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Future ISICR Meetings

2009 Meeting
Joint ISICR/ICS/SLB
Lisbon, Portugal

2010 Meeting
Joint ISICR/ICS
Chicago, Illinois

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One on one: An Interview with Giorgio Trinchieri, Recipient of the 2008 Milstein Award

Thomas Tan

Giorgio Trinchieri received his medical degree from the University of Torino, Italy, in 1973. He was a member of the Basel Institute for Immunology (Basel, Switzerland) and an investigator at the Swiss Institute for Experimental Cancer Research (Epalanges sur Lausanne, Switzerland). From 1979 to 1999 he was at Wistar Institute in Philadelphia and became Hilary Koprowski Professor and Chairman of the Immunology Program; he was also Wistar Professor of Medicine at the University of Pennsylvania. He then served as director of the Schering Plough Laboratory for Immunological Research in Dardilly, France, and an NIH Fogarty Scholar at the Laboratory for Parasitic Diseases, NIAID, before becoming director of the Cancer and Inflammation Program (CIP) and Chief of the Laboratory of Experimental Immunology at NCI in August 2006. As CIP director, he oversees the operations of two major NCI intramural laboratories, the Laboratory of Experimental Immunology and the Laboratory of Molecular Immunoregulation. These two laboratories constitute the major immunologic component of the inflammation and cancer initiative, which spans the NCI's campuses in Frederick and Bethesda and seeks to partner NCI's expertise in inflammation and immunology with its cutting-edge cancer etiology and carcinogenesis program. He has been interested for many years in the interplay between inflammation/innate resistance and adaptive immunity, and in the role of pro-inflammatory cytokines and interferons in the regulation of hematopoiesis, innate resistance and immunity. In 1989, his group at the Wistar Institute discovered Interleukin-12 (IL-12), and he has spent many years characterizing the molecular mechanisms of IL-12 production and action, and the role of this molecule in tumor immu-

(continued on page 2)

*(**Giorgio Trinchieri**, cont. from page 1)*

immunity, infections and autoimmunity. His main focus of research is now the role of inflammation, innate resistance, and immunity in carcinogenesis, cancer progression, and prevention or destruction of cancer.

Questions:
1. Congratulations on receiving this year's Milstein Award. How did you become involved in IL-12 research?

In 1985, my laboratory at the Wistar Institute had just identified that the so-called Differentiation Inducing Factor, which was able to induce differentiation of immature myeloid cells as well as activation of monocyte/macrophages and neutrophils, was not a single factor but rather the combination of different cytokines, particularly IFN gamma as well as tumor necrosis factor and lymphotoxin. In order to continue these studies, we decided to purify lymphotoxin to homogeneity from the supernatant of a human EBV-transformed cell line, RPMI 7788, that was producing large amounts of this cytokine. In a separate line of research, we were using in the laboratory the same cell line as a potent stimulus for the expansion of human Natural Killer (NK) cells and we had identified that the supernatant of that cell lines contained a factor that we called NK cell stimulatory factor (NKSF), able to enhance NK cell cytotoxic activity and to induce IFN-gamma production from NK cells. NKSF was different from the two factors that we have previously discovered to be potent NK cell activators, type I IFN and IL-2. Thus, when a senior post-doc in my laboratory, Dr. Michiko Kobayashi, started the purification of lymphotoxin, I decided to test the fractions for NKSF activity. The first gel filtration fractionation did not separate lymphotoxin from NKSF but a subsequent MonoQ fractionation clearly showed that the two activities were due to distinct proteins. It was only because of Michiko's technical ability and perseverance that NKSF/IL-12 was then purified to homogeneity, shown to be the first described heterodimeric cytokine, and the two chains sequenced. Then, with the instrumental help of Dr. Stan Wolf at Genetics Institute, the two genes encoding IL-12 were cloned.

2. What disease indications do you think would best benefit from therapies targeting IL-12?

As for many cytokines, the road to the clinical use of IL-12 has been rocky with several sad failures in the early clinical trials. Presently, most pharmaceutical companies that have acquired the rights for IL-12 have abandoned the development of IL-12 as a drug after many disappointing attempts in cancer therapy, HIV, HCV, and vaccination for infectious diseases. Still, a NCI appointed panel have recently identified IL-12 as one of the top three most promising biologics for cancer therapy and NCI is coordinating further trials in cancer therapy of IL-12 as a single agent therapy or in combination with other agents, e.g. IL-2. IL-12 still offers a potential usefulness as vaccine adjuvant, not only in cancer vaccines but also in vaccines for infectious diseases, both prophylactic and therapeutic, due to its potent activity as an inducer of IFN-gamma production and of Th1 responses, as well as its ability to favor the generation of memory and effector cytotoxic T cells. But most promising, rather than the use of IL-12 as a drug, is the therapeutic use of IL-12 antagonists, particularly monoclonal antibodies. IL-12 plays an important role in autoimmunity as an inducer of Th1 responses but it was more recently discovered that the potent ability of anti-IL-12 antibodies to reverse many experimental models of autoimmune diseases was due to the ability of the antibodies to neutralize not only IL-12 but also IL-23, a cytokine sharing the p40 chain with IL-12 and important for endowing the recently discovered Th17 cells with pathogenic activity. Antibodies against IL-12 p40 (thus neutralizing both IL-12 and IL-23) have been found to be dramatically effective in clinical trials against psoriasis and colitis and have a potential to replace anti-TNF antagonists as first line therapy in these and possibly other autoimmune diseases.

3. Who was your mentor or role model in your scientific career?

In a scientific career that it is now more than 40 years, I have been in contact with many investigators, colleagues, and friends who have deeply affected my vision and approach to science. Mentors have been important but I do not believe in role models, rather I think it is the daily interaction with every-

*(**Giorgio Trinchieri**, cont. from page 2)*

body in the laboratory as well as collaborators that shape us as scientists and thinkers. The relationship with collaborators, postdoctoral fellows, students, and technicians is really two-way and I think one learns from each of them as much or more than one gives to them. I treasure all those personal interactions more than any scientific accomplishment or success in my career. When I was a young medical student and Prof. Ruggero Ceppellini in 1967 asked me to volunteer as a student in his Institute of Medical Genetics in Turin, it was like he was reading the dreams in my mind. Ruggero taught me to be enthusiastic for scientific discovery, always keeping in mind the medical applications of my work and he gave me a strong interest in human genetics that never left me even when the focus of my work was far from genetics. When I moved to Basel Dr. Niels Jerne taught me to recognize the forest from the trees and that ideas, not technologies, should drive the scientific quest. At the Wistar Institute, Dr. Hilary Koprowski taught me how it is important to recognize that similar immunopathogenetic mechanisms are involved in viral and bacterial infections, cancer, and autoimmunity and the enthusiasm for interdisciplinary and translational research that I learned from him has deeply influenced my scientific work. More recently my dear friend Dr. Alan Sher has tried to make a parasitologist out of me; it was tempting and he almost but not quite succeeded, it is not easy to teach new tricks to an old dog.

4. If you weren't a scientist, what would you be?

I think that the spirit of research is innate and I do not remember even as a child to dream something different. However, what to research is a different question, and I think Anthropology or Archeology was maybe even more attractive for me than Medicine or Immunology.

5. What do you like to do in your spare time?

I like to read, mostly history, archeology, politics, and philosophy. When I can, I like to walk to visit prehistoric or historical sites and I am still very enthusiastic about cave exploration. I did a lot of that when I was a teenager, then with my sons, and now with my granddaughters: not as physically challenging explorations as before but still a lot of fun and one of the occasions to spend as much of my free time as possible with my family.

6. Torino is famous for many things: Fiat (Fabbrica Italiana Automobili Torino), Juventus FC (the great Italian soccer team), and Lavazza (Italy's largest coffee roaster). What do you miss the most about Italy in general now that you're living in Frederick/Bethesda?

I moved from Italy in 1970 but I still like to go back there for vacation every year. I enjoy the culture, the history as well as the food and the wine. But my entire scientific career was outside Italy and I found the challenging and competitive scientific environment in the U.S. the most stimulating I have experienced.

7. What are some of the main differences between the Schering-Plough Laboratory for Immunological Research in France, DNAX and NCI in terms of their respective research environment and culture?

Through the years I have experienced many different research environments in different countries: universities, independent or company-supported research institutes, and intramural NIH centers. To be honest, I mostly miss the academic environment, the interaction with students is always very stimulating and the continuous search for grants and funding might be stressful but really makes one feel that only one's own ability and productivity are eventually important in establishing a successful research group. The independent research institutes offer an environment very similar to the academic one with the advantage of leaving to the investigators' discretion how much time, if any, to devote to teaching and how much to research. The company-supported research institutes can be very exciting scientifically but their environment is very transient and the supporting company may not always let the investigators free to fully pursue their scientific interest. Both the Basel Institute of Immunology and the LIR were at a time extremely challenging places and I spent several wonderful and productive years working in them, but both were eventually shut down by the companies supporting them. The company-supported research institutes are an endangered species and, as all other endangered species are not faring very well in the

*(**Giorgio Trinchieri**, cont. from page 3)*

present economical environment. The NIH intramural program is wonderful because of its unique collection of world-class investigators and the almost unlimited possibilities of collaborations and utilization of state of the art technologies. A bureaucracy that does not always seem to have as its primary scope that of facilitating rapid scientific progress and the lack of the competitive system that drives academic research are the only drawbacks of this otherwise incredibly challenging intellectual and technological environment.

8. What advice would give to those who are contemplating a career in academia versus industry?

They are two different worlds that may be differentially attractive for different investigators. Industry may offer a much better environment and resources for anybody interested in drug discovery and development. These opportunities are not usually offered by academic institutions and only in a very limited way by NIH. Investigators with a very technological interest are also likely to be more successful and better recognized and rewarded in an industry environment. The possibility to pursue drug discovery with generous resources is what attracted me to Schering Plough. However, I found that it is not always possible in industry to combine drug discovery studies with in depth analysis of the biology behind those studies. Also, the freedom of the investigators may be limited and often projects are initiated or abruptly terminated for non-scientific reasons. Smaller biotech companies may offer extremely exciting and challenging environments but again this can be very transient and the investigators in these companies often move very frequently from one company to another. Working in an academic and in an industry environment indeed requires different qualities and the career decision should be made early based on each person's interest and ability; moving to industry because of failure in an academic environment is unlikely to be a good path for a successful career. There are attempts to establish not-for-profit research centers with a strong emphasis on drug discovery and medicinal chemistry. Similar initiatives are also taking places in academic institutions and at NIH. These attempts should be looked upon with interest because they may allow new investigators to pursue careers in treatment-focused and drug discovery research outside industry.

9. What was your role as an NIH Fogarty Scholar at the Laboratory for Parasitic Diseases, NIAID?

I had no administrative responsibilities and it was a wonderful occasion to spend a sabbatical year interacting intellectually with many investigators in the Laboratory and at NIH at large. That gave me a great opportunity to meet and know well many of the NIH scientists that are now my colleagues and collaborators.

10. What are your current priorities as director of CIP at NCI?

In addition to my own research group, I have been given the mission to bring together the 15 senior investigators in the Program and the new recruits to work in a coordinated and interactive way to address the mechanisms underlying the role of inflammation and immunity in controlling tumor initiation, promotion, progression, and dissemination, with the eventual objective to identify therapeutic targets for cancer prevention and treatment.

11. What do you see as the most exciting new development in the field of cancer and inflammation, one which we could realistically harness or manipulate for therapeutic purposes in the not-too-distant future?

One of the important effects of the inflammatory microenvironment that allows or favors cancer progression is the creation of an altered immunological environment in which tumor growth and angiogenesis are stimulated but the development of an effective anti-tumor immunity is prevented. Many of the immunological checkpoints responsible for tumor-mediated immunosuppression have been identified and drugs targeting them are being developed or already being tested in clinical trials in association with other immunotherapeutic or chemotherapy approaches. Other mechanisms involved in cancer initiation or early promotion are also likely to be identified that could be targeted for cancer prevention or adjuvant therapy of minimally residual tumors. Progress in this latter aspect of therapeutic

*(**Giorgio Trinchieri**, cont. from page 4)*

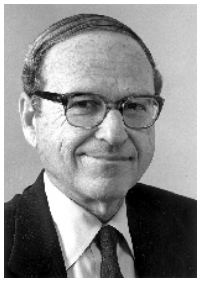
targeting of inflammation-related molecules in cancer prevention is however, expected to be slower.

12. Who would you thank if there was an acceptance speech at the Milstein award ceremony?

No scientific achievement is possible without a team effort for which every member of the team deserves full credit. Thus, the award really recognized the work of all my past collaborators, especially those who were directly involved in the discoveries of Interleukin-12 and of the plasmacytoid Dendritic cells / IFN-producing cells for which the award was given. Personally, I would like to thank my family for bearing with me and always encouraging and supporting me and particularly my wife Simonetta for always reminding me "to just snap out of it" each time I am becoming really obnoxious.

2009 ISICR Awards

The Seymour and Vivian Milstein Award



Seymour Milstein (1920-2001)

Individuals who have made exceptional contributions to research related to interferons and cytokines either in a basic or clinical field. The Seymour and Vivian Milstein awards are made possible by the generous gift of the Milstein family. This award represents a pinnacle of scientific achievement in our field and is an important landmark of the society. Nominations should be communicated to the President of the ISICR by **April 1, 2009** (see below).

Honorary Membership

Nominees should be 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.

We invite your nominations for eligible candidates for The Seymour and Vivian Milstein Award and Honorary Membership, both prestigious symbols of recognition by our society for outstanding achievements. A brief (one to two page) description of the reasons for your nomination and the CV of the nominee should be sent to the ISICR President by **April 1, 2009**:

Eleanor N. Fish, Ph.D.
Canada Research Chair in Women's Health & Immunobiology
Professor, Dept. of Immunology, University of Toronto
67, College Street, Rm. 424
Toronto, Ontario M5G 2M1
Tel: 416 340-5380
FAX: 416 340-3453
e-mail: en.fish@utoronto.ca

The nominations will be collated, and passed on to the Chair of the Awards Committee in April. This committee will then vote for the winners. As specified in the ISICR Constitution, the final vote of the Awards Committee is subject to the approval of the ISICR Board of Directors.

New ISICR Logo

The ISICR has a new logo, courtesy of PBL Biomedical. Many thanks to PBL for providing us with numerous versions for which to select the new society logo.

