She is particularly interested in the development of systemic co-morbidities of chronic inflammation including HIV-associated neurocognitive dysfunction and cardiac-pathogenesis.



Larisa Labzin

University of Bonn

Larisa Labzin is originally from Australia and received her bachelor's degree from the University of Queensland in 2007, after completing her honours thesis in the laboratory of Matt Sweet. She is now a 3rd year PhD student with Eicke Latz at the Institute of Innate Immunity at the University of Bonn, Germany. Her PhD research focuses on the interplay between metabolism and innate immunity, in particular the anti-inflammatory properties of high-density lipoprotein (HDL) in macrophages. She aims to decipher the molecular mechanisms by which HDL inhibits the expression of pro-inflammatory cytokines such as IL-6 and IL-12 and thus better understand the protective effect of HDL in inflammatory diseases.

New Member MINIBIOs *continued*



Prof. Pawan K. Singal, Ph.D., D.Sc.

Director of the Institute of Cardiovascular Sciences, St. Boniface Hospital

Dr. Singal is a Professor of Physiology and is Director of the Institute of Cardiovascular Sciences, St. Boniface Hospital and the University of Manitoba, Winnipeg, Canada. Dr. Singal completed his B.Sc. Hons (1968) and M.Sc. in Biophysics (1970) from Punjab University, India; Ph.D. in Physiology in 1974 from the University of Alberta. After 3 years in Saskatoon, Canada, as a Post-Doctoral Fellow of the Medical Research Council, Dr. Singal joined the Physiology Department at the University of Manitoba as a lecturer, rose through the ranks and has been a professor since 1990. He received a D.Sc. degree in 1994 in Cardiovascular Pathophysiology. He served as Associate Dean for the Faculty of Graduate Studies, University of Manitoba. He is also holder of the Naranjan S. Dhalla Chair established by the St. Boniface Hospital & Research Foundation.

Internationally known for his work on oxidative stress and heart failure, Dr. Singal has made significant contributions in our understanding of the role of cytokines in the sequelae of heart failure due to doxorubicin, chronic pressure overload as well as myocardial infarction. He has published 250 papers, has co-edited 27 books and trained more than 100 students, fellows and visiting scientists. He has been the recipient of more than one million dollars in competitive scholarships and career awards as well as more than 10 million dollars in research grants over a period of 20 years from different agencies including the Heart and Stroke Foundation, Medical Research Council and Canadian Institute for Health Research. He has received more than 60 national and international recognitions. The University of Manitoba has established an award in his name called 'Pawan K. Singal Award for Graduate Students in Cardiovascular Sciences'. His name has been added to the Wall of Fame in the University Centre at the University of Manitoba recognizing his outstanding teaching skills and research.

MEETING APP IS AVAILABLE



Don't forget to download the mobile app, CYTOKINES2013, available in both Apple and Android formats. The use this year will impact on future meeting app availability.

In Memoriam

Charles Chany

1920-2013



Charles was born in 1920 in Budapest, Hungary. The 2nd World War was a very difficult time for him as he was deported to the labor camp in the salt mines in Bor in Jugoslavia; he was one of few who survived. At the end of the war he choose to stay in France for the rest of his life.

He went to Medical School in Paris and after finishing his degree, he chose to study viruses. He was a trainee at the Institute Pasteur in the laboratory of Professor Pierre Lépine and at the same time he was also associated with the Department of Pediatrics in the hospital St Vincent de Paul. He was the first to isolate adenoviruse in France (1955-56) and then spent one year in the laboratory of Dr. Wallace Rowe (discoverer of Adenovirus) at the National Institutes of Health (NIH) in Bethesda, MD.

After his return to France, he started his own laboratory at the hospital St Vincent Paul. Here Charles isolated the first Parainfluenza 3 virus in France and he described the phenomenon of autointerference for this virus. He and his collaborators described the first epidemics of respiratory syncytial virus and adenovirus in France. In his Thesis of Medicine, he described for the first time the pulmonary lesions caused by adenovirus infection.

After those studies, his work was mainly focused on interferon. Together with Ion Gresser, Jacqueline and Edward de Maeyer and Rebecca and Ernesto Falcoff, he was part of the leadership of interferon research in France. Charles was responsible for organizing a very successful Interferon meeting in Portugal in 1973.

His research group focused on different aspects in the IFN field. Among other findings, they showed an inhibitory effect of interferon on the oncogenic properties of polyoma virus and demonstrated the phenotypical reversion of Moloney virus-MSV transformed cells as a result of interferon treatment. Another significant contribution to the interferon field was the development and the use of the human- mouse hybrid cells.

Using these hybrid cells, Charles, together with J de Grouchy, mapped the human Type I interferon genes to chromosome 9. Another interesting finding reported by Charles was the existence of spontaneous interferon production in the placenta during pregnancy.

Charles also made significant clinical contributions outside the Interferon system. Together with the team of Pierre Tiollais, who had cloned the genome of the hepatitis B virus (HBV), they expressed the S antigen of Hepatitis B virus in vitro. This work lead to the development of the current HBV vaccine. After retirement, Charles donated his royalties from the patent of the HBV vaccine to the University of Paris 5 and installed there a laboratory where he, with his wife Françoise Chany Fournier, continued to study natural inhibitors that are able to regulate interferon action in vivo.

Collectively, Charles' initial work contributed to the development of medical virology and his later work resulted in seminal contributions in interferon research. The laboratory which he created at the hospital Saint Vincent de Paul continues to function, now at the Cochin hospital. In addition to his hospital work and his research, Charles also conveyed his interest in interferon research to several generations of medical students and he trained a great number of graduate students. His talks on interferon were always met with great enthusiasm and generated many questions from the audience. He leaves us with the memory of an impassioned researcher, kind teacher and generous man.

Pierre Lebon
Université Paris Descartes, France

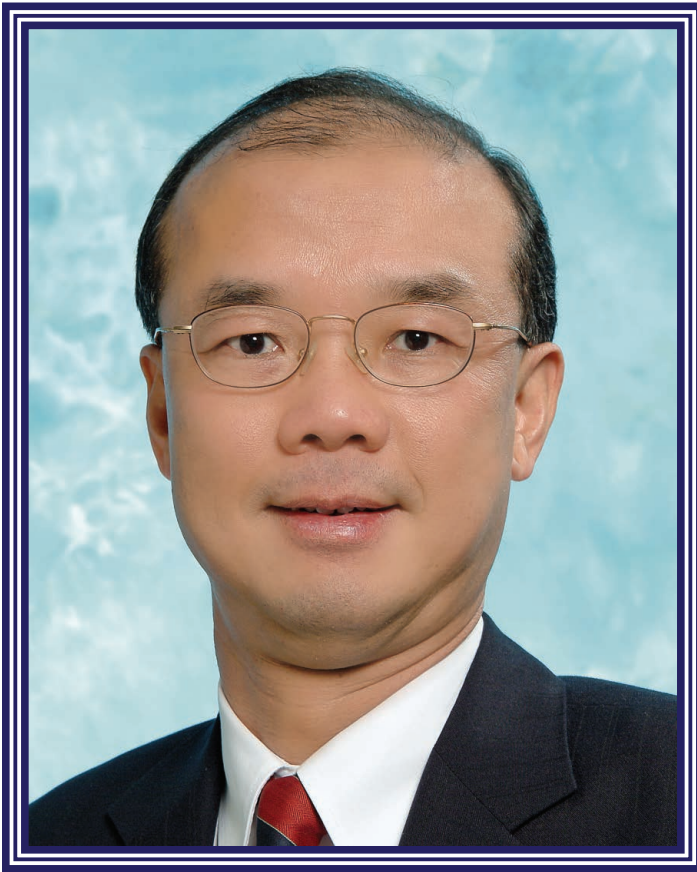
In Memoriam

By Bryan Williams, Monash Institute

Allan SY Lau

1952-2013

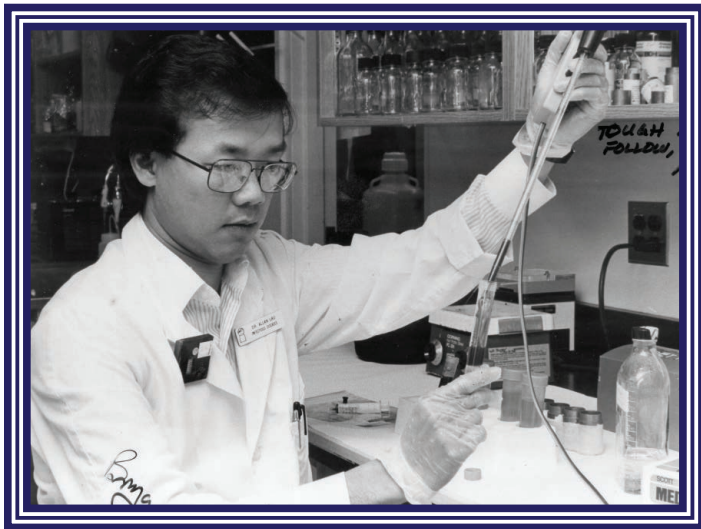
A dedicated interferon and cytokine biologist and infectious disease physician



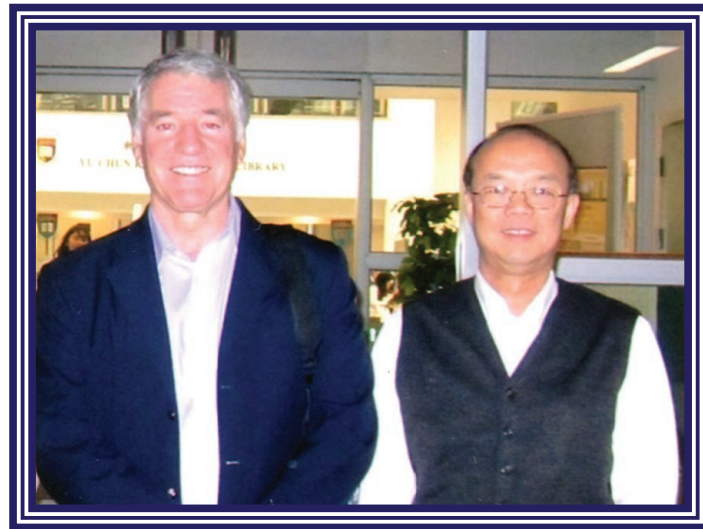
To the shocked surprise of many of his overseas colleagues Allan Lau passed away after a battle with lung cancer on April 21st.

