ISICR

INTERNATIONAL SOCIETY FOR
INTERFERON AND CYTOKINE RESEARCH

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The Seymour and Vivian Milstein Awards

The ISICR wishes to express its deepest gratitude and appreciation for the support of the Milstein Family. This year the **Seymour and Vivian Milstein Awards** support the Milstein Award, the Milstein Young Investigator Awards and, for the first time ever, the Milstein Travel Awards. These awards allow the ISICR to support the strongest science in interferon and cytokine research and permit our members, particularly young investigators, to present their work at our annual meeting. We are honored by their support and dedicate our efforts to supporting excellence in biomedical research through **The Seymour and Vivian Milstein Awards**.

ISICR Award Recipients

Seymour and Vivian Milstein Award Winners

Nancy Reich
Stony Brook University, Stony Brook, NY
nancy.reich@stonybrook.edu
(Mini bio page 2)

Menachem Rubinstein/Daniela Novick (joint award)
Weizmann Institute of Science, Rehovot, Israel
menachem.rubinstein@weizmann.ac.il
daniela.novick@weizmann.ac.il
(Rubinstein mini bio page 2, Novick mini bio page 3)

ISICR Honorary Members

Philip Marcus
University of Connecticut, Storrs, CT
philip.marcus@uconn.edu
(Mini bio page 5)

Kathryn Zoon
National Institute of Allergy and Infectious Diseases, Bethesda, MD
kzoon@niaid.nih.gov
(Mini bio page 4)

*(See **Award Recipients**, page 2)*

*(**Award Recipients**, cont. from page 1)*

Seymour and Vivian Milstein Young Investigator Award Winners

Carole Galligan, Toronto, Canada
Toronto General Research Institute, Toronto, Canada
cgalliga@uhnres.utoronto.ca
(Mini bio page 6)

Joao Marques, Cleveland OH
Cleveland Clinic Foundation, Cleveland, OH
MARQUEJ@ccf.org
(Mini bio page 5)

Youcun Qian, Cleveland OH
Cleveland Clinic Foundation, Cleveland, OH
QIANY@ccf.org
(Mini bio page 6)

Devanand Sarkar, New York, NY
Columbia University Medical Center, New York, NY
ds2039@columbia.edu
(Mini bio page 6)

Chunfu Wang, Dallas , TX
University of Texas Southwestern Medical Center, Dallas, TX
Chunfu.Wang@UTSouthwestern.edu
(Mini bio page 6)

Christina Fleischmann Memorial Award Winner

Dedicated to the memory of outstanding Interferon research scientist, Dr. Christina Fleischmann

Katja Pokrovskaja, Stockholm, Sweden
Karolinska Institute, Stockholm, Sweden
katja.pokrovskaja@cck.ki.se
(Mini bio page 7)

Dr. Nancy Reich, Ph.D.

Dr. Nancy Reich, Ph.D. received her B.A. from Hofstra University and her Ph.D. from the State University of New York at Stony Brook. She then began postdoctoral research in the laboratory of Dr. Jim Darnell at Rockefeller University where she became interested in the IFN signaling pathways. In 1988 she became an Assistant Professor in the Department of Pathology, Stony Brook University and became a Full Professor in 2002. In 2004 she moved to the Department of Molecular Genetics and Microbiology at Stony Brook. Her investigations have led to the discovery of a primary defense response of the cell that is stimulated by dsRNA and is independent of interferon. dsRNA activates a latent transcription factor, designated Interferon Regulatory Factor-3 (IRF-3) that directly induces a subset of interferon stimulated genes. More recently her studies have elucidated mechanisms that regulate nuclear trafficking of the STAT transcription factors activated by interferons and cytokines. Distinct mechanisms regulate localization of STAT1, STAT2, and STAT3, and these findings set the stage for design of inhibitors or activators of STAT function. Dr. Reich has received the Catacosinos Young Investigator Award and the American Cancer Society Junior Faculty Research Award and has participated in numerous NIH study sections. She is also on the Editorial board of the *Journal of Interferon and Cytokine Research*. Dr. Reich credits her success to the efforts of the outstanding graduate students and postdoctoral fellows whose skills and devotion are responsible for the scientific achievements of her research team.

The Reich lab website is:
http://www.path.sunysb.edu/faculty/woz/nreich

Menachem Rubinstein, Ph.D.

Prof. Menachem Rubinstein, Ph. D. was educated as a biochemist, earning his Ph.D. degree from the Weizmann Institute of Science, Rehovot, Israel in 1975. As a postdoctoral fellow and later as a visiting scientist at the Roche Institute of Molecular Biology (Nutley, New Jersey), he developed the RP-HPLC method for protein fractionation, which he utilized for the first purification and characterization of human leukocyte IFN in 1979. This work, which was done in collabora-

*(**Award Recipients**, cont. from page 2)*

tion with Dr. Sidney Pestka, then at the Roche Institute, culminated in the development of Roferon-A™ by Roche. Since 1980, Dr. Rubinstein has been a member of the Department of Molecular Genetics at the Weizmann Institute of Science. In 1983, he was appointed to the Maurice and Edna Weiss Professorial Chair of Cytokine Research. In addition to his research projects and mentoring graduate students at the Weizmann Institute, Prof. Rubinstein served as Chief Scientist of Interpharm Laboratories in Israel from 1987 to 1990. During that period he headed the team that developed recombinant IFN-β (REBIF™) for clinical use.