ISICR
International Society for Interferon & Cytokine Research

NEW ISICR MEMBERS

We welcome these members into the ISICR and look forward to their participation in the ISICR annual meetings and ISICR committees

Mohamed Abdel-Hakeem
Univ of Montreal, Montreal, Canada

Farnam Ajamian
Univ of Alberta, Alberta, Canada

Sebastien Anguille
Univ of Antwerp, Edegem, Antwerp, Belgium

Corey Balinsky
Nat. Inst. Allergy & Infectious Disease, Bethesda, MD

Jennifer Bharucha
NCI-Frederick, Frederick, MD

Catarina Ramo Do Carmo
Imperial College London, United Kingdom

Hui-Chen Chen
Stony Brook Univ, Stony Brook, NY

George Christophi
Upstate Med Univ, Syracuse, NY

Jennifer Drahos
Columbia Univ, New York, NY

Brian Doehle
Univ of Washington, Seattle, WA

Seamus Duffy
Murdoch Univ, Perth, Australia

James Ellison
Auburn Univ, Auburn, AL

Xuan Feng
Univ of Chicago, Chicage, IL

Adriana Filip
Univ of Med & Pharmacy-Iuliu Hatieganu, Cluj - Napoca, Romania

Sinead Flannery
Trinity College, Dublin, Ireland

Claudia Gherman
Univ of Med & Pharmacy-Iuliu Hatieganu, Cluj - Napoca, Romania

Jennifer Gommerman
Univ of Toronto, Toronto, Canada

Geetanjali Gupta
All India Inst of Med Sci, New Dehli, India

Ole Hamming
Aarhus Univ, Aarhus, Denmark

Wei-Chun Huangfu
Univ of Pennsylvania, Philadelphia, PA

Katharine Irvine
Univ of Queensland, Queensland, Australia

Lionel Ivashkiv
Hospital for Special Surgery, New York, NY

Youngtae Jeong
Johns Hopkins Univ Sch of Med, Baltimore, MD

Michael Jones
Shenandoah Biotechnology, Monroe, OH

Joachim Kaysser
Artimmun Analytik, Kelkheim, Germany

*(**New Members**, cont. from page 6)*

Helle Kristiansen
Univ of Aarhus, Aarhus, Denmark

Virginia Maina
Istituto Clinico Humanitas, Milano, Italy

Nicholas Megjugorac
Humigen, Hamilton, NJ

Karoly Mirnics
Vanderbilt Univ, Nashville, TN

Reem Mohammed
Inst of Endemic Diseases, Khartoum, Sudan

Jayaseelan Murugaiyan
Helmholtz Ctr for Envrn Rsch-UFZ,
Leipzig, Bermany

Yoshihiro Okamoto
Chiba Inst of Sci, Choshi, Japan

Anna Overby
Univ of Freiburg, Freiburg, Germany

Shripad Patil
NIH/NIMHANS, Bangalore, India

Dean Pemberton
Murdoch Univ, Perth, Australia

George Perros
Applied Data Rsch, Amherst, NH

Chiara Porta
Istituto Clinico Humanitas, Milano, Italy

Erin Rogerss
Univ of Toronto, Toronto, Canada

Saleela Ruwanpura
Monash Inst of Med Rsch, Clayton, Australia

Monika Sachet
Univ of Vienna Med Sch, Vienna, Austria

Ayca Sayi
Univ of Zurich, Zurich, Switzerland

Fredy Siegrist
F Hoffmann-La Roche Ltd, Basel, Switzerland

Suzanne Thibodeaux
Univ. Texas Heal. Sci. Ctr, San Antonio, TX

Emmanuel Thomas
NIDDK, Bethesda, MD

Cristina Tomas Do Santos
Imperial College London, London, United Kingdom

Elena Shestakova
Lady Davis Inst for Med Rsch, Montreal, Canada

Katrina Sutton
Imperial College London, London, United Kingdom

Joanna Wegrzyn
Virginia Commonwealth Univ, Richmond, VA

Christopher Woelk
Univ of California - San Diego , San Diego, CA

Mumtaz Yaseem
Johns Hopkins Sch of Med, Baltimore, MD

Sherrie Zhang
Biolegend, San Diego, CA

Ying Zheng
Univ of Alabama at Birmingham, Birmingham, AL

Fanxiu Zhu
Florida State Univ, Tallahassee, FL

New Member Minibios

Reem Khalil Bairam

Department of Parasitology, Institute of Endemic Diseases
University of Khartoum
Khartoum,Sudan

Miss Reem Khalil obtained her B.S. (honor) from Faculty of Science, University of Khartoum in 2004. She joined the Institute of Endemic Diseases in 2006 for her postgraduate studies. Now she is finishing her M.S. study project which is focused on the mechanisms of immune responses to human malaria. This includes the study of cytokine profiles during the course of malaria infection and its relation to humoral immune responses, mainly IgE antibody responses.

Xuan Feng, Ph.D.

Research Assistant Professor
Department of Neurology/MC-2030
The University of Chicago
5841 South Maryland Avenue
Chicago, IL 60637 USA

Xuan Feng received her medical training in China. She obtained her Ph.D. in Microbiology and Immunology (advisor Dr. Gretchen Caughman) at Medical College of Georgia (USA), where she characterized the equine herpesvirus type 1 virion-associated host shutoff homolog gene. Her postdoctoral research, with Dr. Anthony Reder at University of Chicago and with Dr. Lee Ratner at Washington University School of Medicine, focused on (1) Gene therapy in animal models for Alzheimer's disease and neuroblastoma with adenovirus and adeno-associated viruses; (2) Identification of a fundamental defect in type I IFN signaling that disrupts immune regulation in clinically progressive multiple sclerosis (MS); (3) Virus and tumor resistance to IFN in an animal model of HTLV-1 infection and in a clinical trial of adult T cell leukemia (HTLV-1 induced ATL). She found that IFN-inhibits HTLV-1 viral replication by blocking viral assembly and release. She also selected and characterized IFN-resistant variants in HTLV-1 infected cells, and how HTLV-1 inhibits IFN signaling by blocking phosphorylation of STAT1, STAT2, and Tyk2. Dr. Feng is now investigating how drugs such as statins interfere with IFN signaling in immune cells, and the mechanism underlying type I IFN resistance in MS. She also has interests in identifying MS-associated viruses and their roles in MS pathogenesis and treatment.

Károly Mirnics

Associate Professor of Psychiatry
Vanderbilt University
8130A MRB III, 465 21st Avenue
South Nashville, TN 37232, USA
http://mirnicslab.vanderbilt.edu/mirnicslab/

Károly Mirnics obtained his medical degree from University of Novi Sad, Yugoslavia. He established his independent research laboratory in 2000 at University of Pittsburgh. The research of this laboratory focuses on immune transcriptome changes across human brain disorders, including schizophrenia, autism, MS and major depression. Furthermore, his research team also uses various animal models to understand the effects of prenatal immune activation on brain development and behavior.

Dr Katrina Sutton

Post-doctoral fellow
Lung Cancer Signal Transduction Group
Molecular Oncology
Division of Surgery, Oncology, Reproductive Biology and Anaesthetics Imperial College, London, W12 0NN

Katrina Sutton was awarded her PhD from the University of London in 2004. Katrina undertook her post-graduate studies at the Institute of Cancer Research in the department of Cancer Research UK Centre for Cancer Therapeutics, under the supervision of Dr. Margaret Ashcroft. During her time at the Institute of Cancer Research she investigated the role of ERK1/2 signalling in the regulation of HIF-1 in

*(**Minibios**, cont. from page 8)*

response to hypoxia and growth factor treatment and identified that ERK1/2 were required for the upregulation of HIF-1 protein in response to IGF-1. Katrina then went on to complete a post-doctoral position at the Kennedy Institute of Rheumatology, under the supervision of Dr Toby Lawrence, where she investigated the role of the alternative NF-κB signaling in the regulation of dendritic cell maturation. Katrina is currently a post-doctoral fellow at Imperial College London under the supervision of Dr Ana Costa-Pereira. She is presently investigating the regulation of the IFN-γ like response induced by IL-6 in the absence of STAT3.

Emmanuel Thomas, M.D., Ph.D.

Research Fellow
Liver Diseases Branch
NIDDK-NIH
Bethesda, Maryland, USA

Dr. Emmanuel Thomas received his medical and scientific training at the University of Miami School of Medicine in Miami, FL. His Ph.D. training was conducted in the Department of Microbiology and Immunology under Dr. Glen N. Barber, and focused on the identification of genes involved in the innate immune antiviral response. After completing his doctoral studies, he participated in the Doris Duke Clinical Research Fellowship under the mentorship of Dr. Michael W. Fried at University of North Carolina Chapel Hill. During this fellowship, Dr. Thomas designed and implemented clinical research protocols aimed at increasing our understanding of the mechanism of action of ribavirin in antiviral therapy against Hepatitis C. He is currently continuing this work in the Liver Diseases Branch at the National Institutes of Health in the lab of Dr. T. Jake Liang as a research fellow.

Christopher Woelk

Assistant Professor
Division of Medical Informatics
Department of Medicine UCSD
San Diego, CA
858-552-8585 extn 7193
http://woelklab.ucsd.edu/

Christopher Woelk is currently an Assistant Professor in the Division of Medical Informatics at the University of California San Diego (UCSD) and is also the Director of the Genomics Core at the UCSD Center for AIDS Research (http://cfar.ucsd.edu/). Previously, he received his B.S. in Biochemistry and Genetics from Nottingham University in the United Kingdom and his Ph.D. from the University of Oxford. He recently joined the ISICR because he has a number of research projects in the cytokine field. Specifically, he is on the hunt to identify more IFN-stimulated host factors with anti-HIV properties and he also studies the evolutionary relationships of IFN molecules across species to better understand how this cytokine has adapted to host defense. There is currently a postdoctoral position open in his lab. Please visit http://woelklab.ucsd.edu/ for more details.

Dr. Mumtaz Yaseen, PhD

Postdoctorate fellow at the Johns Hopkins School of Medicine
Dept. of Viral Oncology and Genetics
Baltimore MD 21213

Dr. Mumtaz Yaseen Balkhi received his PhD from Ludwig Maximillian University (LMU), Munich, Germany in 2007. The topic of the thesis was entitled "Proteomics of Acute Myeloid Leukemia: Cytogenetic Risk Groups Differ Specifically in Their Proteome, Interactome and Posttranslational Protein Modification". The study was based on the idea that proteome of different AML subtypes may be a discriminatory criteria for either treatment induction or measuring disease survival. Moreover, the proteomic analysis discovered survivin as a target of the AML1/ETO fusion protein. The results confirmed for the first time that AML1/ETO directly activates the basal transcription of the survivin gene. Knockdown

*(**Minibios**, cont. from page 9)*

of survivin showed that AML1-ETO mediated inactivation of master myeloid regulator C/EBP alpha biological activity could be restored. This drives myeloid leukaemia cells to terminal differentiation and growth arrest. The reason for joining the ISICR, "my postdoctoral work is focused on investigating the interferon regulatory factor (IRF5) signalling pathways from TLR7/9 and we discovered that IRF5 undergoes K63 linked ubiquitination through the TLR-MyD88-TRFA6-IRAK1 signaling pathway. To understand the transcriptional regulation, we are studying the chromatin modification of histone-like phosphorylation, acetylation and H3K4me3 of the IRF5 enhancesome. Joining the ISICR will provide a good platform for finding related positions and for interaction with other groups".

Members in the News

UW receives nearly $17 million to study emerging respiratory viruses

By Leila Gray
News & Community Relations


Michael Katze

The National Institute of Allergy and Infectious Diseases, one of the National Institutes of Health, has awarded a contract to the UW to use systems biology approaches to comprehensively analyze and model the virus-host interactions and cellular response networks that are induced or altered during the course of acute respiratory virus infection.

This new research program will be led by Michael Katze, UW professor of microbiology and associate director of the Washington National Primate Research Center. Katze will head a multidisciplinary team of researchers from the UW, University of Wisconsin-Madison, University of North Carolina, Oregon Health & Science University, and Pacific Northwest National Laboratory in Richland, Wash. The team will receive about $17 million over five years for the development of computational models of the host response to H5N1 avian influenza virus ("bird flu") and severe acute respiratory syndrome (SARS) associated coronavirus, two highly pathogenic respiratory viruses that represent significant threats to human health and the global economy. These models will be premised on the acquisition of large datasets through high-throughput genomic, proteomic, and metabolomic technologies, using samples from a variety of biological model systems.

The goal is to generate predictive models that can be experimentally validated in an in vivo setting and which will reveal whether influenza and SARS viruses use common strategies to regulate cellular signaling circuitry and evade antiviral defenses. In addition, these large datasets, as well as the modeled interpretations, will be made freely available to the research community via the Internet, thus providing powerful resources for other scientists exploring viral diseases. Systems biology provides global views, or models, of the vast numbers of molecular components and interactions that make up complex functions inside living things. The UW research program is unusual in that, in addition to the traditional simple cell culture models, it will also use mouse and nonhuman primate infection models. These animal models will allow researchers to study disease-relevant complexities, Such information is likely to help translate findings into new clinical initiatives, including new targets for therapeutic intervention. Understanding the initial, innate, antiviral response also has potential in developing alternative vaccine strategies, where such early signals are exploited to induce more robust adaptive immune outcomes. "This program is distinctive in its comparison of different respiratory viruses and the incorporation of animal models," said Katze. "There are few antiviral drugs available and none that work against diverse types of viruses. It would be extremely beneficial to have information that could lead to the rational design of a drug that could be used against a range of different viruses."

INTERFEROME

INTERFEROME is an open access database of types I, II and III Interferon regulated genes (http://www.interferome.org) collected from analyzing expression data sets of cells treated with IFNs. This database of interferon regulated genes integrates information from high-throughput experiments with annotation, ontology, orthologue sequences from 37 species, tissue expression patterns and gene regulatory information to enable a detailed investigation of the molecular mechanisms underlying IFN biology. INTERFEROME fulfils a need in infection, immunity, development and cancer research by providing computational tools to assist in identifying interferon signatures in gene lists generated by high-throughput expression technologies, and their potential molecular and biological consequences.

url: www.interferome.org
link to paper:
PMID: 18996892
http://nar.oxfordjournals.org/cgi/content/full/gkn732v1

There is a lack of bioinformatics resources available for cytokine biologists and INTERFEROME was one of the tools I built to help analyze interferon related microarray/proteomic data sets. Its main function is to identify interferon signatures in high throughput experiments. We've already started working on the next version which will have additional functionality.

To expand the capabilities of interferome we need the interferon community to submit high-throughput datasets to be included in INTERFEROME:

1. microarray or proteomic data from IFN treated (TYPE I,II OR III) cells tissues

2. microarray data from IFN treatment in disease situations (viral infections, cancer, multiple sclerosis, lupus etc)

3. STAT or IRF Chip-ChIP or ChIP-Seq datasets

Other issues with which the ISICR membership may be able to help:

1. Help building interferon regulated gene networks - These networks will help identify how these 2000 IRGs we identified mediate interferon biology. If the IFN community used its collective knowledge, building the IRG network isn't going to be hard. Resources like wikipathways (http://www.wikipathways.org/index.php/WikiPathways) may be useful.