He had never smoked. Allan kept his illness to himself and continued working until his final hospitalization. The loss of a fine colleague at the young age of 61 is hard to come to terms with. His faculty and students treasured him, as a wonderful clinician scientist, teacher and a fine human being. To me he was a loyal, caring, considerate colleague and friend. Allan was born and grew up in Hong Kong, finishing high school before moving to Canada to complete an undergraduate degree at McGill University. He was admitted to Medical School at McGill and completed an MD in the Faculty of Medicine in 1980. It was at McGill that he met and married Maureen, a microbiology graduate and fellow Hong Kong expatriate. From 1980 until 1982 Allan completed a residency in Pediatrics at UCSF before returning to Canada. There he undertook training in Infectious Diseases at the University of Toronto, Hospital for Sick Children, gaining a FRCP specialisation in 1985. It was during this period that I first met Allan and convinced him to undertake his research training in my laboratory. He already had significant laboratory experience and was awarded a Medical Research Council of Canada Fellowship in Immunobiology to study interferons and their receptors. It was clear to me from the outset that Allan was a hardworking and talented researcher. One of the first papers we published together appeared in the Journal of Clinical Investigation (JCI) in 1986 and described the expression of IFN receptors in cells treated with IFN in vitro and in vivo in children with leukemia (1). These studies guided the timing of the clinical dosing of IFNs, avoiding receptor down-regulation. Interestingly, I remember at the time Allan's insistence that the paper was submitted to JCI rather than my preference JBC. He was right and it changed my natural prejudice to what I had, up until that time considered, a light-weight clinical journal! In total we published 6 papers together over the next few years including another article in JCI.

In Memoriam continued



Allan, Hospital for Sick Children, 1986



Allan Lau and Bryan Williams, Hong Kong University, 2010

In 1986, the year he was awarded the Royal College of Physicians, Canada Infectious Disease Young Investigator Award, Allan was appointed Assistant Professor in the Department of Pediatrics, Hospital for Sick Children, and Department of Microbiology, University of Toronto. He set up his laboratory adjacent to mine and began a lifelong interest in IFN, TNF and cytokine signaling in macrophages during infection with different agents, including HIV, TB, and Influenza. In 1992 Allan was recruited to the University of California San Francisco as an Associate Professor in the Department of Pediatrics. This was essentially a research position as Allan did not bother with US clinical accreditation, but rather practiced on an academic license, which left him substantial protected research time. During the 9 years he was in San Francisco his research thrived and he contributed important insights into the regulation of cytokine production. Among these was the discovery that by manipulation of signaling pathways in different cell lines, production of significant natural type I IFNs and other cytokines could be realized. This led to the establishment of GeneTrol Biotherapeutics in 1997, with a proprietary technology platform, based on Allan's discoveries. Bob Lehman (Stanford University) and I served on the Scientific Advisory Board chaired by Allan. This was an exciting time buoyed by Allan's unbounded enthusiasm and supported by a fine cadre of biotechnologists. Unfortunately, despite our best efforts the technology bubble-burst led to the company being closed and assets transferred to another biotech in 2002.

Allan was offered the opportunity to relocate back to his birthplace, Hong Kong by an offer of a position in the Department of Pediatrics, University of Hong Kong. This was an attractive offer as the new Vice Chancellor of the University was a colleague from Toronto, Lap-Chee Tsui. Allan had a keen interest in Chinese culture and was particularly interested in traditional Chinese medicine (TCM). The new position offered an opportunity for him to actively explore the relationship between TCM and cytokines, an uncharted territory. This resulted in a string of patents and a number of papers from his laboratory describing active pure compounds from TCM. The success stimulated Allan's son Jonathan to pursue a PhD in this area after completing his undergraduate studies at the University of British Columbia. At the same time more conventional areas of work were pursued, as evidenced by a paper published last year in PNAS from a graduate student Howard Yim, now a post-doctoral fellow in my lab. Howard is the second student after Sandy Der, (a former ISICR Young Investigator awardee), that Allan has trained and I have benefitted from. Allan served on the ISICR Meetings Committee for a number of years and was a current member of the ISICR Publications Committee. His students and post-doctoral fellows regularly present at the annual ISICR/ICS meetings.

Allan was a generous, caring and considerate individual. He was a fine mentor and established a hardworking and dedicated laboratory. He could be quite conspiratorial but very amusing when discussing competitors. He was a terrific host and loved to arrange visits to his favourite tailor in Hong Kong. We will all miss his cheery smiling, backslapping greetings and of course his science.

REVIEWS OF INTEREST



Atan R, Crosbie DC, Bellomo R. **Techniques of extracorporeal cytokine removal: a systematic review of human studies.** *Ren Fail.* 2013 Jul 19. [Epub ahead of print]

Cox MA, Kahan SM, Zajac AJ. **Anti-viral CD8 T cells and the cytokines that they love.** *Virology* 435 (1):157-169, 2013

Hasselbalch HC. **The role of cytokines in the initiation and progression of myelofibrosis.** *Cytokine & Growth Factor Rev.* 24(2):133-145, 2013

Heim MH. **25 years of interferon-based treatment of chronic hepatitis C: an epoch coming to an end.** *Nat Rev Immunol.* 2013 Jun. doi: 10.1038/nri3463

Kumar P, Chen K, Kolls JK. **Th17 cell based vaccines in mucosal immunity.** *Curr Op in Immunol.* 25(3): 373-380, 2013

Mills KHG, Dungan LS, Jones SA, Harris J. **The role of inflammasome-derived IL-1 in driving IL-17 responses.** *J Leukoc Biol.* 93:489-497, 2013

Le H, Kim W, Kim J, Cho HR, Kwon B. **Interleukin-33: a mediator of inflammation targeting hematopoietic stem and progenitor cells and their progenies.** *Front Immunol.* 2013 May, doi:10.3389

Levick SP, Goldspink PH. **Could interferon-gamma be a therapeutic target for treating heart failure?** *Heart Fail Rev.* Apr 16, 2013.

Liao W, Lin JX, Leonard WJ. **Interleukin-2 at the Crossroads of Effector Responses, Tolerance, and Immunotherapy.** *Immunity,* 38 (1):13-25, 2013

Liu X, Fang L, Guo TB, Mei H, Zhang JZ. **Drug targets in the cytokine universe for autoimmune disease.** *Trends in Immunol.* 34(3):120-128, 2013

Owen JL, Mohamadzadeh M. **Macrophages and chemokines as mediators of angiogenesis.** *Front Physiol.* 4:159, 2013.

Quintas-Cardama A, Verstovsek S. **Molecular Pathways: JAK/STAT Pathway: Mutations, Inhibitors, and Resistance.** *Clinical Cancer Res.* 19 (8):1933-1940, 2013

Rutz S, Eidschenk C, Ouyang WJ. **IL-22, not simply a Th17 cytokine.** *Immunol Rev,* 252: 116-132, 2013

Schulte W, Bernhagen J, Bucala R. **Cytokines in sepsis: potent immunoregulators and potential therapeutic targets-an updated view.** *Mediators Inflamm.* 2013; doi: 10.1155/2013/165974. Epub Jun 18, 2013

Ye S, Wu J, Zhou L, Lv Z, Xie H, Zheng S. **Interleukin-35: The Future of Hyperimmune-Related Diseases?** *J Interferon & Cytokine Res.* 33(6): 285-291, 2013.

Zheng Y, Li H, Yu J, Zhao H, Wang SE, Ren X. **Interferon-λs: Special Immunomodulatory Agents and Potential Therapeutic Targets.** *J Innate Immun.* 5:209-218, 2013



The ArrayExpress Archive of Functional Genomics Data

<http://www.ebi.ac.uk/arrayexpress>

The ArrayExpress Archive of Functional Genomics Data is one of three international functional genomics public data repositories, alongside the Gene Expression Omnibus at NCBI and the DDBJ Omics Archive, supporting peer-reviewed publications. It accepts data generated by sequencing or array-based technologies and currently contains data from almost a million assays, from over 30 000 experiments. The proportion of sequencing-based submissions has grown significantly over the last 2 years and has reached, in 2012, 15% of all new data. All data are available from ArrayExpress in MAGE-TAB format, which allows robust linking to data analysis and visualization tools, including Bioconductor and GenomeSpace. Additionally, R objects, for microarray data, and binary alignment format files, for sequencing data, have been generated for a significant proportion of ArrayExpress data.

BioGPS

<http://biogps.org>

BioGPS is a free extensible and customizable gene annotation portal, a complete resource for learning about gene and protein function. BioGPS was created as a centralized gene portal for aggregating distributed gene annotation resources, emphasizing community extensibility and user customizability. BioGPS serves as a convenient tool for users to access known gene-centric resources, as well as a mechanism to discover new resources that were previously unknown to the user.

Bookshelf

<http://www.ncbi.nlm.nih.gov/books>

Bookshelf is a full-text electronic literature resource of books and documents in life sciences and health care at the National Center for Biotechnology Information (NCBI). Created in 1999 with a single book as an encyclopedic reference for resources such as PubMed and GenBank, it has grown to its current size of > 1300 titles. Unlike other NCBI databases, such as GenBank and Gene, which have a

strict data structure, books come in all forms; they are diverse in publication types, formats, sizes and authoring models. The Bookshelf data format is XML tagged in the NCBI Book DTD (Document Type Definition), modeled after the National Library of Medicine journal article DTDs. The book DTD has been used for systematically tagging the diverse data formats of books, a move that has set the foundation for the growth of this resource. Books at NCBI followed the route of journal articles in the PubMed Central project, using the PubMed Central architectural framework, workflows and processes. Through integration with other NCBI molecular databases, books at NCBI can be used to provide reference information for biological data and facilitate its discovery.

CellLineNavigator: a workbench for cancer cell line analysis

<http://www.medicalgenomics.org/celllinenavigator>

The CellLineNavigator database is a web-based workbench for large scale comparisons of a large collection of diverse cell lines. It aims to support experimental design in the fields of genomics, systems biology and translational biomedical research. Currently, this compendium holds genome wide expression profiles of 317 different cancer cell lines, categorized into 57 different pathological states and 28 individual tissues. To enlarge the scope of CellLineNavigator, the database was furthermore closely linked to commonly used bioinformatics databases and knowledge repositories. To ensure easy data access and search ability, a simple data and an intuitive querying interface were implemented. It allows the user to explore and filter gene expression, focusing on pathological or physiological conditions. For a more complex search, the advanced query interface may be used to query for (i) differentially expressed genes; (ii) pathological or physiological conditions; or (iii) gene names or functional attributes, such as Kyoto Encyclopaedia of Genes and Genomes pathway maps. These queries may also be combined. Finally, CellLineNavigator allows additional advanced analysis of differentially regulated genes by a direct link to the Database for Annotation, Visualization and Integrated Discovery (DAVID) Bioinformatics Resources.

CiteAb: The Antibody Search Engine

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

CiteAb is the largest citation-ranked antibody search engine, regularly updated with new antibodies and citations. We list more than 700,000 antibodies from 50 companies, along with publications that cite them. We feel that citations are the best guide to whether an antibody is likely to work in your laboratory, they are independent and easily verifiable. CiteAb is independent and ranks entirely by citations, nobody can pay to be top ranked...