2. Gene nomenclature issues -there are at least 50+ IRGs without a gene name and most IRGs have more than 20 names

Our database is a community resource and there is potential for it's capabilities to increase with the involvement of the interferon community. We look forward to input from the ISICR membership.

Kind regards,
Shamith

Shamith Samarajiwa BSc.(Biomedical) (Hons.) PhD.
Computational Biology Group, Department of Oncology, University of Cambridge

Cancer Research UK Cambridge Research Institute
Li Ka Shing Centre
Robinson Way, Cambridge CB2 0RE, England

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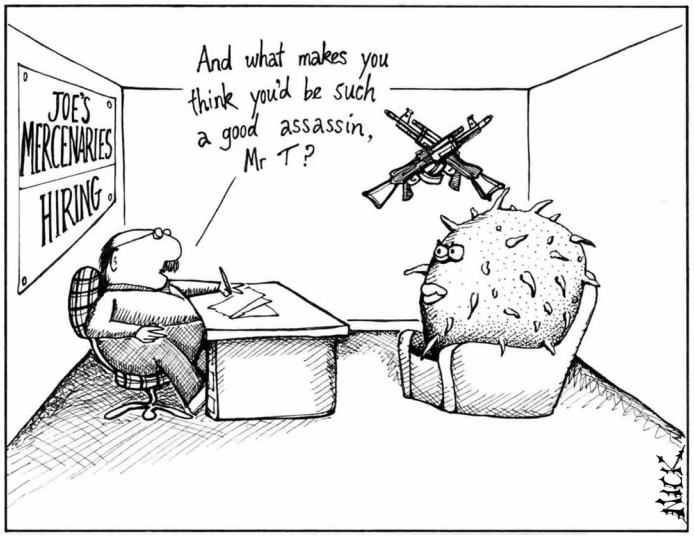

As each disease is finally eradicated, redundant lymphocytes increasingly find themselves looking for other work.

Cartoon by Nick D Kim, nearingzero.net. Used by permission. This image is available in the ISICR slide repository.

Clinical Trials

http://clinicaltrials.gov/ct2/home

Interferon-Alpha Lozenges for Prevention of Relapse in Hepatitis C. Sponsors and Collaborators: Amarillo Biosciences, Inc. CytoPharm, Inc. ClinicalTrials.gov Identifier: NCT00695019

Capecitabine and **Interferon-Alpha** in Metastatic Renal Cell Carcinoma Patients With Failure on Interleukin-2 Based Regimens. Sponsored by: Kidney Cancer Research Bureau Contact: Ilya V. Tsimafeyeu, MD +79265646581 office@kidneytumor.org Natalia N. Petenko, MD +74953249004 petenko@kidneytumor.org ClinicalTrials.gov Identifier: NCT00591188

Interferon-Gamma With **Interferon Alpha** and Ribavirin for Hepatitis C Non-Responders. Sponsored by: Aga Khan University Contact: Zaigham Abbas, FCPS, FACG +92-21-4930051 zaigham@akunet.org ClinicalTrials.gov Identifier: NCT00538811

Study of PEG-rIL-29 (or **PEG-IFN Lambda**) in Subjects With Chronic Hepatitis C Virus Infection. Sponsored by: ZymoGenetics Contact: Sherri Souza (206) 434-4702 seso@zgi.com. ClinicalTrials.gov Identifier: NCT00565539

Treating Patients With Childhood Acute Myeloid Leukemia With **Interleukin-2.** Sponsors and Collaborators: Assistance Publique - Hôpitaux de Paris Chiron Corporation. Principal Investigator: Guy Leverger, M.D. Department of Pediatrics Hematology, Children Armand Trousseau Hospital, 26 Avenue Arnold Netter, 75012 Paris. ClinicalTrials.gov Identifier: NCT00149162

Ultra-Low Dose **Interleukin-2** for Refractory Chronic Graft Versus Host Disease. Sponsors and Collaborators: Dana-Farber Cancer Institute,Brigham and Women's Hospital, Novartis. Principal Investigator: John Koreth, MBBS, D.Phil Dana-Farber Cancer Institute. ClinicalTrials.gov Identifier: NCT00529035

Interferon Alfa and **Interleukin-6** in Treating Patients With Recurrent Multiple Myeloma. Sponsors and Collaborators: Sidney Kimmel Comprehensive Cancer Center National Cancer Institute (NCI) Study Chair: Carol A. Huff, MD Sidney Kimmel Comprehensive Cancer Center ClinicalTrials.gov Identifier: NCT00470093

Interleukin-7 in Treating Patients With Metastatic Melanoma or Locally Advanced or Metastatic Kidney Cancer. Sponsors and Collaborators: NCI - Center for Cancer Research-Medical Oncology National Cancer Institute (NCI) Study Chair: Steven A. Rosenberg, MD, PhD NCI - Surgery Branch. ClinicalTrials.gov Identifier: NCT00492440

Radiolabeled Monoclonal Antibody Plus Rituximab With and Without Filgrastim and **Interleukin-11** in Treating Patients With Relapsed or Refractory Non-Hodgkin's Lymphoma. Sponsors and Collaborators: Mayo Clinic National Cancer Institute (NCI) Study Chair: Thomas E. Witzig, MD Mayo Clinic Investigator: Gregory Wiseman, MD Mayo Clinic. ClinicalTrials.gov Identifier: NCT00012298

Interleukin-12 Gene in Treating Patients With Liver Metastases Secondary to Colorectal Cancer. Sponsors and Collaborators: Mount Sinai School of Medicine.National Cancer Institute (NCI) Principal Investigator: Max W. Sung, MD Mount Sinai School of Medicine. ClinicalTrials.gov Identifier: NCT00072098

A Phase I, Dose-Escalation Study to Assess the Safety and Biological Activity of Recombinant Human **Interleukin-18.** Sponsored by: GlaxoSmithKline Study Director: GSK Clinical Trials, MD GlaxoSmithKline. ClinicalTrials.gov Identifier: NCT00500058

Combination Study Of SB-485232 (**Interleukin 18**) And Doxil For Advanced Stage Epithelial Ovarian Cancer. Sponsored by: GlaxoSmithKline Study Director: GSK Clinical Trials, MD GlaxoSmithKline. ClinicalTrials.gov Identifier: NCT00659178

Interleukin-21 in Treating Patients With Metastatic or Recurrent Malignant Melanoma. Sponsored by: National Cancer Institute of Canada Study Chair: Teresa M. Petrella Edmond Odette Cancer Centre at Sunnybrook. ClinicalTrials.gov Identifier: NCT00514085

AMAZINGLY SIMPLE HOME REMEDIES

1. A mouse trap, placed on top of your alarm clock, will prevent you from rolling over and going back to sleep after you hit the snooze button.

2. If you have a bad cough, take a large dose of laxatives, then you will be afraid to cough.

3. Clumsy? Avoid cutting yourself while slicing vegetables by getting someone else to hold them while you chop away.

4. Avoid arguments with the Mrs. about lifting the toilet seat. Simply use the sink.

5. For high blood pressure sufferers: simply cut yourself and bleed for a few minutes, thus reducing the pressure in your veins. Remember to use a timer.

6. Have a bad toothache? Smash your thumb with a hammer and you will forget about the toothache.

Sometimes, we just need to remember what the rules of life really are: You only need two tools: WD-40 and Duct Tape. If it doesn't move and should, use the WD-40. If it shouldn't move and does, use the Duct Tape.

Remember:

* Everyone seems normal until you get to know them.
* Never pass up an opportunity to go to the bathroom.
* If you woke up breathing, congratulations! You get another chance.

And finally, be really nice to your family and friends; you never know when you might need them to empty your bedpan.

Reviews of Interest

Finley MJ, Happel CM, Kaminsky DE, Rogers TJ. Opiold and nociceptin receptors regulate cytokine and cytokine receptor expression. *Cellular Immunol*. 252: 146-154, 2008

Fontana JM, Bankamp B, Rota PA. Inhibition of interferon induction and signaling by paramyxoviruses. *Immunological Rev*. 225: 46-67, 2008

Girnita DM, Burckart G, Zeevi A. Effect of cytokine and pharmacogenomic genetic polymorphisms in transplantation. *Current Opinion Immunology* 20: 614-625, 2008

Kelchtermans H, Billiau A, Matthys P. How interferon-γ keeps autoimmune diseases in check. *Trends in Immunology* 29: 479-486, 2008

Kim EY, Moudgil KD. Regulation of autoimmune inflammation by pro-inflammatory cytokines. *Immunology Lett*. 120: 1-5, 2008

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Li MO, Flavell RA. TGF-beta: A master of all T cell trades. *Cell* 134: 392-404, 2008

Lu R. Interferon regulatory factor 4 and 8 in B-cell development. *Trends in Immunology* 29: 487-492, 2008

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Mumm JB, Oft, M. Cytokine-based transformation of immune surveillance into tumor-promoting inflammation. *Oncogene* 27: 5913-5919, 2008

O'Connor JC, McCusker RH, Strle K, Johnson RW, Dantzer R, Kelley KW. Regulation of IGF-I function by proinflammatory cytokines: At the interface of immunology and endocrinology. *Cellular Immunol*. 252: 91-110, 2008

*(**Reviews of Interest**, cont. from page 13)*

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Seruga B, Zhang H, Bernstein LJ, Tannock IF. Cytokines and their relationship to the symptoms and outcome of cancer. *Nat Rev Cancer* 8:887-999, 2008

Xu H, Zhang G-X, Ciric B, Rostami A. IDO: A double-edged sword for T_H1/T_H2 regulation. *Immunology Lett*. 121:1-6, 2008

Lymphodrek and Hollywood?

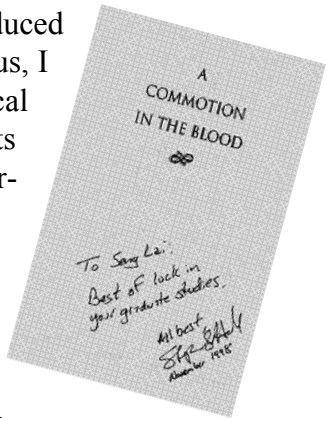
By Thomas Tan

In the 2007-08 Annual Report for the Feinstein Institute for Medical Research it asks: What gives rise to a scientist? "For some, it begins with an idea in childhood: A puzzle to be pieced together to solve a medical mystery. For others, it is sheer fate in young adulthood: A stint at the lab bench that stirs the desire to understand a particular disease and commit to a life of serving science. It is the excitement--the chance for one "eureka" moment promised in each new day--that comes to define the life of a researcher. They know science is a slow process, but they are pushed forward day after day believing that the ultimate dividends could be big."

Check out these 'non-fiction' books written on interferon and cytokine drug discovery and the stories of many such scientists. But don't hold your breath for Hollywood to adopt any of these books for the big screen!

1. **A Commotion in the Blood: Life, Death, and the Immune System**, by STEPHEN S. HALL. 544 pp. New York, Henry Holt, 1997

I first read this book when I was a graduate student. I was researching on molecular mechanisms of viral evasion of the interferon-induced protein kinase, PKR, and thus, I was interested in the historical background and the scientists behind the discovery of interferon. Although only one (appropriately entitled 'The Patron Saint of Cytokines') of the four major chapters recounts the saga of interferon and other cytokines, A Commotion in the Blood remains as one of my favorite books written about the subject because of its human drama-infused 'spy thriller' format. This book also introduced me to an old acronym "lymphodrek" used to first describe cytokines, and I remember shamelessly incorporating it in my daily research vocabulary: "I work on lymphodrek", "Hi, I am a lymphodrekie", etc. Not surprisingly, my copy of A Commotion in the Blood was personally autographed by Mr. Hall himself. Can you say 'geek'?



Product description from Library Journal: "…science journalist Hall chronicles the history of immunotherapy as a treatment for cancer. He begins with a discussion of William Coley's early attempts to treat cancer by deliberately injecting patients with a bacterial culture. He then examines numerous critical advances in the science of immunotherapy such as the discovery of cytokines and the impact of molecular genetics. Hall concludes with a lengthy review of some of the latest attempts at immunotherapy, including monoclonal antibodies, adoptive immunotherapy, and interleukin-12."

2. I**nterferon: The Science and Selling of a Miracle Drug**, by TOINE PIETERS. 264 pp. New York, Routledge, 2005

This book is a little on the pricey side ($180 for hardcover). Better deals may be found at Overstock.com ($144 per hardcover the last time I checked). I have not read *Interferon* yet, but according to Dr. Fran Balkwill of Barts and the London Queen Mary's Medical School: "Pieters

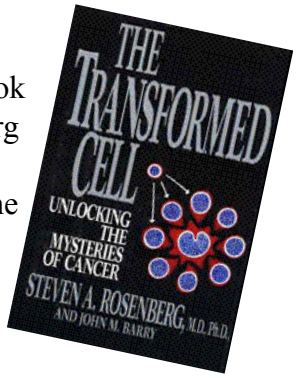
*(**Lymphodrek and Hollywood?**, cont. from page 13)*

focuses on answering one intriguing question: Why does interferon enjoy a public reputation similar to penicillin's even though it remains a treatment confined almost entirely to specialty diseases? In its answer, the book succeeds admirably."

Product description from the Publisher This innovative study charts the beginnings, history and fate of Interferon--one of modern medicine's most famous and infamous drugs. Interferon is part of the medical profession's armory against viral infection, cancer and MS. The story of its development and use is one of survival in the face of remarkable cycles of promise and disappointment as a miracle drug. By telling this story, Toine Pieters' book provides insight into the research, manufacture, and marketing of new biomolecules that mark modern medical science.

Editors note: A number of the images in this book are available as slides from the ISICR slide repository.

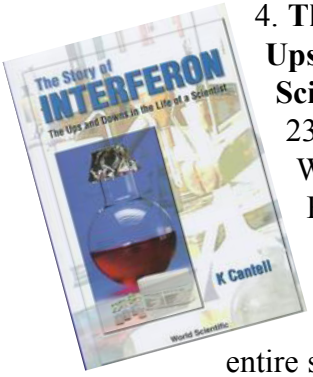
3. **The Transformed Cell: Unlocking the Mysteries of Cancer**, by STEVEN. ROSENBERG and JOHN M. BARRY. 353 pp. New York, G. P. Putnam's Sons, 1992



The blurb on the back of the book says: "In 1968, Steven Rosenberg met a patient who should have died twelve years before - but the widespread untreatable tumours in his liver and stomach had simply disappeared. His cancer, incredibly, had cured itself.

That was the beginning of his thrilling medical quest of all time, the disease that attacks one person in four. From that time on Dr Rosenberg - now Chief of Surgery at America's National Cancer Institute, and a world authority on cancers and their treatment - set out to see if immunotherapy, and later gene therapy, held answers to surgery, radiation and chemotherapy could not provide."

The Transformed Cell is the gripping story of his progress towards solving one of medicine's greatest mysteries. It describes his pioneering treatments (in which the patient's own genes are altered and then-reintroduced into the bloodstream to fight tumours), the trials, triumphs and first tentative evidence of success. Written with scrupulous clarity, cautious optimism, and infectious excitement, it is a compulsive, compassionate and above all human account of the greatest medical breakthrough of our time."



4. **The Story of Interferon: The Ups and Downs in the Life of a Scientist**, by KARI CANTELL. 239 pp. River Edge, N.J., World Scientific, 1997

Every lymphodrek should own or read these memoirs of Finnish doctor Kari Cantell, who devoted his entire scientific life to bringing interferon from the laboratory to the pharmacy shelf. Dr. Cantell takes us through the journey that took more than three decades, involving moments of triumph, tribulation, as well as desperation in the lives of many scientists. For young scientists, there are the lessons of focus, dedication, and persistent hard work. Cantell never patented his procedure or the interferon he manufactured himself which he gave away for clinical studies free of charge. So, don't forget to protect your inventions if you're in it for the fortune!

Product description from the Publisher
The book will give the reader a glimpse of the world of science; how research is carried out in the laboratory and the clinic; how the mind of the scientist operates and how he experiences success and failure; how warm friendships and bitter conflicts develop between investigators; how the involvement of money and politics harms as well as helps research.

The Interferon Story is a richly rewarding book written for ordinary people without a basic knowledge of biology or medicine. It can be read as a thriller describing the struggle of scientists against the most feared diseases of mankind.

WWW

ASiDesigner

http://sysbio.kribb.re.kr:8080/AsiDesigner/menuDesigner.jsf

RNA interference (RNAi) with small interfering RNA (siRNA) has become a powerful tool in functional and medical genomic research through directed post-transcriptional gene silencing. In order to apply RNAi technique for eukaryotic organisms, where frequent alternative splicing results in diversification of mRNAs and finally of proteins, we need spliced mRNA isoform silencing to study the function of individual proteins. AsiDesigner is a web-based siRNA design software system, which provides siRNA design capability to account for alternative splicing for mRNA level gene silencing. It provides numerous novel functions including the designing of common siRNAs for the silencing of more than two mRNAs simultaneously, a scoring scheme to evaluate the performance of designed siRNAs by adopting currently known key design factors, a stepwise off-target searching with BLAST and FASTA algorithms and checking the folding secondary structure energy of siRNAs. To do this, we developed a novel algorithm to evaluate the common target region, where siRNAs can be designed to knockdown a specific mRNA isoform or more than two mRNA isoforms from a target gene simultaneously. The developed algorithm and the AsiDesigner were tested and validated as very effective throughout widely performed gene silencing experiments. It is expected that AsiDesigner will play an important role in functional genomics, drug discovery and other molecular biological research.

The Bioinformatics Links Directory

http://bioinformatics.ca/links_directory/

The Bioinformatics Links Directory features curated links to molecular resources, tools and databases. The links listed in this directory are selected on the basis of recommendations from bioinformatics experts in the field. We also rely on input from our community of bioinformatics users for suggestions. Starting in 2003, we have also started listing all links contained in the NAR Webserver issue.

Cancer and the Immune System: The Vital Connection

Oki K. Dzivenu, D.Phil., and Jill O'Donnell-Tormey, Ph.D.

http://www.cancerresearch.org/Resources.aspx?id=572

The Cancer Research Institute was established in 1953 to foster the field of cancer immunology, which is rooted in the notion that the body's immune system can be mobilized against cancer. From our inception, we have championed the development of new and effective strategies based on the immune system to complement traditional methods of cancer treatment, such as surgery, radiation, and chemotherapy. We are a non-profit intermediary organization that provides funding for individual and collaborative research projects across the country and throughout the world. Our funding strategy is aimed at providing support to investigators throughout various career development stages encompassing a broad spectrum of research such as basic, preclinical, and clinical sciences.

Today, we are more committed than ever to our long-term goal of fostering cancer immunology. We recognize that further advancement in the field depends on increased public understanding of the enormous power of the immune system and its connection to cancer. To help build that critical understanding, we have prepared this guide, which answers a number of commonly asked questions about cancer, the immune system, and the latest trends in immunotherapy. In the first chapter, the reader is introduced to the concept of cancer as the defining term for a panoply of diseases underpinned by two common features. This chapter ends with an introduction to the human immune system and how its normal function and cancer prevention are inextricably linked. We move on to chapter 2 for a discussion of the immune system thus setting the stage for the introduction of immunotherapy in chapter 3. The next three chapters (4-6) constitute a tour de force into almost every form of currently available immunotherapeutic regimens and how they are faring in worldwide clinical trials. The seventh chapter is full of hope: reminding

us of how far we have come and how much further we must travel on this exhilarating but arduous journey of battling cancer. The remainder of the book provides a brief look at the techniques behind the progress we have made in this field of biomedical science. We hope that you will find it enlightening.

DiRE: identifying distant regulatory elements of co-expressed genes

http://dire.dcode.org

Regulation of gene expression in eukaryotic genomes is established through a complex cooperative activity of proximal promoters and distant regulatory elements (REs) such as enhancers, repressors and silencers. We have developed a web server named DiRE, based on the Enhancer Identification (EI) method, for predicting distant regulatory elements in higher eukaryotic genomes, namely for determining their chromosomal location and functional characteristics. The server uses gene co-expression data, comparative genomics and profiles of transcription factor binding sites (TFBSs) to determine TFBS-association signatures that can be used for discriminating specific regulatory functions. DiREs unique feature is its ability to detect REs outside of proximal promoter regions, as it takes advantage of the full gene locus to conduct the search. DiRE can predict common REs for any set of input genes for which the user has prior knowledge of co-expression, co-function or other biologically meaningful grouping. The server predicts function-specific REs consisting of clusters of specifically-associated TFBSs and it also scores the association of individual transcription factors (TFs) with the biological function shared by the group of input genes. Its integration with the Array2BIO server allows users to start their analysis with raw microarray expression data.

IDT SciTools: a suite for analysis and design of nucleic acid oligomers

http://www.idtdna.com/SciTools/SciTools.aspx

DNA and RNA oligomers are used in a myriad of diverse biological and biochemical experiments. These oligonucleotides are designed to have unique biophysical, chemical and hybridization properties. We have created an integrated set of bioinformatics tools that predict the properties of native and chemically modified nucleic acids and assist in their design. Researchers can select PCR primers, probes and antisense oligonucleotides, find the most suitable sequences for RNA interference, calculate stable secondary structures, and evaluate the potential for two sequences to interact. The latest, most accurate thermodynamic algorithms and models are implemented.

Journal of Visualized Experiments

www.myjove.com

JoVE: What is it?
Journal of Visualized Experiments (JoVE) is a peer reviewed, free access, online journal devoted to the publication of biological research in a video format.

JoVE: Rapid Knowledge Transfer
The Journal of Visualized Experiments (JoVE) was established as a new tool in life science publication and communication, with participation of scientists from leading research institutions. JoVE takes advantage of video technology to capture and transmit the multiple facets and intricacies of life science research. Visualization greatly facilitates the understanding and efficient reproduction of both basic and complex experimental techniques, thereby addressing two of the biggest challenges faced by today's life science research community: i) low transparency and poor reproducibility of biological experiments and ii) time and labor-intensive nature of learning new experimental techniques.

JoVE: Addressing Complexity
The complexity and breadth of life science research has increased exponentially in recent years. Research progress and the translation of findings from the bench to clinical therapies relies on the rapid transfer of knowledge both within the research community and the general public. Written word and static picture-based traditional print journals are no longer sufficient to accurately transmit the intricacies of modern research.

JoVE: Lifting the Laboratory Time Sink
As every researcher in the life sciences knows, it can take weeks or even months to learn, perfect, and apply new experimental techniques. It is especially difficult to reproduce newly published studies describing the advanced state-of-the-art techniques. Thus, much time in the laboratory is spent learning techniques and procedures. This is a never ending process for experimental scientists as methodologies in this fast-growing field evolve and change with each coming year (e.g. genomics and proteomics, most dramatically). The time and resource-consuming process of learning and staying current with techniques and procedures is a rate-limiting step in the advancement of scientific research and drug discovery.

JoVE: Integrating Time
JoVE opens a new frontier in scientific publication by promoting efficiency and performance of life science research. Visualization of the temporal component, or the change over time integral to many life science experiments, can now be done. JoVE allows you to publish experiments in all their dimensions, overcoming the inherent limitations of traditional, static print journals, thereby adding an entirely new parameter to the communication of experimental data and research results.

JoVE: Be a Part of a New Movement in Science Publishing
We invite you to actively participate in and contribute to JoVE, a scientific journal and novel tool for the advancement of life science research, by submitting video-articles that visualize your experiments.

Magnolia

http://bioinfo.lifl.fr/magnolia

Magnolia is an advanced multiple alignment program suite for nucleic sequences. It is especially designed for protein-coding RNA sequences or non-coding RNA sequences. It tries to determine the putative function of the sequences before aligning them. Magnolia extracts information from the similarities and differences in the data, and searches for a specific evolutionary pattern. It combines two evolutionary models.

- **Protea** for *protein-coding sequences*. In this first model, the selection pressure tends to preserve the encoded amino acid sequence. For this reason, the mutations are governed by the redundancy of the genetic code: silent mutations or mutations leading to similar amino acids are privileged between codons of the correct reading frame. So it is possible to identify coding sequences by looking for a global conservation of common reading frames.

- **caRNAc** for *non-coding RNA genes*. In this latter model, the selection pressure tends to preserve the spatial structure of the molecule. The secondary structure, formed by isosteric base pairs, is more highly conserved than is the sequence. This means that mutations should retain the ability to form base pairs into energically favourable stems. In this context, caRNAc looks for a significantly conserved common secondary structure. If the sequences are classified as protein coding sequences, then the nucleic multiple alignment is built from the hypothetical amino-acid sequences using ClustalW. This process is able to handle frameshifts. If the sequences are classified as non-coding RNA genes, then the multiple alignment takes into account both the primary structure and the predicted common secondary structure of the RNA sequences.

The Predikin webserver: improved prediction of protein kinase peptide specificity using structural information

http://predikin.biosci.uq.edu.au/pkr/

The Predikin webserver allows users to predict substrates of protein kinases. The Predikin system is built from three components: a database of protein kinase substrates that links phosphorylation sites with specific protein kinase sequences; a perl module to analyse query protein kinases and a web interface through which users can submit protein kinases for analysis.

The Predikin perl module provides methods to (i) locate protein kinase catalytic domains in a sequence, (ii) classify them by type or family, (iii) identify substrate-determining residues, (iv) generate weighted scoring matrices using three different methods, (v) extract putative phosphorylation sites in query substrate sequences and (vi) score phosphorylation sites for a given kinase, using optional filters. The web interface provides user-friendly access to each of these functions and allows users to obtain rapidly a set of predictions that they can export for further analysis.

Regulatory Sequence Analysis Tools

http://rsat.ulb.ac.be/rsat/

The regulatory sequence analysis tools is a software suite that integrates a wide collection of modular tools for the detection of cis-regulatory elements in genome sequences. The suite includes programs for sequence retrieval, pattern discovery, phylogenetic footprint detection, pattern matching, genome scanning and feature map drawing. Random controls can be performed with random gene selections or by generating random sequences according to a variety of background models (Bernoulli, Markov). Beyond the original word-based pattern-discovery tools (oligo-analysis and dyad-analysis), we recently added a battery of tools for matrix-based detection of cis-acting elements, with some original features (adaptive background models, Markov-chain estimation of P-values) that do not exist in other matrix-based scanning tools. The web server offers an intuitive interface, where each program can be accessed either separately or connected to the other tools. In addition, the tools are now available as web services, enabling their integration in programmatic workflows. Genomes are regularly updated from various genome repositories (NCBI and EnsEMBL) and 682 organisms are currently supported. Since 1998, the tools have been used by several hundreds of researchers from all over the world. Several predictions made with RSAT were validated experimentally and published.

SuperPred

http://bioinformatics.charite.de/superpred/

The drug classification scheme of the World Health Organization (WHO) [Anatomical Therapeutic Chemical (ATC)-code] connects chemical classification and therapeutic approach. It is generally accepted that compounds with similar physicochemical properties exhibit similar biological activity. If this hypothesis holds true for drugs, then the ATC-code, the putative medical indication area and potentially the medical target should be predictable on the basis of structural similarity. We have validated that the prediction of the drug class is reliable for WHO-classified drugs. The reliability of the predicted medical effects of the compounds increases with a rising number of (physico-) chemical properties similar to a drug with known function. The web-server translates a user-defined molecule into a structural fingerprint that is compared to about 6300 drugs, which are enriched by 7300 links to molecular targets of the drugs, derived through text mining followed by manual curation. Links to the affected pathways are provided. The similarity to the medical compounds is expressed by the Tanimoto coefficient that gives the structural similarity of two compounds. A similarity score higher than 0.85 results in correct ATC prediction for 81 of all cases. As the biological effect is well predictable, if the structural similarity is sufficient, the web-server allows prognoses about the medical indication area of novel compounds and to find new leads for known targets.

Availability: the system is freely accessible at http://bioinformatics.charite.de/superpred. SuperPred can be obtained via a Creative Commons Attribution Noncommercial-Share Alike 3.0 License.