The more publications that are submitted to CiteAb the more useful it will be to the research community. Submitting your publication will also increase the profile of your work. Citation information can easily be added using our online submission tool.

We want to list your antibodies. We are happy to list any primary antibodies, there is no charge for listing and we only require a simple data file from you. If you would like to list your antibodies then please get in touch.

CiteAb is based in the beautiful city of Bath, UK. CiteAb was founded by Dr Andrew Chalmers in the Department of Biology and Biochemistry at the University of Bath and is run as a collaborative project between the University of Bath and Storm Consultancy.

We are very grateful to everybody at the University of Bath that helped in setting up CiteAb. In particular the Research Development and Support Office and the Department of Enterprise and Knowledge Exchange who have provided funding and support. We want to thank the antibody companies, Xenbase and all our users for providing data.

No Guarantees. We hope CiteAb can help you start the process of finding the right antibody, but a condition of use is that we offer no guarantees that an antibody will work in your laboratory and are not liable should an antibody fail to work. CiteAb is for research antibodies only.

Clinical Connection

<http://www.clinicalconnection.com/Default.aspx>

We Bring Clinical Trials to YOU! ClinicalConnection.com connects its 400,000+ members with clinical research trials. Join now to be notified when new clinical trials are available.

Clone DB: an integrated NCBI resource for clone-associated data

<http://www.ncbi.nlm.nih.gov/clone/>

The National Center for Biotechnology Information (NCBI) Clone DB is an integrated resource providing information about and facilitating access to clones, which serve as valuable research reagents in many fields, including genome sequencing and variation analysis. Clone DB represents an expansion and replacement of the former NCBI Clone Registry and has records for genomic and cell-based libraries and clones representing more than 100 different eukaryotic taxa. Records provide details of library construction, associated sequences, map positions and information about resource distribution. Clone DB is indexed in the NCBI Entrez system and can be queried by fields that include organism, clone name, gene name and sequence identifier. Whenever possible, genomic clones are mapped to reference assemblies and their map positions provided in clone records. Clones mapping to specific genomic regions can also be searched for using the NCBI Clone Finder tool,

which accepts queries based on sequence coordinates or features such as gene or transcript names. Clone DB makes reports of library, clone and placement data on its FTP site available for download. With Clone DB, users now have available to them a centralized resource that provides them with the tools they will need to make use of these important research reagents.

DIANA-LncBase: experimentally verified and computationally predicted microRNA targets on long non-coding RNAs

www.microrna.gr/LncBase

Recently, the attention of the research community has been focused on long non-coding RNAs (lncRNAs) and their physiological/pathological implications. As the number of experiments increase in a rapid rate and transcriptional units are better annotated, databases indexing lncRNA properties and function gradually become essential tools to this process. Aim of DIANA-LncBase is to reinforce researchers' attempts and unravel microRNA (miRNA)-lncRNA putative functional interactions. This study provides, for the first time, a comprehensive annotation of miRNA targets on lncRNAs. DIANA-LncBase hosts transcriptome-wide experimentally verified and computationally predicted miRNA recognition elements (MREs) on human and mouse lncRNAs. The analysis performed includes an integration of most of the available lncRNA resources, relevant high-throughput HITS-CLIP and PAR-CLIP experimental data as well as state-of-the-art in silico target predictions. The experimentally supported entries available in DIANA-LncBase correspond to > 5000 interactions, while the computationally predicted interactions exceed 10 million. DIANA-LncBase hosts detailed information for each miRNA-lncRNA pair, such as external links, graphic plots of transcripts' genomic location, representation of the binding sites, lncRNA tissue expression as well as MREs conservation and prediction scores.

PhosphoNET: Human Phospho-Site Knowledge Base

<http://www.phosphonet.ca/>

PhosphoNET is an open-access, online resource developed by Kinexus Bioinformatics Corporation to foster the study of cell signalling systems to advance biomedical research in academia and industry. PhosphoNET is the world's largest repository of known and predicted information on human phosphorylation sites, their evolutionary conservation and the identities of protein kinases that may target these sites. PhosphoNET presently holds data on over 950,000 known and putative phosphorylation sites (P-sites) in over 23,000 human proteins that have been collected from the scientific literature and other reputable websites. Over 19% of these

phospho-sites have been experimentally validated. The rest have been predicted with a novel P-Site Predictor algorithm developed at Kinexus with academic partners at the University of British Columbia and Simon Fraser University.

With the PhosphoNET Evolution module, this website also provides information about cognate proteins in over 20 other species that may share these human phospho-sites. This helps to define the most functionally important phospho-sites as these are expected to be highly conserved in nature.

With the Kinase Predictor module, listings are provided for the top 50 human protein kinases that are likely to phosphorylate each of these phospho-sites using another proprietary kinase substrate prediction algorithm developed at Kinexus. Our kinase substrate predictions are based on deduced consensus phosphorylation site amino acid frequency scoring matrices that we have determined for each of ~500 different human protein kinases. The specificity matrices are generated directly from the primary amino acid sequences of the catalytic domains of these kinases, and when available, have proven to correlate strongly with substrate prediction matrices based on alignment of known substrates of these kinases. The higher the score, the better the prospect that a kinase will phosphorylate a given site. Over 30 million kinase-substrate phospho-site pairs are quantified in PhosphoNET.

PTMcode: a database of known and predicted functional associations between post-translational modifications in proteins

<http://ptmcode.embl.de>

Post-translational modifications (PTMs) are involved in the regulation and structural stabilization of eukaryotic proteins. The combination of individual PTM states is a key to modulate cellular functions as became evident in a few well-studied proteins. This combinatorial setting, dubbed the PTM code, has been proposed to be extended to whole proteomes in eukaryotes. Although we are still far from deciphering such a complex language, thousands of protein PTM sites are being mapped by high-throughput technologies, thus providing sufficient data for comparative analysis. PTMcode aims to compile known and predicted PTM associations to provide a framework that would enable hypothesis-driven experimental or computational analysis of various scales. In its first release, PTMcode provides PTM functional associations of 13 different PTM types within proteins in 8 eukaryotes. They are based on five evidence channels: a literature survey, residue co-evolution, structural proximity, PTMs at the same residue and location within PTM highly enriched protein regions (hotspots). PTMcode is presented as a protein-based searchable database with an interactive web interface providing the context of the co-regulation of nearly 75 000 residues in > 10 000 proteins.

SwissRegulon, a database of genome-wide annotations of regulatory sites

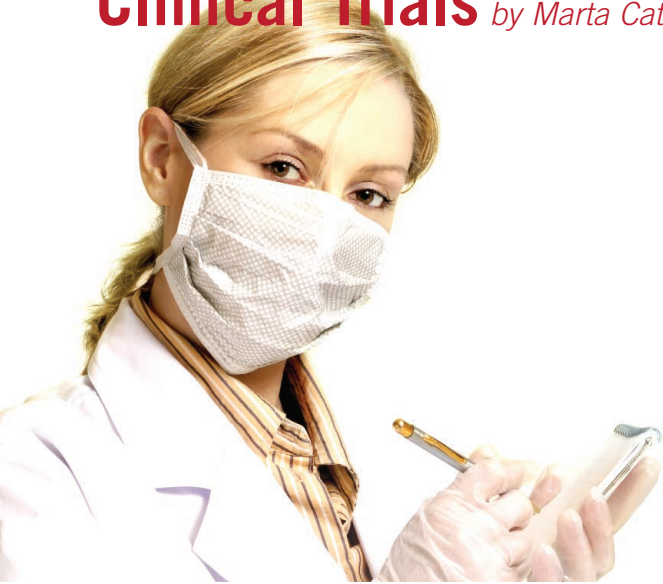
<http://swissregulon.unibas.ch>

Identification of genomic regulatory elements is essential for understanding the dynamics of cellular processes. This task has been substantially facilitated by the availability of genome sequences for many species and high-throughput data of transcripts and transcription factor (TF) binding. However, rigorous computational methods are necessary to derive accurate genome-wide annotations of regulatory sites from such data. SwissRegulon is a database containing genome-wide annotations of regulatory motifs, promoters and TF binding sites (TFBSs) in promoter regions across model organisms. Its binding site predictions were obtained with rigorous Bayesian probabilistic methods that operate on orthologous regions from related genomes, and use explicit evolutionary models to assess the evidence of purifying selection on each site. New in the current version of SwissRegulon is a curated collection of 190 mammalian regulatory motifs associated with similar to 340 TFs, and TFBS annotations across a curated set of similar to 35 000 promoters in both human and mouse. Predictions of TFBSs for *Saccharomyces cerevisiae* have also been significantly extended and now cover 158 of yeast's similar to 180 TFs. All data are accessible through both an easily navigable genome browser with search functions, and as flat files that can be downloaded for further analysis.

YM500

<http://ngs.ym.edu.tw/ym500/>

YM500 is an integrative database containing analysis pipelines and analysis results for 609 human and mice smRNA-seq results, including public data from the Gene Expression Omnibus (GEO) and some private sources. YM500 collects analysis results for miRNA quantification, for isomiR identification (incl. RNA editing), for arm switching discovery, and, more importantly, for novel miRNA predictions. Wetlab validation on > 100 miRNAs confirmed high correlation between miRNA profiling and RT-qPCR results ($R = 0.84$). This database allows researchers to search these four different types of analysis results via our interactive web interface. YM500 allows researchers to define the criteria of isomiRs, and also integrates the information of dbSNP to help researchers distinguish isomiRs from SNPs. A user-friendly interface is provided to integrate miRNA-related information and existing evidence from hundreds of sequencing datasets. The identified novel miRNAs and isomiRs hold the potential for both basic research and biotech applications.



Hu Mik-Beta-1 (anti-CD122, IL-2 receptor beta) to Treat HTLV-1-Associated Myelopathy/Tropical Spastic Paraparesis

Principal Investigator: Steven Jacobson, Ph.D. National Institute of Neurological Disorders and Stroke (NINDS), NIH.

Contact: Steven Jacobson, Ph.D.

Phone: (301) 496-0519

jacobsons@mail.nih.gov

ClinicalTrials.gov Identifier: NCT00076843

Safety and Tolerability of Intravenous Dose of MEDI-546 (anti-IFN- α receptor) in Japanese Subjects With Systemic Lupus Erythematosus

Principal Investigator: Stephen Yoo, MD. MedImmune LLC

Contact: AstraZeneca Clinical Study Information.

Phone: 800-236-9933

information.center@astrazeneca.com

ClinicalTrials.gov Identifier: NCT01559090

Interferon Alfa Sensitivity in HIV/HCV Persons Before and After HIV Meds

Principal Investigator: David L Thomas, MD, MPH. Infectious Diseases, Johns Hopkins University

Contact: Rosie Silva.