Universal Virus Database

http://www.ncbi.nlm.nih.gov/ICTVdb/index.htm

The Universal Virus Database, ICTVdB, is authorized by the ICTV (International Committee on Taxonomy of Viruses) and has been constructed by Cornelia Büchen-Osmond, from 1991-2000 in the Bioinformatics Group, Australian National University, in consultation with the ATCC and supported by the NSF. In 2001, ICTVdB moved to the Biosphere 2 Center, the Western Campus of the Earth

Institute, Columbia University of New York USA. The directory of ICTVdB is an Index of Viruses, a list of approved virus names linked to virus descriptions coded from information in Virus Taxonomy: *The Seventh Report of the International Committee on Taxonomy of Viruses*, van Regenmortel et al. (eds) Academic Press (2000), and includes updates subsequently approved by ICTV. It also incorporates the plant virus database VIDEdB and is illustrated with EM pictures, diagrams and images of symptoms contributed by virologists around the world. Recommended by Kevin Ahern in *Genetic Engineering News*

A Web Atlas of Cellular Structures Using Light and Confocal Microscopy

http://www.itg.uiuc.edu/technology/atlas/

This web site displays a series of light and confocal micrographs illustrating a variety of subcellular structures and organelles. We hope to provide a useful educational resource for people interested in cytology who do not have access to advanced imaging technologies or cell biological expertise. We have employed a cultured epithelial cell line, CV1-monkey kidney cells, for these experiments and stained for such organelles as the Golgi apparatus, the endoplasmic reticulum, nucleus, mitochondria, and several cytoskeletal elements. Protocols for each staining as well as a description of the microscopes utilized are provided. Confocal and fluorescent microscopy images help to reveal the intriguing structures of the cell. We hope also to demonstrate the high quality imaging techniques available for such visualization. This project has been made possible with the support of the Beckman Institute of Advanced Science and Technology's Imaging Technology Group at the University of Illinois at Champaign-Urbana.

Sheela Konda, Steve Rogers, and Daniel E. Weber

Summer Intern program: Amgen Scholars Europe

www.amgenscholars.com

Amgen is delighted to announce the launch of Amgen Scholars Europe - a $2.5 million investment by the Amgen Foundation in a two-year pilot undergraduate research program. The program will provide more than 100 selected undergraduate students from across Europe the opportunity to engage in a hands-on summer research experience under top academic scientists at three world class universities. Modeled on the existing and very successful U.S. program - which attracted over 2,300 applicants from nearly 500 U.S. colleges and universities in 2008 - the European expansion brings the Amgen Foundation's global commitment to Amgen Scholars to $27.5 million.

The program - which is already implemented at 10 premier universities in the United States - will be hosted in Europe by:

- University of Cambridge, UK;
- Karolinska Institute, Stockholm, Sweden
- Ludwig-Maximilians-University, Munich, Germany.

Each host institution will select participants from colleges and universities from 46 countries throughout Europe. In addition to their research opportunity, all participating students will take part in an annual three-day symposium at the University of Cambridge, where they will have the opportunity to hear firsthand from leading scientists working in industry and academia, and to network with other Amgen Scholars from throughout Europe.

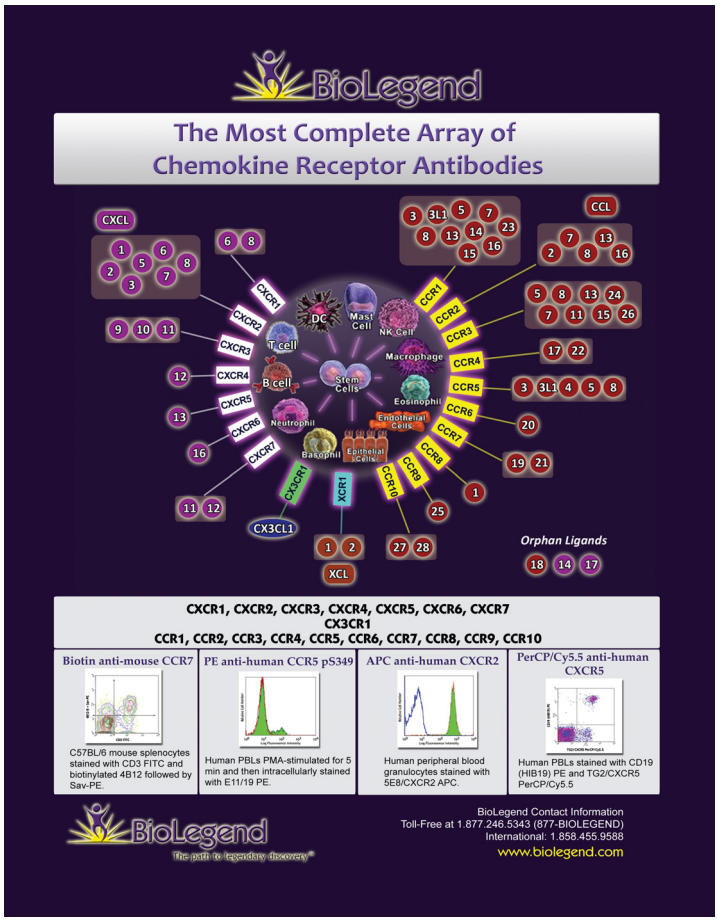
With the expansion of Amgen Scholars, we hope to strengthen undergraduate science education in Europe by increasing the number of meaningful research opportunities for students. Our hope is that Amgen Scholars Europe will be a pivotal experience that will encourage students to pursue further education and training in the sciences and enable them to discover their future potential as scientists.

This initiative underlines our strong commitment to Europe and our desire to extend the Amgen Foundation's philanthropic programs around the world. We believe it will form an important part of our reputation-building activities in Europe.

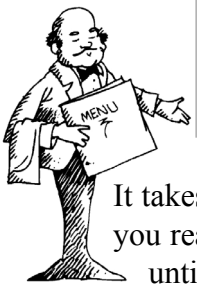
WWW (continued)

For more information about Amgen Scholars, including application deadlines and eligibility criteria, please visit the website listed above.

Since 1991, the Foundation has made more than $125 million in grants to nonprofit organizations throughout the United States, Puerto Rico and Europe that impact society in inspiring and innovative ways. Over the last two years, the Amgen Foundation has expanded its support to nonprofit organizations chartered in Europe. To date, the Foundation has granted more than $1 million to nonprofits throughout Europe including support for organizations in France, Germany, Ireland, Italy, Spain, Switzerland and the UK.



BioLegend is an ISICR Silver sponsor. Be sure to mention the ISICR when placing an order with BioLegend to be eligible for an ISICR member discount on your purchases.



YOUR AGE BY DINNER & RESTAURANT MATH
DON'T CHEAT BY SCROLLING DOWN FIRST!

It takes less than a minute. Work this out as you read. Be sure you don't read the bottom until you've worked it out!

1. First of all, pick the number of times a week that you would like to go out to eat. (more than once but less than 10)

2. Multiply this number by 2 (just to be bold).

3. Add 5.

4. Multiply it by 50.

5. If you have already had your birthday this year add 1758.....If you haven't, add 1757.

6. Now subtract the four-digit year that you were born.

You should have a three digit number. The first digit of this was your original number. (i.e. How many times you want to go out to restaurants in a week.)

The next two numbers are YOUR AGE ! ----------
(Oh YES it is!)

THIS IS THE ONLY YEAR (2008) IT WILL EVER WORK.

(Editor's Note: This statement cannot be verified but does it really matter????)

ISICR Meetings of Interest

Methods in Cytokine Biology

March 12, 2009

Sponsored by the NIH Cytokine Interest Group and the National Cancer Institute Center for Excellence in Immunology

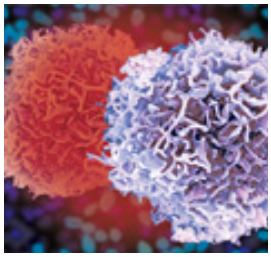
Lipsett Auditorium
Bldg. 10
NIH campus
Bethesda, MD

The full program will be announced in early 2009. There is no charge to attend this meeting but registration will be required. For more information, contact Howard Young at younghow@mail.nih.gov.

Cytokine Therapies: Novel Approaches for Clinical Indications

March 26-27, 2009
http://www.nyas.org

Presented by the Food and Drug Administration and the New York Academy of Sciences

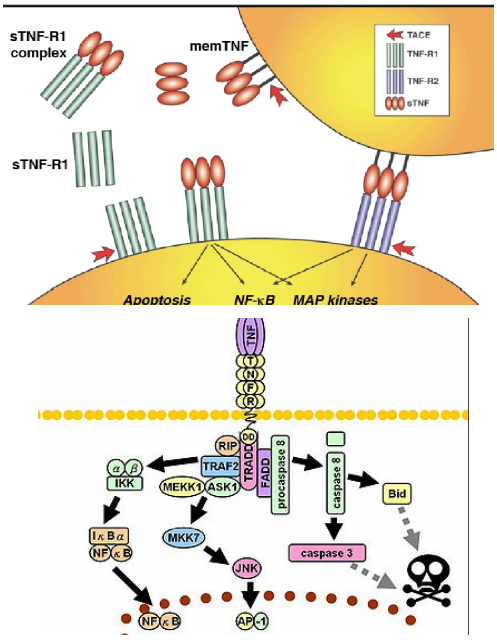


Despite outstanding therapeutic promise and sound scientific rationale, most cytokine therapies have largely failed to establish clinical utility. This meeting is designed as a forum to critically assess the factors that are limiting the clinical development of cytokines as therapeutic agents. It will cover the successes and failures of recombinant cytokines as therapeutic agents for treating human diseases, including various cancers and autoimmune diseases, and will provide a forum to review the scientific and clinical basis of both successful and unsuccessful attempts to develop cytokines as therapeutic agents. The goal is to identify areas for improvement and to coordinate, develop and disseminate novel approaches to current scientific hurdles that are limiting the development of many cytokine products.

12th International TNF conference

April 26-29, 2009
http://www.tnf2009.org/

Euroforum Escorial (http://www.euroforum.es/en/), San Lorenzo de El Escorial near Madrid, Spain



The biennial TNF-family conferences have been held over the past 20 years, from the time that TNF was cloned. These meetings have followed the enormous progress in this field. Much is now known about the members of the TNF ligand and receptor families, their signaling proteins, mechanisms of action and cellular functions.

The 12th TNF International Conference, to be held in April 2009, will focus on the physiological, pathophysiological, and medical significance of these important regulators. Sessions at the meeting will specifically address their involvement in immunity, development, apoptosis, autoimmunity, cancer, and infection, the normal function and pathology of the neuronal system, as well as major unresolved questions about their mechanisms of action.

A New ISICR Recipe

The most dangerous cake recipe in the world

5 MINUTE CHOCOLATE MUG CAKE

4 tablespoons flour
4 tablespoons sugar
2 tablespoons cocoa
1 egg
3 tablespoons milk
3 tablespoons oil
3 tablespoons chocolate chips (optional)
a small splash of vanilla extract
1 large coffee mug

Add dry ingredients to mug, and mix well. Add the egg and mix thoroughly. Pour in the milk and oil and mix well. Add the chocolate chips (if using) and vanilla extract, and mix again. Put your mug in the microwave and cook for 3 minutes at 1000 watts. The cake will rise over the top of the mug, but don't be alarmed! Allow to cool a little, and tip out onto a plate if desired. EAT! (this can serve 2 if you want to feel slightly more virtuous).

And why is this the most dangerous cake recipe in the world? Because now we are all only 5 minutes away from chocolate cake at any time of the day or night!

ISICR Committee Minutes

ISICR Board of Directors Meeting Minutes
Cytokines 2008/Montreal Canada
Sunday October 12, 2008
15:30 - 17:30, Chaudiere Room

Attendees: Eleanor Fish - President, Leonidas Platanias - President-elect , Thomas Hamilton - Secretary, Robert Friedman - Treasurer, BOD members: Keiko Ozato ,Nancy Reich, George Stark; Otto Haller - Past President; Past Presidents: Samuel Baron, Ferdinando Dianzani, Sidney Pestka, Bryan R.G. Williams, Howard Young, Kathryn C. Zoon; Meetings Committee Chair-Christine Czarniecki; Publications Committee Chair-Robert Fleischmann, Jr.; Awards Committee Chair-Robert H. Silverman Staff Present: Lisa Hetherington

I. Call to Order. Meeting was called to order at 15:33 Eastern time by Eleanor Fish
- a. Reminder about joint Board meeting with the ICS on Wednesday

II. Awards Committee report (Robert Silverman and Kathryn Zoon)
- a. Propose changes to selection process for Milstein Award
  - i. Solicit nominations (via blast email) by April 1st
  - ii. Awards Committee will select top three and will recommend to Board by May 1st
    1. Will obtain more information on nominees
      - a. Nomination letter
      - b. Three independent reference letters
        - iii. Awards Committee will perform additional research if needed and will follow up with findings and recommendations to Board to June 1st

III. Report on FASEB activities (Lisa Hetherington)
- a. Eleanor introduces Lisa Hetherington to the Board
- b. Lisa reports on FASEB activities over the past year
- c. Recommendation among Board that the ISICR directory be available online only. Discussions occurred about the pros and cons of this proposal.
- d. Motion approved to continue print only if advertising revenue contributes towards 80% of printing costs.

*(**ISICR Committee Minutes**, cont. from page 24)*

IV. Proposal for Joint ICS/ISICR Meetings Committee- Christine Czarniecki
a. Report on 2007 meeting.
b. BOD approved the creation of a Joint ICS/ISICR Meetings Committee
c. Resolution that the Meetings Committee begin to explore the possibility of contracting with a meeting organization company to manage future meetings.

V. Student Membership
a. Motion approved to drop free student member= ship, and offer a 3 year membership for $30

VI. BioLegend Offer
a. Silver sponsor this year. Biolegend wants to network with society and offer ISICR members (US and Canada) a 30% discount on products
b. Decision reached that BioLegend can use ISICR email to announce the promotion upon approval of the email content by the BOD

VII. Standards Committee - no report

VIII. Secretary's Report (Tom Hamilton)
a. The positions for Secretary (Tom Hamilton) and Treasurer (Bob Friedman) were renewed for additional 3 year terms by unanimous approval of the International Council and the BOD.
b. In 2009 the following positions will be open for election:
i. President-elect
ii. 3 "at-large" BOD positions
c. International Council
i. International Council appointments come from individual chapters. IC meeting occurs with general membership meeting.
ii. Discussion of International Council function.
1. IC provides nominations for ISICR elections
2. Fundraising
3. Opportunity for international representative to voice opinions
iii. Eleanor to contact each IC representative and ask for input on how to be more effective and how to stimulate more interest in participating in society affairs

IX. Treasurer's Report (Bob Freidman)
a. Over the years, it is noted that total capital varies from $190K - $210K, and currently, total capital is at $194K
b. Bob will circulate email of budget for approval

X. New logo discussion - deferred

XI. Publications Committee (Bob Fleischmann, Jr.)
a. Impact factor is at 2.667; the highest ever
b. Turnover of editorial board and associate editor continues as in past years
c. Number of pages and number of manuscripts have declined. There is a strong need for members to submit papers for possible publication.
d. New ideas to increase submissions were discussed
i. Approach members to send invited reviews for consideration for publication
ii. Peruse posters at annual meeting, ask presenter that they consider submitting their work to the journal
e. Because of complaints about review process and complexity, journal will now offer streamlined and effective review. Will offer specific constructive critique on how to get the article published. This new process will be reinforced with reviewers.
f. Special topics issue for next year. Journal would like to hear ideas

XII. Other business (Howard Young)
a. Website - FASEB soon to offer content management system so Howard can update website directly
b. Grant application for ISICR summer internships- letter of inquiry sent to Invitrogen Foundation but the Foundation has suspended operations until merger with Applied Biosystems is complete. Invitrogen delayed decisions until first quarter 2009
c. Recognition to Howard Young for producing and editing outstanding newsletters over the past 15 years

XIII. Meeting adjourned 17:30 Eastern time by Eleanor Fish

ISICR Awards Committee Minutes
1:45-3:15 PM Sunday October 12, 2008
Fairmont The Queen Elizabeth Hotel, Chaudiere

Present: Robert Silverman (Chairperson), Katherine Zoon (Co-chair), Daniela Novick, Peter Staeheli, Eleanor Fish (ex officio)
Absent: Jeanne Wietzerbin, Takashi Fujita, Michael Gale

*(**ISICR Committee Minutes**, cont. from page 24)*

In 2008 about $50,000 was distributed to participants at the annual meeting in Montreal for Seymour & Vivian Milstein Travel Awards. Amounts of the travel awards were based on the quality of the abstracts, the distance the person had to travel and the number of awards given per lab.

In addition, there was one winner of The Seymour and Vivian Milstein Award (Dr. Giorgio Trinchieri); two Honorary Members (Dr. George Galasso and Dr. Paula Pitha-Rowe); four winners of The Seymour and Vivian Milstein Young Investigator Award (Toby Lawrence, Tao Lu, Cesar Munoz-Fontela, & Takeshi Saito), a winner of The Christina Fleischmann Award to Young Women Investigator (Yueh-Ming Loo), and four winners of the Ludwig Boltzmann Award jointly awarded by the ISICR, ICS and ECS (Saurabh Chattopadhyay,Joao Marques, Bryan Williams and Ganes Sen).

Changes to the process of selecting The Seymour and Vivian Milstein Award were agreed upon and recommended to the Board of Directors. These include soliciting nominations from the General Membership by April 1st to allow additional time to obtain letters, deliberate and interact with the Board towards making a final selection of the winner(s).

Respectfully submitted,
Robert Silverman, Co-Chair

ISICR Meetings Committee and ICS Meetings Committee Minutes
October 12, 2008
Montreal, Canada

The meeting was called to order on Sunday, October 12, 2008. The following attendees at this meeting represented the ISICR Meetings Committee: Yoichiro Iwakura, Santo Landolfo, Allen Lau, Nancy Reich, Michael Tovey, Leon Platanias. The following attendees represented the ICS: Scott Durum, Alberto Mantovani, John Schrader, John Sims, David Wallach. Also attending were guests from the ISICR Board of Directors (Eleanor Fish) and from the Montreal Meeting Organizing Committee (John Hiscott and Gabriella Di Pancrazio). The meeting was co-chaired by Christine Czarniecki (ISICR) andCarl Ware (ICS)

2008 - Montreal, Canada
Translating Science into Health: Cytokines in Cancer, Inflammation and Infectious Disease
John Hiscott presented an update on the 2008 Joint ISICR/ICS meeting in Montreal.
This meeting is the 7th joint meeting of the two societies. The conference dates were October 12-16, 2008 at the Fairmont Queen Elizabeth Hotel. There were a total of 800 participants coming from 40 countries. The number of abstracts submitted was 450. All invited speakers received travel funds and waived registration fees. Total expenses are estimated to be $487,000 (Canadian) and total income is estimated to be $500,000 (Canadian) including: seed funds of $10,000 (US) from ISICR and $10,000 (US) from ICS; 50 Sponsors (mostly from North America) and 24 exhibitors.

After final accounting, any remaining funds will be split evenly between the two societies.

In discussions, John expressed the opinion that when considering future meetings seed funds of $25,000 (US) from each society is a reasonable amount. The website used for this meeting (***Cytokines 2008***) was built upon the site used for ***Cytokines 2007***. The site was structured to provide continuity with the previous site, hopefully to become a "one stop" resource for this and future Conferences. John and Gabriella found the site to work well and ISICR and ICS committee members strongly recommend that future meeting continue with this same cite structure.

2009 - Lisbon, Portugal
Scott Durum assisted by Michael Tovey presented the update for the 2009 Joint Meeting of the SLB, ICS and ISICR which will take place at the Lisbon Congress Center in Lisbon, Portugal on October 17-21, 2009. The theme of the conference is "Cellular and Cytokine Interactions in Health and Disease". Letters have been sent to invited speakers. In choosing the 49 invited speakers, with a further 50% of speakers to be chosen from submitted abstracts, the Organizing Committee strove for balance between outstanding established scientists and new exciting work from younger scientists. An effort was also

*(**ISICR Committee Minutes**, cont. from page 25)*

made to choose different speakers from those present at Montreal in order to give other people a chance to speak. The program was established so as to provide a balance between the interests of the membership of all three societies. Invited speakers were chosen on the basis of scientific excellence and suitability for a particular topic. An effort was made to reduce gender bias. The pros and cons of waiving registration fees was discussed and speakers were asked to pay the registration if they had funds to do so. The budget has been prepared using the Vienna Meeting as a model and an estimate of 800 attendees. The expected income is $665,250 (US). Earlier this year, the three participating Societies provided seed funds of $20,000 each to the Lisbon Organizers for deposit into a Euro bank account in order to pay the scheduled installments on the Lisbon Conference Center throughout the 18 months leading up to the Lisbon meeting. Expenses are estimated at 629,640 (US). The Administrative management for the meeting will be done by a local company in Lisbon called "Leading" and FASEB in the US. This arrangement was established by SLB.

There was discussion of what has worked well, administratively, for the Montreal Meeting with suggestions that the Lisbon Organizers continue with: the same website, collection of registrations, publishing of Abstracts and Program by Elsevier.

There was discussion about the high costs of using a Conference Center vs a Hotel. Lisbon did not have any Hotels large enough to accommodate the needs for this meeting and thus the Congress Center was chosen. However, the Meetings Committee must consider this point when choosing future locations, as use of Hotels for our Meetings appears to be more cost-effective.
Post meeting note : To date 43 of the 49 invited speakers have agreed to speak at the Lisbon meeting.

2010 - Chicago, Illinois, USA
Leon Platanias provided the update for the 2010 joint ISICR/ICS meeting. The meeting will take place at the Hyatt Regency in Chicago's "Magnificent Mile" on October 3-7, 2010. The Theme of the meeting is "Cytokines and Cancer". The International Organizing committee will be established in the next few months. A gala dinner is being planned at the Robert Lurie Comprehensive Cancer Center.

The Preliminary Budget as presented indicated total expenses of $519,000 (US) with estimated income as $550,000 (US). The contract for the hotel has been executed with an acceptable number of rooms. The negotiating rate appears to be the same for Montreal and Chicago (commitment of 1 room per 50 conference attendees.)

Suggestions made in discussions included broadening the theme of the meeting to include other diseases so as to enhance interest of potential attendees. The process of selecting the scientific organizing committee was discussed with the recommendation of the criteria of choosing members of the committee should be high scientific quality and visibility and experience in fund raising, with the result of providing a balanced program.

2011 and beyond - Copenhagen
Michael Tovey presented a proposal for a future meeting from Kurt Berg who was not present. The theme of the meeting is "New Developments and Applications of the Cytokine Network in Human Medicine." A two-track format was suggested comprising joint plenary sessions together with workshops on both basic science and the role of cytokines in the physiopathology and treatment of chronic hepatitis C, multiple sclerosis, and diabetes. Copenhagen is a compact city with good conference and hotel facilities and an efficient transport system. There are good flight connections to the North America, Asia, and the rest of Europe. The city of Copenhagen offers assistance to organizations choosing Copenhagen as a conference venue. Michael visited three down-town conference venues all three of which were suitable for the joint ISICR/ICS meeting. A date in September was suggested as optimum for both weather and daylight. The Meetings Committee felt that Copenhagen would be a possible venue for the 2011 meeting provided that Kurt Berg was confident that he would be able to raise sufficient funds to underwrite the meeting and that he was assisted by an international committee in the preparation of the scientific program. Michael offered to contact a number of members of the ISICR and ICS who would be prepared to join such a Scientific

*(**ISICR Committee Minutes**, cont. from page 26)*

Organizing Committee and get feedback from Kurt Berg.

The Committee Members agreed to a "tentative" approval for Copenhagen dependent upon the revised proposal from Kurt Berg. Carl Ware and Christine Czarniecki presented this proposal to the ICS and ISICR Boards, respectively.
[Post meeting notes: Both BODs voted in favor of this "tentative" proposal - with the caveat of receiving additional information from Kurt Berg and an International Organizing Committee. The committee has also received additional inquiries and is expecting proposals for Florenza, Italy and Geneva, Switzerland.
Proposal for a Joint ISICR/ICS Meetings Committee
Prior to this committee meeting the attendees, who represented both the ISICR and ICS, were provided with detailed proposals for: (i) a Joint Meetings committee; and (ii) a Guideline for Contents of Meetings Proposals. At this committee meeting, the attendees voted unanimously in favor of the proposals and it was agreed that the Committee Co-Chairs would present the proposals to the Board of Directors (BODs) of each of the societies.

In summary, the charge of this new Committee is to: (i) evaluate and vote on all proposals for future annual meetings held jointly between the International Cytokine Society (ICS) and the International Society for Interferon and Cytokine Research (ISICR) and convey that vote to the BODs of each Society as a recommendation for final approval by those BODs; and (ii) review and evaluate progress and financial budget statements of the currently approved meetings. The committee will be comprised of 14 voting members [7 "active" (dues paying) members of each Society], non-voting members representing future "approved" planned meetings, and 2 voting co-chairs (one representing each Society). Voting members will be chosen by the Presidents of each respective Society in consultation with the current co-chairs. A guideline has been established that describes the contents of a Meetings Proposal that will be presented to the committee for vote.

[Post meeting note: Both BODs voted in favor of the proposals for the new Joint ISICR/ICS Meetings Committee]

There was no other business to discuss and the Meeting was adjourned.

Respectfully submitted, Christine Czarniecki
Chair, ISICR Meetings Committee and
Carl Ware, Chair, ICS Meetings Committee

ISICR Meetings Committee Minutes
October 12, 2008
Montreal Canada

Note: The information below, regarding the 2007 ISICR Meeting in Oxford, UK, was discussed by the ISICR Meetings Committee(by email) prior to the Montreal Committee Meeting and presented to the ISICR BOD in Montreal.

2007 - Oxford, United Kingdom - The Anniversary Meeting
This meeting marked the 50th anniversary of the discovery of Interferon by Alick Isaacs and Jean Lindenmann and it was preceded by a pre-Meeting Symposium entitled "History of the Interferons" on September 15, 2007. The ISICR Meetings Committee expresses thanks to Dr. Graham Foster and his colleagues on the Organizing Committee for their efforts in the planning of this important Anniversary Meeting.

The responsibility for administrative/financial accounting for this meeting was divided between the local Organizers and FASEB. It should be noted that the FASEB was not under contract to provide services for the Oxford Meeting and only provided registration services for the meeting as other arrangements had not been made. The only fees the FASEB received were a transaction fee for registrations to cover direct costs for the service. A detailed, consolidated final report was not provided to the ISICR Meetings Committee. The reports that were provided to the Committee by the Organizers and FASEB (showing local transactions in Oxford as well as payments made from FASEB on behalf of the Organizers with the consent of ISICR) indicated some confusion regarding payments made on behalf of ISICR and payments made on behalf of the Meeting. Any payments that were to be paid from ISICR funds for ISICR-paid activities should not

*(**ISICR Committee Minutes**, cont. from page 27)*

appear in a finance statement for the Meeting. For all future meetings it is critical that: (i) there is a clear separation of accounting for the activities that are funded by the Society and activities that are funded by the Meeting Organizers; and (ii) a detailed financial report be prepared by the Meetings Organizers and submitted to the Meetings Committee and ISICR Board. The ISICR Meetings Committee Members strongly recommended that for future meetings FASEB, or any other Conference Management Organization, should submit a detailed estimate for the organization of a meeting with the costs for each line item clearly stated. There was also a recommendation that the accounts of all future meetings be audited.

The information provided to the Meetings Committee utilized a conversion rate of US$2.00 = GBP1.00 and indicated a total income of $336,452 (US) which included: $40,000 from ISICR as seed funds; $175,070 from registration fees (main and Pre-Meetings); $13,142 from exhibitors; $48,000 from sponsors/Pharmaceutical companies. After all expenses were paid, the ISICR received one check in the amount of GBP 20,571.37 - which at that time (May 2008), the US dollar value received was $39,775.

A breakdown for registration was not provided but from the data provided, the ISICR Meetings Committee estimates the following: approximately 300 paid registrations for the main meeting and 70 for the Pre-Meeting.

Respectfully submitted,
Christine Czarniecki
Chair, ISICR Meetings Committee

ISICR Membership Committee Minutes
Sunday, October 12, 2008

Present: Eleanor Fish, Acting Chair, Ana Gamero, Howard Young

The membership committee reviewed the membership statistics for 2008. As in past years, membership is stable but is not increasing. It was also pointed out that feedback from the FASEB office has indicated that other societies that have offered free student memberships have dropped that option as it has not proven to retain students as members. Based on that input, the committee voted to eliminate the free student membership and replace it with a 3 year minimum membership at a cost of $30. In addition, Emeritus membership options for 1, 2 or 3 years, at a substantially reduced price, will be added to the 2009 membership options.

Respectfully submitted,
Eleanor Fish, Acting Chair

ISICR Publications Committee Minutes
Sunday, October 12, 2008

Members Present:
Bob Fleischmann, Chair
Deborah Vestal
Ganes Sen, Editor-in-Chief JICR
Tom Hamilton, Editor-in-Chief JICR
Eleanor Fish, Ex Officio

The meeting of the Publications Committee was called to order at 11:30 am. The low turnout of committee members was acknowledged to be due to a late change in the meeting time by the organizing committee that several committee members didn't see.

Tom Hamilton (on behalf of himself and Ganes Sen) provided his report of the Status of the Journal of Interferon and Cytokine Research (JICR) to the Publications Committee. The highlights of their report were as follows:

1. With 1/3 of year 2008 to go, the JICR is down somewhat from past years in terms of both the number of articles accepted for publication and the number of pages published. There is concern that the Associate Editors and the Members of the Editorial Board have not been as supportive of the JICR as they should be.
2. The impact factor of the JICR continues to increase. It was 2.667 in 2007, up from 2.094 in 2005 and 2.472 in 2006.
3. In keeping with the terms of our contract, it was once again time for replacement or renomination of Associate Editors and Editorial Board Members.