Phone: 410-502-7134

rsilva6@jhmi.edu

ClinicalTrials.gov Identifier: NCT01285050

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

Principal Investigator: Frank Maldarelli, M.D. National Cancer Institute (NCI)

Contact: Frank Maldarelli, M.D. Phone: (301) 435-8019

fmali@mail.nih.gov

ClinicalTrials.gov Identifier: NCT01295515

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.

Contact: Kristy Scott, BS.

Phone: 434-982-6714

ks4ww@hscmail.mcc.virginia.edu

ClinicalTrials.gov Identifier: NCT00977145

Effects of Interferon-gamma on Sepsis-induced Immunoparalysis

Principal Investigator: Peter Pickkers, MD, PhD. Radboud University. Nijmegen, Netherlands.

Contact: Peter Pickkers, MD, PhD.

Phone: 0031-24-362378

P.Pickkers@ic.umcn.nl

ClinicalTrials.gov Identifier: NCT01649921

Consequences of Anti-interleukin 6 Immunotherapy Treatment for Rheumatoid Arthritis on Periodontium (ParoPAR)

Principal Investigator: Assem SOUEIDAN, PhD. Nantes University Hospital. Nantes. France.

Contact: Assem SOUEIDAN, PhD

assem.soueidan@chu-nantes.fr

ClinicalTrials.gov Identifier: NCT01806974

Evaluation Effects of Treatment With IL-6R Inhibitor on Clinical Response and Biomarkers in Patients With Rheumatoid Arthritis (RA) Not Responding to DMARDs and/or a First Biological Agent

Principal Investigator: Gianfranco Ferraccioli, Prof. Dipartimento di Reumatologia, Università Cattolica del Sacro Cuore, Roma. Italy

Contact: Giovanni Lapadula, Prof.

Phone: +39 080 5478866

info@oegisea.it

ClinicalTrials.gov Identifier: NCT01835613

Efficacy of Tocilizumab (anti-IL-6 receptor) in Primary Sjögren's Syndrome. (ETAP)

Principal Investigator: Jacques-Eric Gottenberg. Hôpitaux Universitaires de Strasbourg. Strasbourg, France.

Contact: Jacques-Eric Gottenberg.

Phone: 3 88 12 81 89 ext 0033

jacques-eric.gottenberg@chru-strasbourg.fr

ClinicalTrials.gov Identifier: NCT01782235

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

Contact: Jeffrey S Miller, MD.

Phone: (612)-625-7409

Mille011@umn.edu

ClinicalTrials.gov Identifier: NCT01385423

Use of IL-15 After Chemotherapy and Lymphocyte Transfer in Metastatic Melanoma

Principal Investigator: Steven A Rosenberg, M.D. NIH Clinical Center. Surgery Branch, NCI, NIH.

Contact: June Kryk, R.N.

Phone: (301) 451-1929

ncisbirc@mail.nih.gov

ClinicalTrials.gov Identifier: NCT01369888

TNF- α Inhibitors and Antibody Production in Patients With Psoriasis

Principal Investigator: Peter Jensen, MD, University Hospital, Gentofte, Copenhagen. Denmark.

Contact: Lone Skov, MD, PhD.

Phone: +4539773204

lone.skov.02@regionh.dk

ClinicalTrials.gov Identifier: NCT01657513

CYTOKINES & CELLS ONLINE PATHFINDER ENCYCLOPEDIA

www.copewithcytokines.org

2013 Media Kit (COPE Version 31.4)

Content Provider for the Life Science Community since 1997

31,400+ entries | 84,890+ citations | 1,137,890+ value-added information cross-references

COPE averages 3000 - 4000 page views per day.

COPE is a multidisciplinary, award-winning, manually curated research tool and educational source.



Cope is a private initiative, not a company. I operate this free resource from a developing country with difficulties.

Continuing free access will depend on increased support from individuals and non-profit societies. Please make a donation!

Cellular Communication at its Best

Major topic-oriented subdictionaries in this version include:

| | | |
|--|---|--------------|
| Angiogenesis | ~ | 835 entries |
| Apoptosis & cell death | ~ | 2255 entries |
| CD antigens | ~ | 3720 entries |
| Cell lines in cytokine research | ~ | 275 entries |
| Cell types & expression profiles | ~ | 2380 entries |
| Chemokines | ~ | 420 entries |
| Cytokine species specificities | ~ | 390 entries |
| Cytokine levels in biological fluids | ~ | 985 entries |
| Cytokine topics | ~ | 80 entries |
| Dual identity proteins & cryptides | ~ | 1210 entries |
| Hematology | ~ | 785 entries |
| Hormones | ~ | 670 entries |
| Innate immunity defense peptides | ~ | 2610 entries |
| Metalloproteinases | ~ | 390 entries |
| Modulins & virulence factors | ~ | 1015 entries |
| Pattern recognition receptors | ~ | 920 entries |
| Protein domains/sequence motifs | ~ | 300 entries |

Support Open-Access COPE through Advertising

Practically everyone in the extremely complex world of communication biology and "biomedomics" consults COPE. COPE is ranked and respected as a scientific "High Quality Content" resource and used widely.

Capture Your Market

Attract the professionals you want to reach on COPE.

- Get multiple exposures on 75,000+ COPE web pages
- Get relevant, targeted, viable high-quality customer leads
- Create, ensure, and maintain global marketplace visibility

Advertising on COPE - the Affordable Imperative

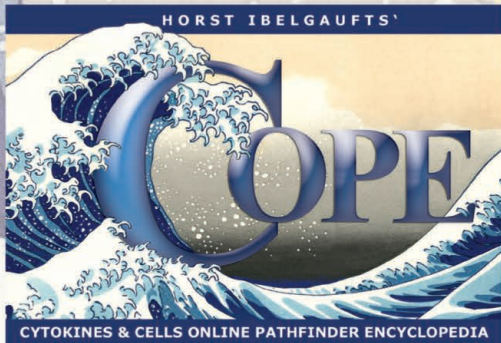
COPE users are potential customers. Researchers may order tomorrow what they look up in COPE today.

COPE Advertising Options:

- 1) Standard rotating banner (4 months minimum) \$650/month
- 2) 1-year educational grant (includes 2 free banners)
Please inquire for rate.
- 3) Other options available (including consulting, coaching, creative writing). Please write in for further info and rates.

For Further Information:

Reach Prof. Dr. Horst Ibelgauf, the creator of COPE, at cytokines@copewithcytokines.org.



Comments from top scientists and journals

- "... a kind of Rosetta stone" (Trends in Biochemical Sciences)
- "... much needed research tool" (Trends in Cell Sciences)
- "... classic resource" (Nature Reviews Immunology)
- "... outstanding contribution" (Jeff A Bluestone, Immune Tolerance Network)
- "... comprehensive site. ... gathers, consolidates, and puts information into perspective" (Howard Young, International Society of Interferon and Cytokine Research)
- "... goldmine when it comes to terminology, scientific concepts, new developments, and the manifold cross-connections in this field" (Matthias von Herrath, La Jolla Institute for Allergy and Immunology)
- "... Herculean task well done" (Joost J Oppenheim, NIH)
- "... strong points: comprehensive; weak points: none" (Society of Endocrinology Newsletter)

Things to do in San Francisco

By Bob Friedman

There is no city more colorful and exciting to visit than San Francisco. It is culturally stimulating, a wonderful place to walk around and observe the life of this beautiful city. There are a large number of great restaurants and bars in almost all of its unique neighborhoods. It's a fine place to get a map and wander about in. You can easily get around the city by public transport. The San Francisco Municipal Railway system consists of busses, streetcars, light rail, and cable cars. The fare is \$2, with a significant reduction if you are over 65. Exact change is required and free transfers good for 90 minutes after issue are available.



A partial list of its many wonderful attractions might include:

- Golden Gate Park containing an aquarium at The California Academy of Sciences, a fine art collection at the De Young Museum, and a Botanical Garden. This is a great place to spend a day.
- Mission San Francisco de Asis was founded in 1776, and was part of the string of missionaries set up in California by the Jesuits, when it still belonged to Spain.
- Golden Gate Bridge is a nice place to walk across with beautiful views along the way.
- Alcatraz is a big tourist attraction. It was the former domicile of such colorful characters as Al Capone and Machine Gun Kelly. You must take a ferry to get there, and since it's a very popular site it's best to make reservations for a visit well in advance (415) 981-7625.
- A Cable Car Ride from Powell to Market Street is a must do in this town.
- Lombard Street is said to be the crookedest street in the world.
- Chinatown is a colorful place for shopping and taking a walk.
- Two other art museums are certainly worth a visit: The Asian Art Museum and The Legion of Honor in Lincoln Park.
- A CityPass can be purchased which will cover the cost of both transportation in town and admissions for any of the attractions above where there is an entry fee.

As noted above this is a great town for walking. A trip around town might include as a minimum Union Square, Jackson Square, North Beach (includes Little Italy), Coit Tower, Telegraph Hill, Golden Gate Bridge, Oakland Bay Bridge, Fisherman's Warf, and Ghiradelli Square. Segway tours of Golden Gate Park are available at (415) 474-3130.




International Cytokine and Interferon Society

A WORLD COMMUNITY. Can you guess the language? Look for the answers elsewhere in the newsletter.

- | | |
|--|--|
| 1. Citokineve Ndërkombëtare dhe interferon Shoqëria | 9. Nemzetközi citokin és interferon Society |
| 2. আন্তর্জাতিকি Cytokine এবং Interferon সমসাইটি | 10. ಇಂಟರ್ನಿಯಾಷನಲಿ ಸೈ ಓ ಕೆನೆ ಮತತು ಇಂಟರ್ಫೆರಾಸಿ ಸು ಸೈ ಓ |
| 3. Međunarodni citokinima i Interferon društvo | 11. 국제 사이토 카인 인터페론 사회 |
| 4. 国际细胞因子和干扰素协会 | 12. Tarptautinė citokinų ir Interferonas draugija |
| 5. International tsütokiini interferoon Selts | 13. Międzynarodowa cytokin i Interferon Society |
| 6. <i>සාද්‍රව්‍යවිභවන</i> Cytokine <i>හා</i> <i>ගිවුරුහුරුතරිබ</i> <i>සාපිතයාලතුවා</i> | 14. ಅಂತ್ರ್ಜತ್ಯಯ ಸಜೈಕಿನ್ ಮರಿಯು ಇಂಟರ್ಫೆರಿಸ್‌ಸಜೈಟಿ |
| 7. Διεθνής κυτταροκινών και ιντερφερόνη Κοινωνία | 15. ไทโตไคน์สัมบูรณ์ระหว่างประเทศและสังคม |
| 8. अंतर्राष्ट्रीय Cytokine और इंटरफेरॉन सोसायटी | 16. Uluslararası Sitokin ve İnterferon Toplum |

WHEN YOUR PCR ISN'T WORKING, YOUR PROJECT IS GOING SLOWLY AND YOUR LABMATES ARE BECOMING A BIT ANNOYING, REMEMBER ANYTHING IS POSSIBLE.....