*(**ISICR Committee Minutes**, cont. from page 28)*

Three Associate Editors rotated off and were replaced by four new Associate Editors who were approved by the Publications Committee prior to the Annual Meeting. Several changes in the Editorial Board were also approved by the Publications prior to the Annual Meeting.
4. A Special Topics issue on Viral Evasion of IFN Defenses will be published in the next year. Other Special Topics issues are invited from the membership of the ISICR.

There was extended discussion about the perceived lack of support by Associate Editors and Members of the Editorial Board for the JICR and the ISICR. A motion was made and passed to establish the following suggested criteria for future nominees for Editorial Board membership.

ISICR membership
ISICR Annual Meeting participation
JICR reviewer
JICR author

Eleanor Fish proposed that the membership of the ISICR be approached about submitting review articles based upon the dissertation literature reviews of their graduating PhD students. This was heartily endorsed by all present.

Eleanor Fish proposed that the members of the Editorial Board visit the poster sessions and invite presenters who had outstanding posters to submit their research as manuscripts for publication in the JICR.

A motion was made and passed to accept the report of the Editors-in-Chief and to commend them for their outstanding service on behalf of the JICR and of the ISICR.

Having no other business, the meeting was adjourned at 12:10 pm.

Respectfully submitted,
Bob Fleischmann, Chair

ISICR Standards Committee Minutes
Sunday, October 12, 2008
Fairmont Queen Elizabeth Hotel
Montreal, Canada

Committee members attending: Michael Tovey, Darren Baker, representing Vijay Jethwa, and Sidney Grossberg (Chairman). Other Committee members (not in attendance) include: Guido Antonelli, Masayoshi Kohase, Tony Meager, Aida Prync, and Huub Schellekens. Arrangements were made for group teleconference participation.

Sidney Grossberg called the meeting to order at 15:00 hours. He noted that Norman Finter retired from the Committee in the past year after having served for two decades with great distinction and conscientious dedication, providing a remarkable breadth of knowledge, valuable judgments, and sage advice; Norman and his contributions will be sorely missed.

Before addressing items of the meeting agenda previously distributed, Dr. Grossberg provided a summary overview of the purpose and activities of the ISICR Standards Committee. The Committee was established two decades ago by the then ISICR President Ernest Borden to make recommendations regarding interferon standards and standardization as well as deal with related matters that might be referred to the Committee. The Committee has been a source of information and recommendations to the ISICR membership, and thereby to the international cytokine scientific community as well as to the World Health Organization (WHO), the U.S. National Institutes of Health (NIH), pharmaceutical manufacturers, regulatory agencies, and most recently to BEI Resources. To our knowledge, there is no other non-governmental group that deals with such matters in the cytokine field. It was thought worthwhile to inform the European and U.S. Pharmacopoeia organizations of the Committee's activities, and offer, as appropriate, its expertise on matters affecting cytokines, standards, and standardization.

I. Interferon-β Manufacturers Collaborative Neutralizing Antibody Study

The Committee discussed at length the report of the European Medicines Evaluation Agency (EMEA) of the European Union (EU) Biological Working Party (BWP) dated 13 February 2008 (attached). It is hoped that the methodology and results of this study,

*(**ISICR Committee Minutes**, cont. from page 29)*

which took more than seven years to plan and complete, will be published in full. In summary, serum samples obtained by the three major IFN-β manufacturers from patients with IFN-β neutralizing antibody titers previously screened as negative, high, medium, and low were redistributed in a blinded fashion by NIBSC to the laboratories of the manufacturers of Avonex (IFN-β1a), Betaferon (IFN-β1b), and Rebif (IFN-β1a). Testing was to be performed by both antiviral bioassay and the MxA assay that utilizes a secondary protein ELISA dependant on a monoclonal antibody provided by Novartis. From the results of the study, the BWP recommended that the MxA assay be used by the manufacturers, especially for the evaluation of neutralizing antibodies (NAbs). The Committee discussed in detail a number of aspects of the BWP report. It is not currently known whether these manufacturers are currently using the MxA assay as recommended. It would be helpful to know the basis for the report's recommendation that a single antigen (Avonex, IFN-β1a) be used to measure NAbs no matter which product or subtype of IFN-β the patient was treated with. The Committee noted that there were newer, more rapid gene-reporter assays of greater utility than the MxA assay (Lallemand et al., *Journal of Interferon and Cytokine Research*, 28:393-404, 2008 and Lam et al., *Journal of Immunological Methods*, 336:113-118,2008). It was thought appropriate to try to obtain data summaries directly from the manufacturers involved to be able to better evaluate the basis for the recommendations, especially since there is no certainty that the results of the full study will be published.

II. European Union Neutralizing Antibodies in Multiple Sclerosis Program (NABINMS)

This rather extensive EU project was described briefly in last year's Standards Committee meeting minutes, about which further information can be obtained at its website, www.nabinms.eu. Whether the grant due to expire this year has been extended for an additional year is not known. The results of this collaborative initiative are not yet available.

Dr. Tovey informed the Committee of additional European initiatives, such as the EU Innovative Medicines Initiative (IMI), intended to improve predictability of immunogenicity, which includes a standardization program for immunogenicity analyses, development of predictive tools, and sharing of acquired knowledge. These research efforts are being supported by funds from the EU and multiple biopharmaceutical companies through integrated consortia.

III. Availability of Reference Reagents from BEI Resources

The current ISICR Newsletter contains an article by Dr. Grossberg that includes a tabulation of Reference Reagents, Standard Preparations, and antisera that are now available through BEI Resources. These reagents were obtained from various sources and produced by support from the U.S. National Institute of Allergy and Infectious Diseases. The article provides information as to how application should be made to BEI Resources, for which approval must be obtained prior to requests for reagents, as detailed in the ISICR Newsletter article (attached).

IV. Needs for New Reference Antisera

The Committee was asked to advise BEI Resources concerning the need for possible replacement of certain antisera for which supplies are becoming low: (1) Sheep antiserum to Mouse L-Cell Interferon, (2) Sheep Antiserum to Human Fibroblast Interferon, (3) Calf Antiserum to Human Lymphoblastoid Interferon-α, (4) Rabbit Antiserum to Mouse Interferon-γ, and (5) Rabbit Antiserum to Human Interferon-γ. After considerable discussion, the Committee recommended that BEI Resources consider obtaining from currently available commercial sources those antisera where exact substitutes having the needed range of reactivities are available, especially Rabbit Antiserum to Human Interferon-β and Mouse Monoclonal Antibody (mAb) to Human Interferon-β, provided the antibody preparations have demonstrable ELISA, western blot, and neutralizing antibodies; descriptions of highly characterized anti-HuIFN-β mAbs with multiple reactivities have been published and are presumably available. Commercially available Rat Monoclonal to Mouse Interferon-γ and Rabbit Purified Immunoglobulin to Human Interferon-γ appear to be suitable substitutes for those reagents. It was not thought useful to

*(**ISICR Committee Minutes**, cont. from page 30)*

replace the Calf Serum to Human Lymphoblastoid Interferon-α or similar antibody preparations.

Dr. Tovey suggested that consideration be given to establishing as possible reference reagents or standards the products of two poxviral genes that neutralize IFNs: (1) the soluble receptor secreted glycoprotein related to protein B18 from vaccinia virus that inhibits human type I interferons but not type III interferons, and (2) the recently described Yaba-like disease virus protein that neutralizes both type I and type III interferons. The B18 glycoprotein can inhibit a broad range of interferons including murine IFN-α, whereas Y136 protein inhibits only primate and not rodent type I interferons. Production of these proteins should not be a problem since their genes have been cloned (Huang et al., *PNAS*, 104:9822, 2007 and Symons et al., *Cell*, 81:551, 1995). The Committee felt that further consideration should be given to the production of these potentially useful interferon inhibitors as reference reagents.

V. New Standards and Reference Reagents

Dr. Meager provided the following information from NIBSC:

1. TRAIL (tumor necrosis factor-related, apoptosis-inducing ligand). A summary report was presented to WHO ECBS recommending that an International Reference Reagent (IRR) be established for TRAIL in October 2007. The WHO ECBS established the TRAIL preparation 04/166 as the IRR for TRAIL in November 2007.
2. Reference materials for Neurotrophin-3 (NT-3), IL-23, IFN-λ1 (IL-29), IL-24, IL-27, and BLyS (B-lymphocyte stimulator) are in various stages of preparation at NIBSC. Further sources of these cytokines are being actively sought.
3. A suitable bioassay for BLyS has been developed (McClements et al., Journal of Immunological Methods, 337:63-70, 2008).
4. The potential need for reference materials for IL-17F, IL-21, IL-22, and certain PEGylated cytokines, e.g., IFN-α2, is recognized.

VI. Standards for New or Modified (e.g. PEGylated) Interferons

Dr. Ron Bordens had directed the Committee's attention to the problems of standardization of interferonsmodified by the addition of polyethylene glycol (PEG). Dr. Meager provided comments that preliminary results from antiviral and reporter gene assays suggest non-parallelism in dose responses between PEGylated IFN-α2 products and the International Standards for IFN-α2a or IFN-α2b. The Committee discussed at length the varieties of attributes of PEGylation that can alter the biological or molecular properties of the interferons, such as the chemistry used to conjugate the PEG to the protein, the length and/or branching of the side-chain, the site(s) of modification and their proximity to receptor binding sites, the differences in retained antiviral activity following PEGylation, the effects of PEGylation on pharmacokinetics, and reactivity with neutralizing antibodies. Since these factors differ significantly between the PEGylated IFN preparations, the Committee felt that a single standard preparation would not be appropriate, but that a given PEGylated IFN should serve as its own standard. However, with the possible advent of biosimilar PEGylated IFNs, where multiple manufacturers may produce the same form, a standard preparation to cover the original and biosimilar version(s) may be appropriate, for which additional biological, chemical, and physical information may be required.

VII. Standardization of Biosimilar (Follow-on or Generic) Interferons

The world-wide problem of generic replacements of protein biologicals on which the original patents are expiring was brought to the attention of the Committee by WHO and briefly discussed by the Committee last year. Substantial concerns remain about biological equivalence and safety of such substitutes for currently approved IFN products, especially in countries without appropriate regulatory controls. Europe has apparently established a regulatory pathway for follow-on biologics, but appropriate legislation is pending in the U.S. The Committee commented that it is most unlikely that current manufacturers will involve themselves in providing appropriate information for the satisfactory production of such follow-on materials. Dr. Meager had indicated that NIBSC has undertaken to study some IFN-β1a products with respect to biological potency

*(**ISICR Committee Minutes**, cont. from page 31)*

estimated by *in vitro* bioassays and molecular characteristics assessed by immunoblotting and high performance liquid chromatography.

There being no additional discussion items, Dr. Grossberg informed the Committee that this is his 21st year as Chairman of the Committee, a matter he has discussed with ISICR President Eleanor Fish, who has appointed Dr. Michael Tovey as the new Chairman to begin in 2009. The meeting was adjourned at 17:30 hours.

Respectfully submitted,
Sidney E. Grossberg, Chair

BIOLOGICS WORKING PARTY MEETING
on 11-13 February 2008
Chairman: Prof. J-H Trouvin

BWP report to the CHMP

Interferons and neutralising antibodies (in multiple sclerosis)

1st phase of the project: Development of a standardised assay methodology for the determination of neutralising antibodies.

Background information
Currently three interferon (IFN) beta preparations are registered for the treatment of certain stages of multiple sclerosis (MS). Two preparations (Rebif and Avonex) are produced from mammalian cells (CHO) and one preparation (Betaferon) from bacteria (E. coli). The two CHO-derived beta interferons are glycosylated products. The E. coli derived product, which is not glycosylated and differs in two amino acid residues from the CHO expressed products, has about 10 % of the specific activity of the CHO-derived products. All three products differ in formulation, dosing schedule and route of administration. All three products have been reported to induce neutralising antibodies (NABs) in MS-patients (from 5 to more than 50% after one year of treatment). There have been reports suggesting that these antibodies may be associated with a loss of efficacy of treatment.

With respect to the effect of NAB on the safety and efficacy of Interferon beta used for the treatment of MS, there are two separate, but related issues to be addressed:
- the incidence of NAB formation
- if and at what level do these antibodies have real biological effects such as inhibition of efficacy

At its July 1999 meeting, the CPMP appointed Dr. Huub Schellekens (NL) as the co-ordinator for the first phase of the project dedicated to the development of a standardised assay methodology for measuring neutralising antibodies. Given the nature of this topic, the BWP was asked to provide the CPMP with recommendations on the proposals to be developed in collaboration with the 3 Marketing Authorisation Holders (MAHs).
On 17 February 2000, a BWP/CPMP adopted recommendation was sent out to the 3 Marketing Authorisation Holders (Ares-Serono, Biogen and Schering AG) with the following proposals:
- the MAHs were asked to introduce as a common assay the viral cytopathic effect (CPE) inhibition based assay analysed according to the Kawade principle.
- the MAHs were asked to collaborate in the blind panel testing approach

During the development of the common assay, the progress was closely monitored and discussed at:
- April 2000 BWP (session with MAHs to agree upon a common approach)
- December 2000 BWP (report from co-ordinator and start of exchange of sera)
- June 2001 BWP (report from co-ordinator on first results on serum titers using in-house assays)
- July 2001 BWP (adoption of BWP report on the report of the co-ordinator dated June 2001)
- July 2002 BWP (report from co-ordinator on further blind exchange of sera and advantages of the MxA assay; adoption of BWP report)
- November 2002 BWP (session with MAHs to report on the MxA assay as a suitable common assay and to agree on a time table to finalise the development and validation of the common assay)

*(**ISICR Committee Minutes**, cont. from page 32)*

- December 2002 BWP (adoption of BWP report on the MxA assay and the outstanding issues)
- July 2004 BWP (session with MAHs to report on the validation of the MxA assay and the blind panel testing)
- September 2007 BMWP/BWP Workshop on Immunogenicity Assessment of Therapeutic Proteins

Common assay methodology
Following a recommendation from the CHMP/BWP, the MAHs agreed to validate a common bioassay based on viral CPE inhibition and the Kawade principle in addition to their established in-house methods. The assays used by Serono and Biogen (both viral CPE-assays) were shown to be dependent on the interferon used in the assay. The assay used by Schering/Berlex (MxA- ELISA assay) however, seemed independent of the interferon used. Although this observation could not be confirmed by further experiments in the laboratories of the different MAHs, based on this initial finding the MxA-assay was selected for further development as the common assay and it has been decided to continue to develop this assay, because of its advantages, i.e. no need for viruses, easier to standardise, possibility to automate and safer methodology. In addition, practical problems were raised regarding the distribution and importation of the viruses in the required different geographical areas for the CPE assay.

Briefly, in the MxA-assay, A549 cells[1] seeded in well plates are incubated with a mixture of sera and challenge IFN. The IFN stimulates the intracellular production of the MxA protein. The cells are then lysed and the amount of MxA is measured with an ELISA using a rat monoclonal antibody (MAb) to capture and a biotinylated mouse MAb for detection. The titer is calculated using the Kawade equation, defining the titer as the dilution of serum that reduces the amount of Laboratory Units (LU) of IFN by 90% (1 LU = EC50 i.e. 50% MxA induction).

The MxA assay validation has been finalised and showed good inter- (1.9 - 5.3%) and intra-lab (0.4 - 4.4%) reproducibility of the assay, estimated by the Coefficient of Variation (CV %). As part of the validation, the relative sensitivity of the assay was tested in the labs of the three MAHs using a limiting dilution assay with the international reference preparation for IFN beta.

The use of Betaferon as a challenge antigen produced consistently lower titers than Avonex, Rebif or the natural interferon beta standard. Futhermore, the detection limit was shown to be dependent on the challenge antigen, with Avonex and Rebif as a challenge antigen being more sensitive. As a last step in the assay development and validation, a panel of sera were sent by the MAHs to NIBSC (November 2003), which were subsequently blinded and distributed (62 samples) to the MAHs by NIBSC (January 2004). The panel was tested against all three authorised interferon beta preparations and the natural interferon beta standard. Testing showed 100% concordance in terms of positive and negative assay results across the three MAHs with the natural interferon beta standard as a challenge antigen. A high concordance was also demonstrated when the CHO derived beta-interferons were used as a challenge antigen. Also the titres obtained for all sera were largely concordant when the natural interferon beta standard or the CHO derived beta-interferons were used as a challenge antigens; the use of *E. coli* derived interferon-beta (Betaferon) resulted in lower titres.

Because of the limited supply of the natural interferon beta standard, it cannot be chosen as a challenge antigen for future routine testing; NIBSC was requested to undertake a statistical analysis so a decision could be made on which of the three beta-interferons should be chosen as a challenge antigen for the common assay. Following timely provision of the data by the MAHs to NIBSC, a summary of this statistical analysis for discussion by BWP was submitted on 28 August 2007. The statistical analysis comparing the viral CPE assay and the MxA assay was also performed. The statistical analysis conducted by NIBSC shows that the CHO derived interferon beta as a challenge should be the standard antigen in both assays. The MAHs agreed in principle to publish the MxA assay method after the statistical analysis has been finalised.

[1] *Continuous cell line derived from human alveolar carcinoma.*

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Previously, it was highlighted that discussions concerning the use of the common assay identified two main goals that could be considered:

- Harmonise the section on antibodies in the different SPCs by expressing titres and incidence of development of antibodies based on the common assay. This can be achieved by retesting (a representative part of) the sera collected during the clinical trials on which the SPCs are based or by using samples from more recent studies using preparations and formulations that are currently being used.
- Correlate titres obtained by the common assay with clinical effects.

Availability of materials and reagents
Novartis has confirmed that the MxA ELISA assay and the MxA antibody are no longer protected by patents in Europe. NIBSC indicated that they will conduct a collaborative study in order to compare the antibody produced by Novartis with the previously used antibody made by Biogen. Initially NIBSC will also produce and make available a first batch of antibody produced from hybridoma. EDQM indicated that, in principle is willing to take over the larger-scale production of the antibody reagent in the future, provided that the hybridomas are made available.

Conclusions
A potential common assay methodology for the determination of neutralising antibodies was successfully developed. When using CHO derived antigen the MxA assay correlated well with the CPE method. The final development of an antigen independent assay necessitated overcoming difficulties with the availability of viral stocks for the initial assay method. The availability of the test methodology and reagents is resolved. It was also remarked that sponsors may be able to use other methods that utilise updated technologies for the quantification step of the assay (e.g. mRNA quantification). However, it should be stressed that in case the sponsors use those new technologies, they will have to demonstrate how the new assay compares to the agreed upon common assay, so as to guarantee standardisation in the expression of the results in antibody formation and incidence rate (to be reported in product literature).

The first phase of the project as requested for the CHMP has been completed.

BWP recommendation to the CHMP

- In view of the satisfactory outcome of the statistical analysis of the validation results, the MxA assay has been developed on the understanding that the description of the method and reagents are publicly available. The MAHs should be encouraged to publish the method.
- The statistical report presented by NIBSC confirmed that the MxA assay is a suitable standardised test method for the assay of interferon beta neutralizing antibodies, and CHMP may consider:
  -the harmonisation of the section on antibody formation in the SPCs of the respective products by expressing titres of antibody formation and incidence rate based on the common assay;
  -consider pathways to achieve the second goal, i.e. correlating titres obtained by the common assay with clinical consequences[2].
- Agree that this report is copied to the MAHs and to make it public on the EMEA website.

[2] Please note that in the new EC Framework Programme there is a call in the area of biopharmaceuticals, which emphasises the collaboration between scientists, industry, regulatory authorities and others.

Availability of Interferon and Cytokine Reference Reagents, Antisera, and Standards

Sidney E. Grossberg, Chairman, ISICR Standards Committee

Investigators, pharmaceutical manufacturers, and commercial laboratories should be aware of the new National Institutes of Health repository for cytokine reference reagents, antisera, and some World Health Organization (WHO) International Standards, for which new request procedures, explained below, are now required. Such materials are essential for the standardization of cytokine products, as well as in bioassays for conversion of Laboratory Units to International Units, neutralization assays, establish of relative sensitivity of bioassays, immunologic

*(**ISICR Committee Minutes**, cont. from page 34)*

identification of cytokines, among other uses. As before, the National Institute for Biological Standards and Control (NIBSC), www.nibsc.ac.uk (South Mimms, Hertfordshire, UK) remains an excellent source for cytokine reagents and WHO International Reference Preparations.

For many years the U.S. National Institute of Allergy and Infectious Diseases (NIAID) had maintained a repository for interferon standards, antisera, and some WHO International Reference Preparations that had been prepared for the NIH. These had been maintained by contract with different companies, e.g., KamTek. More than a year ago, such materials were transferred along with many other types of biological materials to BEI Resources (Biodefense and Emerging Infections Resources Repository), which was established to control under a single authority the distribution of all reference biological materials, including those agents that might be used for criminal, terrorist, or other nefarious purposes, in addition to antisera and other benign reference reagents, such as interferons. BEI Resources has contracted with the American Type Culture Collection (ATCC) for the distribution of these materials, but approval to receive materials must first be obtained by application to BEI Resources.

General information and instructions for application are available at www.beiresources.org (previously listed in the ISICR Standards Committee meeting minutes as www.bioresources.com). You and your institution must first apply to BEI Resources to obtain approval before you will be able to obtain materials of any sort. Although we have been told that their application procedure has been improved, it may still be slow. You should obtain and complete the required forms listed at their registration page, http://beiresources.com/registration/index.cfm. The Material Transfer Agreement (MTA) that your institution must file with the application expressly forbids sharing materials outside the institution. The Indemnification clause about liability stated in the standard form MTA can be modified, but you or your institutional official may need to negotiate modifications in the language if it conflicts with your institutional rules. In principle, this should be resolved without too much difficulty for Biocontainment Level 1 class of materials, to which interferons and antisera belong. Once the approval process has been completed, which may take a month or more, the ordering process, which can be accomplished through the internet, is relatively straightforward and efficient. A person at the repository who has been helpful in the past is Patrick Bodishbaugh, contact@bioresources.org, phone 1-800-359-7370. The NIH Project Officer, Susan Peacock, can be contacted if necessary at peacocksusan@niaid.nig.gov, 1-301-451-5093.

A Product Information Sheet taken from the NIAID catalog describing the reference reagent is supposed to be linked to the web site product page, but may be incomplete. In the past, an NIH Reference Reagent Note accompanied the reference material, standard, or antiserum that had been prepared for the NIH. Such Reference Notes provided valuable scientific information about reference reagent preparation, purification, characterization, and assignment of potency along with supporting data. BEI Resources staff have indicated their intention to supplement Product Information Sheets with information available from the Reference Reagent Notes.

Dr. Connie Young of BEI Resources has graciously provided the following table for the information of the ISICR membership.

NIAID Research Resources for IFN Research

BEI Number	Product	NIAID Number	On Web	Additional info/paper	Date of Ref Note
NR-3072	Freeze-Dried Human Anti-Human IFN Alpha Antibody Ref	G037-501-572	Yes	No. 44	Feb-95
NR-3073	Freeze-Dried Human Anti-Human IFN Beta Antibody Ref	G038-501-572	Yes	No. 45	Feb-95
NR-3074	Freeze-Dried Rabbit Ref IFN	G019-902-528	Yes	No. 10A	Dec-73 rev Jun-80
NR-3076	Freeze-Dried Ref Murine IFN Alpha	Ga02-901-511	Yes	No. 40	Mar-87
NR-3077	Freeze-Dried Ref Human IFN Alpha (Namalwa/Sendai)	Ga23-901-532	Yes	No. 30	Jan-84
NR-3078	Freeze-Dried Ref Human IFN Alpha (Leukocyte/Sendai)	Ga23-902-530	Yes	No. 29	Jan-84
NR-3079	Freeze-Dried Ref Murine IFN Beta	Gb02-902-511	Yes	No. 41	Mar-87
NR-3080	Freeze-Dried Ref Human IFN Beta	Gb23-902-531	Yes	No. 35	Mar-87
NR-3081	Freeze-Dried ref Murine IFN Gamma	Gg02-901-533	Yes	No. 42	Mar-87
NR-3082	Freeze-Dried Ref Murine IFN Alpha/Beta	Gu02-901-511	Yes	No. 39	Mar-87
NR-3083	Freeze-Dried Ref Human Recombinant Alpha 2 IFN	Gxa01-901-535	Yes	No. 31	Jan-84
NR-3085	Freeze-Dried Ref Human Recombinant IFN Beta/ser	Gxb02-901-535	Yes	No. 37	Mar-87
NR-3086	Freeze-Dried Human IFN Gamma Ref	Gxg01-902-535	Yes	No. 43	Feb-95
NR-3087	Sheep Antiserum to Mouse L-Cell IFN	G024-501-568	Yes	No. 19	Aug-80
NR-3088	Control Antiserum (Sheep) to Mouse L-Cell IFN	G025-501-568	Yes	No. 20	Aug-80
NR-3089	Sheep Antiserum to Human Leukocyte IFN	G026-501-568	Yes	No. 22-R	Mar-81 rev Sep-95
NR-3090	Control Antiserum (Sheep) to Human Leukocyte IFN	G027-501-568	Yes	No. 23	Mar-81
NR-3091	Sheep Antiserum to Human Fibroblast IFN	G028-501-568	Yes	No. 24	Mar-81
NR-3092	Control Antiserum (Sheep) to Human Fibroblast IFN	G029-501-568	Yes	No. 25	Mar-81
NR-3093	Calf Antiserum to Human Lymphoblastoid IFN Alpha	G030-501-553	Yes	None	
NR-3094	Rabbit Antiserum to Mouse Gamma IFN	G032-501-565	Yes	No. 32	Aug-84
NR-3095	Control Antiserum to Mouse Gamma IFN	G033-501-565	Yes	No. 33	Aug-84
NR-3096	Rabbit Antiserum to Human Gamma IFN	G034-501-565	Yes	No. 34	Aug-84
NR-4283	Control Antiserum (Calf) to Human Lymphoblastoid IFN Alpha	G031-501-553	Yes	None	

International Society for Interferon & Cytokine Research, Inc. COMPARATIVE BALANCE SHEETS As of September 30, 2008

2008
ASSETS
11100 - Cash - Bank of America 105,270.73 $
11111 - Business Interest Maximzer 51,081.39
11112 - Bank of America CD 103,739.10
12200 - Interfund 11000 (2,442.50)
12800 - Accounts Receivable - 2008 Annual Meeting 10,000.00

TOTAL ASSETS 267,648.72 $

LIABILITIES
21800 - Due to Publisher-Print Only - $
23109 - Deferred Dues - 2009 7,310.00
23110 - Deferred Dues - 2010 2,590.00
23111 - Deferred Dues - 2011 680.00
23112 - Deferred Dues - 2012 680.00
23113 - Deferred Dues - 2013 50.00
23901 - Temporary Restricted Contribution Recorded in Current Year 61,500.00

TOTAL LIABILITIES 72,810.00 $

CAPITAL
31100 - Retained Earnings 152,006.91
Current Year Profit (Loss) 42,831.81

TOTAL CAPITAL 194,838.72

TOTAL LIABILITIES & CAPITAL 267,648.72 $

International Society for Interferon & Cytokine Research, Inc. Consolidated Statements of Revenues and Expenses For the 3rd Quarter Ended September 30, 2008

Y-T-D
Revenue As of 09/30/2008
42200 - Interest - Savings Accounts and CDs 450.51 $
43101 - Dues - Life Member 1,000.00
43102 - Dues - Post Doc 700.00
43103 - Dues - Student 270.00
43104 - Dues - Emeritus 250.00
43108 - Dues - 2008 20,166.00
43901 - Corporate Contributions 10,000.00
44000 - Income From Spring Meeting 39,774.74

Total Revenue 72,611.25 $

Expenses
52200 - Addressing, Mailing, and Shipping 123.38
52300 - Telephone Expense 324.44
53200 - Printing and Graphics 2,632.53
53300 - Office Supplies/Computer EQ Under $5,000 94.48
53900 - Professional Services 10,233.00
53903 - Computer Services Expense 510.87
53909 - Financial Services 10,874.97
53921 - Email-Internet Charges 73.24
53922 - Web Related Charges 2,313.50
53964 - Contracted Priority Shipping 43.33
55103 - Awards - Other 429.10
59900 - Miscellaneous Expenses 449.25
59966 - Credit Card Discount & Handling Fees 1,630.46
59977 - Misc. Expense - Bank Charges 46.89

Total Expenses 29,779.44 $

Net Profit (Loss) 42,831.81 $

ISICR 2009

Join the ISICR for our joint meeting with the International Cytokine Society and the Society for Leukocyte Biology at the Lisbon Conference Center, Lisbon, Portugal - October 17-21, 2009.

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Track II: Disease Immunopathogenesis Mechanisms. 8 sessions include: Therapeutic Application of Cytokine Antagonistso Viral pathogenesis and interactions with Toll-Like receptors: HIV, CMV, HCV • Pathogen interactions with Toll-like receptors: TB and Malaria • Sensing Fungal infection and host response • Chronic Inflammatory Disease

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