Courtesy of Stephanie Vogel

In Spanish, an equivalent saying is: Cuando las ranas críen pelo (When frogs grow hair)
Or Cuando las gallinas críen dientes (When chicken grow teeth)

FINDING NOVEL IMMUNE GENES WITH NEXT GENERATION GENOMIC TOOLS: how RNA-sequencing helped us to discover interferon- λ 4 (IFNL4)



Ludmila Prokunina-Olsson, PhD
prokuninal@mail.nih.gov

Investigator, Laboratory of Translational Genomics, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD, US

Finding novel human genes in the era when most of the genes are already discovered is a difficult task. More specifically finding novel immune genes has additional challenges. These genes might be expressed only transiently and in highly specific conditions, such as during acute response to infection. The expression pattern of these genes might be restricted to specific cells, resulting in very low expression levels when measured in total tissue samples or mixed cell populations.

So, how do new genes get found? New genes might be predicted computationally based on the presence of plausible splicing sites supporting open reading frames (ORFs). The existence of these ORFs can be also supported by ESTs (expressed sequenced tags) which represent fragments of sequenced cDNAs. New genes can be found based on sequence similarity with known transcripts, by bioinformatics search through GenBank database or by hybridization of probes with cDNA libraries.

However, our recent discovery of the human interferon- λ 4 (IFNL4) gene proved that the gene prediction, existence of ESTs or similarity to other related genes was neither necessary nor sufficient for identification of novel immune genes. We discovered IFNL4 in the search for a molecular phenotype of a genetic association with clearance of hepatitis C virus infection (HCV) detected for a single nucleotide polymorphism (SNP)

rs12979860, previously known as “the IL28B marker”. The associated SNP is located upstream of the IFNL3 gene (renamed from IL28B) and close to 3 other related genes in the same family, IFNL1, IFNL2 and a non-coding pseudogene. This family of highly related proteins which now form a family of interferon- λ proteins (also known as type-III interferons) was discovered 10 years. We wondered about the possibility of something else existing in this region – a novel splicing form of a known transcript or something totally unknown. To answer this question we used RNA-sequencing, an agnostic and unbiased discovery tool based on sequencing of the whole transcriptome of a tissue sample. Expression analysis with microarrays, a traditional way of genome-wide expression analysis, allows simultaneous detection of a large number of probes covering many known or predicted genes and splicing forms, but this approach is limited by the content of the array. In contrast, RNA-sequencing is a unique discovery tool to explore the known and unknown transcriptome, including splicing diversity, levels of expression and the presence of transcribed genetic variants. This approach gives an overwhelming amount of data which requires careful validation and interpretation. Depending on the library construction, RNA-sequencing can provide information on mRNA transcripts, small and non-coding RNAs, as well as pseudogenes and RNA repeats, which can contaminate the results. For our experiment, we created an in-vitro system in which IFNL region would be expected to be expressed.

We used fresh primary human hepatocytes treated with PolyIC for 0, 1, 2, 4, 8 and 24 hours. We confirmed that this treatment induced the expression of all IFNL transcripts (IFNL1, IFNL2, IFNL3, and the pseudogene is expressed at low levels even without treatment). Analysis of RNA-sequencing reads in this region was difficult because of the high similarity between the IFNL transcripts and a number of transcribed genetic variants which are considered as mismatches. Genome alignment based on the customized settings revealed induction after 2-24 h of treatment, visualized as a pile of reads right upstream of the IFNL3 and in the area where rs12979860 is located. This step took 2 months, including the sample preparation, RNA-sequencing and analysis. The validation step took 9 months. RNA-sequencing can provide a rough estimation of transcript splicing diversity. This process becomes complicated in the presence of multiple alternative exons. Eventually, we determined transcription and translation start sites and cloned 10 alternative transcripts. The most unusual feature of this transcribed region was that it is fully controlled by a genetic variant in the first exon. The di-nucleotide variant (TT/ Δ G) included a deletion of one nucleotide (G/ Δ G) and a substitution at the next position (T/G). The presence of the Δ G allele supports 4 open reading frames which, depending on the alternative exons, may generate alternative proteins of 179, 170, 131 and 107 aa. The protein of 179 aa, which includes 5 exons, shares 29% amino acid identity with IFNL3 and other IFNL proteins, and was designated IFNL4, based on its functional properties. The Δ G allele that creates the IFNL4 protein is the functional variant that explains and improves the association of rs12979860 (IL28B). rs12979860 is also a IFNL4 variant, but located in the first intron of the gene. Using IFNL4 (Δ G/TT) instead of rs12979860 is most informative in individuals of African ancestry, where this variant is present in one or two copies in 90% of individuals. Interestingly, the

other allele (TT) of the same genetic variant, introduces a frame-shift resulting in a totally different protein after the first 22 amino acids. We have cloned 2 full-length putative open-reading frames with this allele, of 143 and 124 aa, but the predicted proteins have no similarity to any known proteins, no specific domains and showed no specific functions in our assays. Thus, in this novel transcribed region, only one transcript can generate an interferon-type protein, IFNL4. Due to its low sequence homology, IFNL4 had not been discovered together with the rest of the IFNL family of genes in this region. IFNL4 gene was not predicted because the reference version of the human genome has the TT allele which does not support the IFNL4 open reading frame.

How many other immune genes remain to be discovered? While this question remains open, it is now clear that RNA-sequencing is a very powerful discovery tool complementary to carefully designed biological experiments. Our RNA-sequencing data has demonstrated that additional leads might result in new gene discoveries after validation and characterization similar to what we have done for IFNL4.

Reference:

[A variant upstream of IFNL3 \(IL28B\) creating a new interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus.](#)

Prokunina-Olsson L, Muchmore B, Tang W, Pfeiffer RM, Park H, Dickensheets H, Hergott D, Porter-Gill P, Mumy A, Kohaar I, Chen S, Brand N, Tarway M, Liu L, Sheikh F, Astemborski J, Bonkovsky HL, Edlin BR, Howell CD, Morgan TR, Thomas DL, Rehermann B, Donnelly RP, O'Brien TR.

Nat Genet. 2013 Feb;45(2):164-71. doi: 10.1038/ng.2521. Epub 2013 Jan 6.



Rusinova I, Forster S, Yu S, Kannan A, Masse M, Cumming H, Chapman R, **Hertzog PJ.** (2013). *INTERFEROME v2.0: an updated database of annotated interferon-regulated genes.* **Nucleic Acids Res.** 41(Database issue):D1040-6 PMID: 23203888 :

Interferome v2.0

(<http://interferome.its.monash.edu.au/interferome/>) is an update of an earlier version of the Interferome DB published in the 2009 NAR database edition. Vastly improved computational infrastructure now enables more complex and faster queries, and supports more data sets from types I, II and III interferon (IFN)-treated cells, mice or humans. Quantitative, MIAME compliant data are collected, subjected to thorough, standardized, quantitative and statistical analyses and then

significant changes in gene expression are uploaded. Comprehensive manual collection of metadata in v2.0 allows flexible, detailed search capacity including the parameters: range of -fold change, IFN type, concentration and time, and cell/tissue type. There is no limit to the number of genes that can be used to search the database in a single query. Secondary analysis such as gene ontology, regulatory factors, chromosomal location or tissue expression plots of IFN-regulated genes (IRGs) can be performed in Interferome v2.0, or data can be downloaded in convenient text formats compatible with common secondary analysis programs. Given the importance of IFN to innate immune responses in infectious, inflammatory diseases and cancer, this upgrade of the Interferome to version 2.0 will facilitate the identification of gene signatures of importance in the pathogenesis of these diseases.

CYTOKINES AS THERAPEUTIC AGENTS IN CANCER



Miranda L Hanson

Fellow, Laboratory of Molecular Immunoregulation
Cancer and Inflammation Program
National Cancer Institute

Cytokines are involved in almost every important biological process, including inflammation, immunity, cell proliferation, migration, fibrosis, repair, and angiogenesis (1, 2). An aberration in cytokines, their receptors, and/or the signaling pathways can result in a wide variety of diseases such as, psoriasis, inflammatory bowel disease, rheumatoid arthritis, asthma, and cancer.

Basic and clinical research involving the use of recombinant cytokines and their antagonists as therapeutics continues to thrive. While cytokines have been studied extensively for the last 35 years, there has been increased interest over the past two decades in controlling the immune system to reduce cancer progression. In particular, there has been a pursuit to characterize cytokines and manipulate their intricate signaling networks to develop cancer treatments.

Currently, only two cytokines have achieved FDA approval as single agents for cancer treatment- high-dose IL-2 for renal cell carcinoma and metastatic melanoma and IFN- α for the adjuvant therapy of Stage III melanoma. IL-2 immunotherapy was approved in 1992 for metastatic renal cell carcinoma and in 1998 for metastatic melanoma. IL-2 treatment can result in complete remission of 5%–10% of patients with these diseases, with lack of recurrence for as long as 25 years and potential cures of 70% of these individuals, with complete tumor regression (3). The exact mechanisms of this therapy remain to be elucidated, but increased cytotoxicity and changes in tumor blood flow are likely causes.

Gaining FDA approval in 1995, IFN- α produces antitumor effects in several hematological malignancies and solid tumors, such as hairy cell leukemia, chronic myelogenous leukemia, follicular non-Hodgkin lymphoma, cutaneous T-cell lymphoma, kidney cancer, melanoma, and Kaposi's sarcoma (4). In malignant melanoma, randomized clinical trials established that IFN- α reduces the risk of recurrence following surgical removal of localized lymph node metastases (5,6). The mechanisms responsible for the antitumor activity

of IFN- α remain unclear, but likely include direct effects on tumor cells as well as immune stimulation.

Cytokines play multifunctional roles in the promotion and regulation of the tumor response, therefore developing effective cytokine-based treatments for cancer is quite the undertaking. While cytokine treatment may show promise in the lab and/or the clinic, systemic infusion of cytokines can produce significant side effects which results in dose-limiting toxicity. Additionally, systemic cytokine administration has achieved only modest therapeutic benefits so far, possibly due to the administration technique not accurately reflecting the cytokine's behavior in the tumor microenvironment. In an attempt to manipulate cytokine function in a more physiological relevant way, researchers have modified the cytokine environment directly at tumor sites. Peritumoral injection of specific cytokines, particularly IL-2, enhances tumor rejection through a well-orchestrated host reaction involving neutrophils, eosinophils, macrophages, NK cells and lymphocytes (7). Other cytokines that have been delivered locally include IL-12 and GM-CSF. IL-12 was found to amplify tumor rejection by promoting TH1 responses, inhibiting angiogenesis, and increasing lymphocyte cytotoxicity (8). GM-CSF improved tumor antigen presentation by increasing the activation of DCs, macrophages, granulocytes, and NKT cells (9,10). GM-CSF is also being tested against cancer as a non-specific immunotherapy and as an adjuvant given with other types of immunotherapies. Clinical trials of GM-CSF, alone or with other immunotherapies, are being done in patients with many different types of cancer.

Cytokines such as vascular endothelial growth factor (VEGF) that have pro-oncogenic characteristics, are being targeted by anti-cytokine therapy. The proliferative studies of VEGF's function (11-13) have confirmed the critical role of this cytokine in oncogenic processes, thus making the VEGF family of cytokines and their receptors optimal targets for anti-cytokine therapy in various cancers such as pancreas, kidney, breast, lung, prostate cancers, multiple myeloma, acute

myelogenous leukaemia, myelofibrosis, and chronic lymphocytic leukemia. TNF- β and TGF- β antagonists are also potential anticancer therapeutics.

The therapeutic potential of many cytokines such as IL-17, IL-23, and TGF- β is in question because they have dual functions as tumor promoters and tumor suppressors. Other cytokines, like IL-27, have been definitively classified as being antitumor (14), but have both pro- and anti-inflammatory properties, which complicates therapeutic use. Further evaluation of these cytokines' multifunctional roles in different environments is necessary to accurately assess their therapeutic value. The dual role of the immune system in cancer suggests that cytokine-based therapies should target multiple pathways to increase the protective, anti-tumor host response while dampening the regulatory pathways. Using this strategy may lead to more effective and well-tolerated therapeutics.

1. Vilcek, J., and Feldmann, M. 2004. Historical review: cytokines as therapeutics and targets of therapeutics. *Trends Pharmacol. Sci.* 25:201–209.
2. Oppenheim, J.J. 2001. Cytokines: past, present, and future. *Int. J. Hematol.* 74:3–8.
3. Rosenberg, SA. 2012: Raising the Bar: The Curative Potential of Human Cancer Immunotherapy *Sci Transl Med.* 4:127.
4. Chronic Myeloid Leukemia Trialists Collaborative Group 1997. Interferon α versus chemotherapy for chronic myeloid leukemia: a meta-analysis of seven randomized trials. *J. Natl. Cancer Inst.* 89, 1616–1620.
5. Kirkwood, J. et al. 1996. Interferon α -2b adjuvant therapy of high risk resected cutaneous melanoma: the Eastern Cooperative Oncology Group Trial EST 1684. *J. Clin. Oncol.* 14, 7–17.
6. Kirkwood, J. M. et al. 2001. High-dose interferon α -2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III melanoma: results of intergroup trial E1694/S9512/C509801. *J. Clin. Oncol.* 19, 2370–2380.
7. Forni, G. et al. 1988. Helper strategy in tumor immunology: expansion of helper lymphocytes and utilization of helper lymphokines for experimental and clinical immunotherapy. *Cancer Metast. Rev.* 7, 289–309.
8. Boggio, K. et al. 1998. Interleukin 12-mediated prevention of spontaneous mammary adenocarcinoma in two lines of her-2/neu transgenic mice. *J. Exp. Med.* 188, 589–596.
9. Mach, N. et al. 2000. Differences in dendritic cells stimulated in vivo by tumors engineered to secrete granulocyte-macrophage colony-stimulating factor or flt3-ligand. *Cancer Res.* 60, 3239–3246.
10. Gillessen, S. et al. 2003. CD1d-restricted T cells regulate dendritic cell function and antitumor immunity in a granulocyte-macrophage colony-stimulating factor-dependent fashion. *Proc. Natl Acad. Sci. USA* 100, 8874–8879.
11. Ferrara N, Houck K, Jakeman L, Winer J, Leung D. 1991. The vascular endothelial growth factor family of polypeptides. *J Cell Biochem.* 47: 211-8.
12. Ferrara N, Houck K, Jakeman L, Leung D. 1992. Molecular and biological properties of the vascular endothelial growth factor family of proteins. *Endocr Rev* 13: 18-32.
13. Gerber H-P, Ferrara N. 2003. The role of VEGF in normal and neoplastic hematopoiesis. *J Mol Med* 81: 20-31.
14. Murugaiyan G, Saha B. 2013. IL-27 in tumor immunity and immunotherapy. *Trends Mol Med.* 19(2):108-16.



International Cytokine and Interferon Society

Answers to “Can you guess the language?” from page 21

- | | |
|-------------|----------------|
| 1. Albanian | 9. Hungarian |
| 2. Bengali | 10. Kannada |
| 3. Bosnian | 11. Korean |
| 4. Chinese | 12. Lithuanian |
| 5. Estonian | 13. Polish |
| 6. Georgian | 14. Telugu |
| 7. Greek | 15. Thai |
| 8. Hindi | 16. Turkish |

IFN- α AND LUPUS: GUILTY BY ASSOCIATION OR A PRIMARY CULPRIT?



Jarrat Jordan¹ and ChiChi Huang²

¹Estrela Venture, Janssen Research & Development, LLC

²Antibody Drug Discovery, Janssen Research & Development, LLC

Progress of current clinical trials targeting type I IFNs

The type I IFN family of cytokines all signal through a ubiquitously expressed heterodimeric receptor (IFNAR) resulting in antiviral, antiproliferative and immunomodulatory effects. In humans, type I IFN is composed of 12 IFN- α protein subtypes and a single functional protein for IFN- β , IFN- ϵ , IFN- κ , and IFN- ω . Induction of type I IFN occurs in response to both sterile and microbial ligands. The antiviral and anti-proliferative properties of type I IFN have been exploited in the clinic for infectious disease and oncologic indications and more recently pharmaceutical companies are developing approaches to antagonize type I IFN (primarily IFN- α) for autoimmune indications including Systemic Lupus Erythematosus (SLE). In this article, we will summarize evidence suggesting a potential role of type I IFN in SLE pathogenesis and discuss our perspective on recent clinical data examining agents targeting type I IFNs in SLE patients.

IFN- α is a compelling target for SLE.

A relationship between IFN- α and SLE was first described in 1979 when this cytokine was demonstrated to be elevated in the serum of SLE patients (1, 2). More recently, a type I IFN gene signature, defined by the upregulation of hundreds of IFN-inducible transcripts, has been extensively described in a subset of SLE patients which in some cases has been reported to positively correlate with both clinical and serological features of disease (3-7). Several genetic associations affecting the type I IFN pathway have also been identified in the SLE population and mechanistic studies have revealed that IFN- α modulates the expression of a number of gene products implicated in pathogenic mechanisms of SLE. For example, IFN- α can induce the expression of BlyS, an important B cell survival factor and the target of belimumab which is the first and only FDA approved drug for SLE in over 50 years (8, 9). Indeed, a positive correlation has been reported between type I IFN activity and levels of soluble BlyS in the SLE patient sera (10-12). Furthermore, blockade

of IFN- α in SLE patients resulted in a decrease in BlyS gene expression in the small number of lesional skin biopsies examined (13). In concert with IL-6, IFN- α was also shown to be important for the generation of Ig-secreting plasma cells (14). Outside of direct effects on the B-cell compartment, IFN- α exhibits effects on other important processes implicated in lupus pathogenesis. For example, type I IFN can induce the differentiation of monocytes to antigen-presenting DCs (15). Importantly, Blanco et al. demonstrated that the addition of a neutralizing IFN- α antibody significantly reduced the capacity of pediatric SLE patient sera to induce monocyte to DC differentiation demonstrating a potential role of this cytokine in decreasing tolerance to self-antigens. Arguably, the most notable example suggesting a causal relationship between type I IFN and SLE is the observation that some patients undergoing recombinant IFN- α therapy for infectious and oncologic indications exhibit autoantibodies and lupus manifestations which subside after therapy is discontinued (16, 17).

What have we learned from blocking IFN- α in SLE patients?

There are several current early stage clinical trials in SLE investigating agents targeting type I IFN, including three monoclonal antibodies neutralizing multiple subtypes of IFN- α , an IFN- α vaccine approach and an antagonist anti-interferon receptor 1 (IFNAR1) monoclonal antibody which would be expected to block signaling induced by all type I IFN (Table 1). Considering the difficulty to directly quantify type I IFN due to low serum abundance and the diversity of this 16 member family, various type I IFN specific gene signatures are being utilized to assess the pharmacodynamics (PD) of IFN inhibitors in clinical development as summarized in Table 1. These trials have demonstrated dose-dependent PD effects however, none of these antagonists completely neutralized the type I gene signatures in all SLE patients. It is important to note that no significant side effects were revealed in these early trials.

A type I IFN gene signature is present in several rheumatic diseases and is stably elevated in approximately half of the adult SLE population. Stratifying SLE patients based on a type I IFN signature is an attractive option to consider for clinical trials using therapeutic agents targeting this pathway given the substantial heterogeneity and long list of clinical trial failures seen in this disease. One logical approach to stratify patients most amenable for an IFN- α inhibitor would be to enrich for patients having evidence of pronounced elevation of type I IFN-induced transcripts in whole blood. While the IFN- α antagonists in clinical development have all reduced the levels of variously defined type I IFN signatures present in some SLE patients prior to drug dosing, a robust clinical impact of IFN- α antagonism remains to be demonstrated using traditional instruments to measure disease activity (Table 1). Phase 2 trial data using a monoclonal antibody antagonist targeting multiple IFN- α subtypes (rontalizumab) has recently been presented (18). In this trial, SLE patients were stratified into 2 predefined groups (IFN signature high and IFN signature low) based on the baseline gene expression level of 3 type I IFN signature genes (18). Remarkably, only the patient group having low levels of IFN signature gene expression exhibited a significant treatment response both in terms of IFN signature gene suppression and in improvement in the signs and symptoms of SLE. The failure to show a clinically meaningful impact in patients having more pronounced type I IFN signature expression in conjunction with the inability to reduce signature expression in this group to the levels seen in the group of patients having lower levels of signature gene expression raises some important questions.

Why is there a reduced PD response with anti IFN- α treatment in SLE patients classified as having more pronounced type I IFN signature expression?

There are at least three potential explanations why high IFN signature levels were not inhibited by anti-IFN alpha inhibition. First, suboptimal dosing of rontalizumab may normalize signature levels in the low type I IFN signature group, but is unable to neutralize the higher levels of circulating IFN in patients in the signature high group. While this explanation seems feasible the authors of this study have indicated that this is not the case (18). Second, it is also conceivable that type I IFNs not neutralized by rontalizumab could be contributing to the total IFN activity in SLE patients with high IFN signature expression. The type I IFN family consists of 12 IFN- α subtypes in addition to IFNs- β , ϵ , κ and ω and type I IFN signatures currently cannot distinguish which type I IFNs are driving the response. The failure of this IFN- α specific antagonist to down-modulate the high IFN gene signature to low levels may support this notion. To this point, it is

interesting to note that the anti IFN- α antagonist sifalimumab, which dose-dependently inhibits the type I IFN signature in SLE patients, was unable to exhibit significant suppression of this same signature in chronic psoriasis. This also suggests that other type I IFNs besides IFN- α may be driving the IFN signature (19). Indeed, it has been reported that IFN- ω gene expression is elevated in SLE and the existence of autoantibodies against both IFN- α and IFN- ω are prevalent in SLE patients. Thus, these and perhaps other type I IFNs may be contributing to the total IFN activity seen in some SLE patients (20, 21). With the clinical development of Medi-546 an anti-IFNAR1 antagonist by MedImmune it is just a matter of time to test this hypothesis. IFNAR1 blockade would be expected to suppress signaling induced by all type I IFNs and likely normalize the type I IFN signature in all SLE patients if dosed at sufficient levels. This may result in efficacy in a much larger SLE population than observed with rontalizumab which down-modulated clinical activity only in patients with low levels of IFN signature expression. In conjunction with potential clinical benefits of broader inhibition of the type I IFN family, one must carefully monitor the impact of this approach on host defense. For example, IFN- β plays a central role in acute antiviral response although evidence supporting a potential role in lupus is not clear (22, 23).

A third explanation for the inability of anti IFN- α therapies to completely suppress the type I IFN signature in patients with higher levels of signature expression is the possibility that the signature can also manifest through type I IFN-independent mechanisms. Interestingly, recent phase 1 results from Amgen indicate that anti IFN- γ (AMG 811) treatment down-modulated some of the down-stream chemokines and IFN signature elevated in SLE patients (24). It has also been recently suggested that trex1 deficiency can result in a type I IFN signature which may not require type I IFN secretion (25). Of note, approximately 2% of SLE patients harbor mutations in the trex1 gene (26). A key point from the emerging data is that more studies are needed to better understand and improve the type I IFN signature in terms of selectivity and relevance to SLE disease activity.

Where do we go from here?

With a host of type I IFN antagonist approaches in clinical development, it is a very exciting time for the field and perhaps for the patient as the true role of type I IFN in lupus pathogenesis may ultimately be revealed. Integration of patient clinical and serological data before and after IFN inhibitor treatment with genomic and transcriptomic deep sequencing data will likely lead to refinement of the IFN gene signature and perhaps more precise biomarkers to identify patients that would benefit from type I IFN inhibitor treatments.

Table 1. Type 1 IFN antagonists in clinical trials.

Data was collected from clinicaltrials.gov and current as of 07.14.2013.

Only trials using these agents for an SLE indication are listed with the exception of NCT00930683.

| Therapeutic | Company | Current Stage | IFN Signature Utilized | Results | References |
|---|--------------------|---------------|--|--|------------|
| MEDI-545 (Sifalimumab) IFN- α antagonist mAb | MedImmune | Ph2b | 21 gene | Ph1: (NCT00299819) Dose-dependent but not complete suppression of IFN-signature Slight efficacy in exploratory analyses | 27 |
| | | | 21 gene | Ph1b: (NCT00482989) Maximum average inhibition of elevated IFN gene signature of 38.7% | 28 |
| | | | 21 gene | SELENA-SLEDAI and BILAG scores not significantly different than placebo group | |
| | | | Ph2a: (NCT00657189) Maximum suppression of elevated IFN gene signature up to 40% SELENA-SLEDAI and BILAG scores not significantly different than placebo group | 29 | |
| | | | Ph2: (NCT01031836)* Ph2: (NCT00979654) active Ph2b: (NCT01283139) active | | |
| MEDI-546 IFNAR1 antagonist mAb | MedImmune | Ph2 | 5 gene | Ph1: (NCT00930683) complete** Ph2: (NCT01559090) recruiting (NCT01438489) recruiting (NCT01753193) enrolling by invitation | 30 |
| RhuMab (Rontalizumab) IFN- α antagonist mAb | Genentech | Ph2 | 7 gene | Ph1: (NCT00541749) Dose-dependent but not complete suppression of IFN signature | 31 |
| | | | 3 gene | Ph2: ROSE (NCT00962832) Greater suppression of IFN signature in pre-specified IFN signature low group compared to IFN signature high group Clinical efficacy only in IFN signature low group (SRI, flare rates and steroid burden) | 18 |
| AGS-009 IFN- α antagonist mAb | Argos Therapeutics | Ph1 | 27 gene | Ph1: (NCT00960362) dose-proportional down-modulation of signature in patients with elevated signature at baseline No exploratory efficacy measurements were reported | 32 |
| IFN-alpha-kinoid Vaccine against IFN- α | NEOVACS | Ph1-2 | 21 gene | Ph1-2: (NCT01058343) Downregulated IFN-induced genes in SLE patients overexpressing IFN-inducible genes at baseline No significant difference in SLEDAI-2K or BILAG compared to placebo group | 33 |

*Current status of this trial is unknown.

**This trial enrolled adult subjects with scleroderma.

1. J. J. Hooks *et al.*, Immune interferon in the circulation of patients with autoimmune disease. *N Engl J Med* **301**, 5 (Jul 5, 1979).
2. O. T. Preble, R. J. Black, R. M. Friedman, J. H. Klippel, J. Vilcek, Systemic lupus erythematosus: presence in human serum of an unusual acid-labile leukocyte interferon. *Science* **216**, 429 (Apr 23, 1982).
3. E. C. Baechler *et al.*, Interferon-inducible gene expression signature in peripheral blood cells of patients with severe lupus. *Proceedings of the National Academy of Sciences of the United States of America* **100**, 2610 (Mar 4, 2003).
4. L. Bennett *et al.*, Interferon and granulopoiesis signatures in systemic lupus erythematosus blood. *The Journal of experimental medicine* **197**, 711 (Mar 17, 2003).
5. M. C. Dall'era, P. M. Cardarelli, B. T. Preston, A. Witte, J. C. Davis, Jr., Type I interferon correlates with serological and clinical manifestations of SLE. *Annals of the rheumatic diseases* **64**, 1692 (Dec, 2005).
6. T. P. Karageorgas, D. D. Tseronis, C. P. Mavragani, Activation of type I interferon pathway in systemic lupus erythematosus: association with distinct clinical phenotypes. *Journal of biomedicine & biotechnology* **2011**, 273907.
7. T. B. Niewold, J. Hua, T. J. Lehman, J. B. Harley, M. K. Crow, High serum IFN-alpha activity is a heritable risk factor for systemic lupus erythematosus. *Genes and immunity* **8**, 492 (Sep, 2007).
8. G. J. Dennis, Belimumab: a BlyS-specific inhibitor for the treatment of systemic lupus erythematosus. *Clinical pharmacology and therapeutics* **91**, 143 (Jan).
9. M. B. Litinskiy *et al.*, DCs induce CD40-independent immunoglobulin class switching through BlyS and APRIL. *Nature immunology* **3**, 822 (Sep, 2002).
10. L. L. Ritterhouse *et al.*, B lymphocyte stimulator levels in systemic lupus erythematosus: higher circulating levels in African American patients and increased production after influenza vaccination in patients with low baseline levels. *Arthritis and rheumatism* **63**, 3931 (Dec, 2011).
11. B. Richardson *et al.*, Development of A Quantitative PCR Method to Determine Interferon Signature Metric Status in SLE Patients: Distribution and Clinical & Serological Associations in Two Lupus Clinical Trials. *ACR/ARHP 2012 Annual Meeting Abstract* **620**, (2012).
12. A. Seyhan *et al.*, Impact of baseline Interferon pathway activation on widespread gene expression changes with disease flare in lupus patients: interim report from the BOLD (Biomarkers of lupus disease) study. *Ann Rheum Dis.* **14**, 74 (2012).
13. Y. Yao *et al.*, Neutralization of interferon-alpha/beta-inducible genes and downstream effect in a phase I trial of an anti-interferon-alpha monoclonal antibody in systemic lupus erythematosus. *Arthritis and rheumatism* **60**, 1785 (Jun, 2009).
14. G. Jego, V. Pascual, A. K. Palucka, J. Banchereau, Dendritic cells control B cell growth and differentiation. *Curr Dir Autoimmun* **8**, 124 (2005).
15. P. Blanco, A. K. Palucka, M. Gill, V. Pascual, J. Banchereau, Induction of dendritic cell differentiation by IFN-alpha in systemic lupus erythematosus. *Science* **294**, 1540 (Nov 16, 2001).
16. M. Biggioggero, L. Gabbriellini, P. L. Meroni, Type I interferon therapy and its role in autoimmunity. *Autoimmunity* **43**, 248 (Apr).
17. L. M. Burdick, N. Somani, A. K. Somani, Type I IFNs and their role in the development of autoimmune diseases. *Expert Opin Drug Saf* **8**, 459 (Jul, 2009).
18. W. P. Kennedy *et al.*, Efficacy and safety of rontalizumab (anti-interferon-alpha) in sle patients with restricted immunosuppressant use: results of a randomized, doubleblind, placebo-controlled phase 2 study. *The 10th International Congress on SLE, Buenos Aires, Argentina Oral Presentation* **5**, 022, (April 20th, 2013).
19. R. Bissonnette *et al.*, A randomized, double-blind, placebo-controlled, phase I study of MEDI-545, an anti-interferon-alfa monoclonal antibody, in subjects with chronic psoriasis. *Journal of the American Academy of Dermatology* **62**, 427 (Mar, 2010).
20. G. M. Han *et al.*, Analysis of gene expression profiles in human systemic lupus erythematosus using oligonucleotide microarray. *Genes and immunity* **4**, 177 (Apr, 2003).
21. K. H. Ching *et al.*, Two major autoantibody clusters in systemic lupus erythematosus. *PLoS one* **7**, e32001.
22. R. Baccala *et al.*, Anti-IFN-alpha/beta receptor antibody treatment ameliorates disease in lupus-predisposed mice. *Journal of immunology* **189**, 5976 (Dec 15, 2012).
23. J. Hua, K. Kirou, C. Lee, M. K. Crow, Functional assay of type I interferon in systemic lupus erythematosus plasma and association with anti-RNA binding protein autoantibodies. *Arthritis and rheumatism* **54**, 1906 (Jun, 2006).
24. D. A. Martin *et al.*, Safety, Pharmacokinetics and Pharmacodynamics of AMG 811 (anti-IFN-gamma): Results of a Phase I Single Dose Study in Subjects with Systemic Lupus Erythematosus. *The 10th International Congress on SLE, Buenos Aires, Argentina Oral Presentations* **5**, 023, (April 20th, 2013).
25. M. Hasan *et al.*, Trex1 regulates lysosomal biogenesis and interferon-independent activation of antiviral genes. *Nature immunology* **14**, 61 (Jan, 2013).
26. M. A. Lee-Kirsch *et al.*, Mutations in the gene encoding the 3'-5' DNA exonuclease TREX1 are associated with systemic lupus erythematosus. *Nature genetics* **39**, 1065 (Sep, 2007).

Happy Birthday, Jan

Your landmark contributions to our understanding of cytokines and their actions that have extended from the laboratory to the bedside are impressive, beginning with your studies of type I and II interferons and including your work on additional cytokines including tumor necrosis factor. Your seminal work on generating monoclonal antibodies to cytokines, and their development as diagnostics and therapeutics as well as research tools has had a huge interest on the field of cytokines, both from a basic research standpoint but more particularly from the spectacular clinical successes. Of particular relevance to our Society membership is your work on the antibody against TNF, and the development of Remicase, an anti-inflammatory therapeutic for rheumatoid arthritis which is benefitting millions of patients. Your fundamental scientific contributions that emerged from studies to answer basic biologic questions has given rise to new therapies for inflammatory diseases and is very likely to provide substantial clinical benefit to additional patients in the future. We wish you the best for continued success in your current areas of focus, including the mission of the Vilcek Foundation that recognizes creative promise of young foreign-born scholars with records of exceptional early achievement that are naturalized citizens or permanent residents of the USA.

On behalf of our Society's membership, we wish you the Best for Your 80th and for the Years to Come!



Charles E. Samuel

Co-President, ICIS 2013

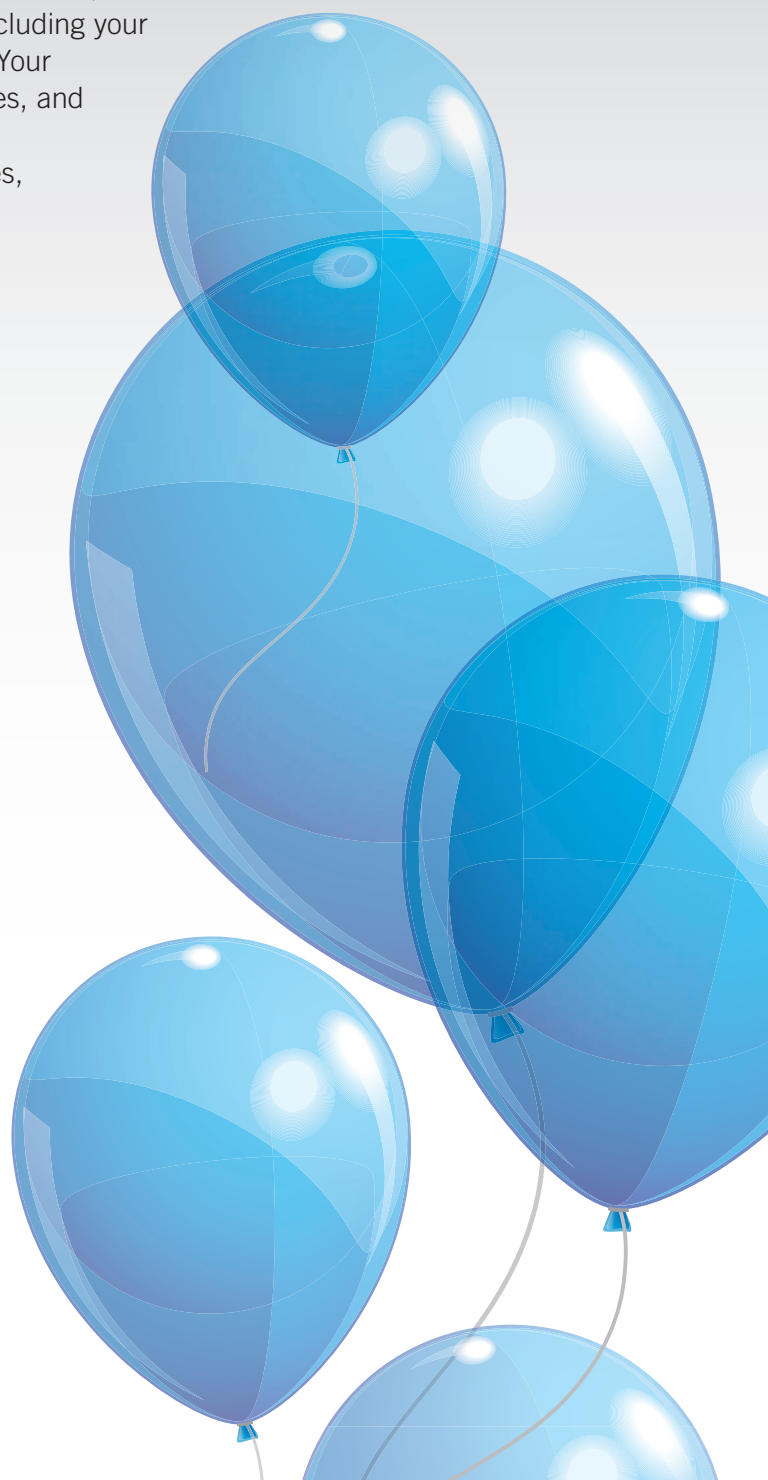
C. A. Storke Professor, UC Santa Barbara



Luke O'Neill

Co-President, ICIS 2013

Director, Trinity Biomedical Sciences Institute, Dublin



Happy Birthday, George

Your seminal contributions to the scientific community are impressive, spanning several areas of biological chemistry and including both fundamental mechanistic discoveries as well as the development of widely utilized methodologies. Of particular relevance to our Society membership is your co-discovery with Jim Darnell of the Jak-Stat signal transduction pathway. Your combined genetic and biochemical analyses unequivocally established the utilization of Jaks and Stats in overlapping combinations for signal transduction by type I and II interferons, and many cytokines, a pathway subsequently shown to be operative in many additional physiologic settings beyond interferon signaling. The discovery of this pathway has given rise to new therapies for inflammatory diseases and is very likely to provide substantial clinical benefit to patients in the future. In addition, the development of the universally-used Northern and Western techniques for analysis of specific RNAs and proteins and the co-discovery of gene amplification in mammalian cells represent landmark contributions. We wish you the best for continued success in your current areas of work including the modification of promoter-bound transcription factors by chromatin remodeling enzymes.

On behalf of our Society's membership, we wish you the Best for Your 80th and for the Years to Come!

Charles E. Samuel

Co-President, ICIS 2013
C. A. Storke Professor, UC Santa Barbara

Luke O'Neill

Co-President, ICIS 2013
Director, Trinity Biomedical Sciences Institute, Dublin

Cleveland Clinic
Lerner Research Institute

A Celebration of Fundamental Discoveries in Molecular and Cellular Biology

A Symposium in Honor of the 80th Birthday of
George R. Stark, Ph.D.

Featured speakers

Session 1 (8 am): James Alwine • Andrei Gudkov • Yukihito Ishizaka • Bryan Williams • chaired by James Darnell
 Session 2 (10:30 am): Mark Jackson • Xiaoxia Li • Martin McMahon • Nima Sharifi • chaired by Geoff Wahl
 Session 3 (1:30 pm): Richard Padgett • Richard Hanson • James Wells • Steven Reed • chaired by Robert Lehman
 Session 4 (4 pm): Robert Silverman • Ganes Sen • George Stark • chaired by Thomas Hamilton

September 20, 2013
Bunts Auditorium • Cleveland Clinic
Program begins at 8:00 am

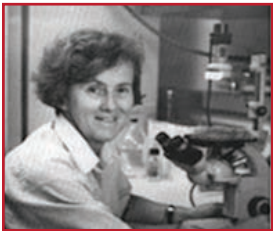




PAULA PITHA-ROWE

Dr. Pitha-Rowe has been working in the field of the innate immune response for most of her life, with recent focus on the transcription factors of IRF family. Her team was the first to identify and clone IRF-3 and have shown the critical role of IRF-3 and IRF-7 in the innate antiviral response. They were also the first to clone and functionally characterized IRF-5 both in vitro and in vivo and have shown its role in the induction of inflammatory and antiviral cytokines. They have shown that in vivo IRF-5 plays a critical role in B cells differentiation, IgG2a response and in the TH-1 mediated response to Leishmania infection. These data indicate that IRF-5 may be one of the mediators of a cross talk between innate and adaptive immune responses. Most importantly, the characterization of IRF-5 function is of clinical importance, since distinct genetic variations in IRF-5 gene were shown to be associated with many autoimmune diseases including lupus.

Her previous work on the effect of Interferon on retroviral and HIV-1 infection demonstrated that interferon inhibits HIV-1 replication and induces genes that play a critical role in the intrinsic resistance to HIV-1 infection. Her laboratory was the first that constructed inducible lentiviral vectors for HIV-1 gene therapy that has been further developed and clinically tested by VirxSys.



Cancer Defense Against Virus Offense

A Symposium to Honor Paula Pitha-Rowe, Ph.D.
October 11, 2013

CYTOKINES 2014

SAVE THE DATES:
OCTOBER 26-29, 2014
MELBOURNE, AUSTRALIA

For further information contact conveners:
Brendan Jenkins brendan.jennkins@monash.edu
or Paul Hertzog paul.hertzog@monash.edu



Seminar BINGO!

To play, simply print out this bingo sheet and attend a departmental seminar.

Mark over each square that occurs throughout the course of the lecture.

The first one to form a straight line (or all four corners) must yell out **BINGO!!** to win!



SEMINAR BINGO

| | | | | |
|--|---|---|--|---|
| Speaker bashes previous work | Repeated use of "um..." | Speaker sucks up to host professor | Host Professor falls asleep | Speaker wastes 5 minutes explaining outline |
| Laptop malfunction | Work ties in to Cancer/HIV or War on Terror | "...et al." | You're the only one in your lab that bothered to show up | Blatant typo |
| Entire slide filled with equations | "The data <i>clearly</i> shows..." | FREE Speaker runs out of time | Use of Powerpoint template with blue background | References Advisor (past or present) |
| There's a Grad Student wearing same clothes as yesterday | Bitter Post-doc asks question | "That's an interesting question" | "Beyond the scope of this work" | Master's student bobs head fighting sleep |
| Speaker forgets to thank collaborators | Cell phone goes off | You've no idea what's going on | "Future work will..." | Results conveniently show improvement |

JORGE CHAM © 2007

WWW.PHDCOMICS.COM

Courtesy of "Piled Higher and Deeper" by Jorge Cham
www.phdcomics.com

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

Signals



International Cytokine &
Interferon Society

9650 Rockville Pike
Bethesda, MD 20814-3998
USA