At the Weizmann Institute, Prof. Rubinstein joined forces with Prof. David Wallach's team to purify and sequence the two soluble TNF receptors, one of which (TNFR2) is the active core of the anti-inflammatory drug Enbrel™. Prof. Rubinstein and his long-time colleague Dr. Daniela Novick have discovered and isolated many soluble cytokine receptors, including sIL-6R, sIFNγR, sTNFR2 and sIFNAR2. Based on the protein sequence of the later, Dr. Batya Cohen of Rubinstein's team cloned the IFN receptor IFNaR2. In collaboration with Dr. Charles Dinarello, Prof. Rubinstein, Dr. Daniela Novick, and PhD student Soo-Hyun Kim discovered and cloned the IL-18-binding protein, a natural inhibitor of IL-18. Later, they showed its role in various inflammatory diseases. IL-18-binding protein is now undergoing extensive clinical development as a potential treatment for various autoimmune diseases. In recent years, Prof. Rubinstein has mainly focused on studying transcriptional regulation of genes coding for cytokines and their receptors. Prof. Rubinstein joined ISICR at its inception and in 1995, he initiated the ISICR web site (Currently: http://www.isicr.org). He also serves on the editorial board of *The Journal of Interferon and Cytokine Research*. He has published over 120 papers and his honors include the Ionel Saniel Career Development Chair and the Maurice and Edna Weiss Chair of Cytokine Research.

Rubinstein lab web page:
http://www.weizmann.ac.il/molgen/members/rubinstein.html

Daniela Novick, Ph.D.

Dr. Daniela Novick, Ph.D. was born in Poland in 1948, a daughter to two Auschwitz and death march survivors. In 1957 the family immigrated to Israel. In 1967, Dr. Novick served in the Israeli air force. She is a mother of two and a grandmother of one. Dr. Novick received a M.S. degree in Microbiology in 1972 from the Tel-Aviv University and in 1973, she was a Research Assistant in the Department of Medicine, University of Cambridge, England. Dr. Novick received the Ph.D. degree in 1979 from The Weizmann Institute of Science, Rehovot, Israel and the topic of her thesis was "Experimental Autoimmune Myasthenia Gravis". At present, Dr. Novick holds the position of tenured Senior Staff Scientist in the Department of Molecular Genetics, at the Weizmann Institute, Rehovot, Israel. Since 1993, she has been repeatedly elected as a representative for over 100 staff scientists at the Weizmann.

In 1979 Dr. Novick joined the laboratory of Prof. Michel Revel and together with Prof. Rubinstein she generated a battery of monoclonal antibodies to IFN-α, -β and -γ, a pioneering achievement for the early 80's. In fact, these antibodies have facilitated the development of large-scale purification and monitoring of all these IFNs, but mainly IFN-β, which is in global use for the treatment of multiple sclerosis.

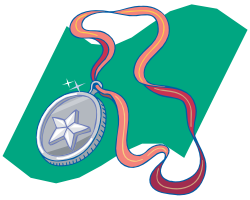
Since 1987, in the laboratory of Prof. Rubinstein, Dr. Novick's research focuses on cytokines and their receptors. In 1989, following a collaboration with the group of Prof. David Wallach, on the purification and characterization of soluble TNF receptors, the TBPI and TBPII, Dr. Novick introduced a new topic to the lab: "Soluble cytokine receptors in normal human fluids" (J. Exp. Med. 170: 1409, 1989). Since then she purified and characterized four additional receptors: the soluble IL-6 receptor, the soluble IFN-γ receptor, the soluble LDL receptor and the soluble IFN-α/β receptor, thus converting from hypothesis to a fact, the prediction that almost every cell surface receptor has a soluble homolog. These observations have established the notion that soluble receptors are normal constituents of body fluids and may serve as

*(**Award Recipients**, cont. from page 3)*

carriers, or antagonists, or agonists of their corresponding cytokines including the IFNs. Of note is Dr. Novick's unique approach that led to the isolation of the soluble IFNα/β receptor from normal human urine, bringing to an end the long sought-after ligand-binding subunit of the IFN- α/β receptor (Novick et al, Cell 77:391, 1994), later renamed IFNAR2.

In 1997, in collaboration with Prof. Dinarello laboratory, Dr. Novick discovered, purified and characterized the IL18-binding protein (Novick et al., Immunity 1999 10:127). The IL18BP is not the soluble receptor for IL18 but rather deviates from the "classical" soluble receptors, as it is not a homologue of the IL-18 receptor. This naturally occurring, novel regulator of mainly the Th1 but also of Th2 response, brought a new level of understanding of control of IFN-γ activity. IL-18BP was found to be active in several model diseases such as rheumatoid arthritis, ischemic heart disease, atherosclerosis and Crohn's disease. Part of Dr. Novick's work has been translated into clinically useful therapies. Her research expertise made a major contribution to the isolation and development of two widely used biologicals, IFN-beta and tumor necrosis factor soluble receptor p75, each of which has reduced the severity of multiple sclerosis and rheumatoid arthritis for hundreds of thousands of patients.

Currently, Dr. Novick is studying the binding protein for a novel proinflammatory cytokine, the IL-32. Dr. Novick has published over 80 research papers and 15 reviews and book chapters and also holds the corresponding patents. She was awarded the Excellency Prize for Senior Staff Scientists in 1999. All in all, Dr. Novick is convinced that the past 25 years of unique expertise team-work, mainly with Prof. Rubinstein, and the ongoing research support by Ares-Serono group of companies, are the key to this team's major impact on both basic and applied science.



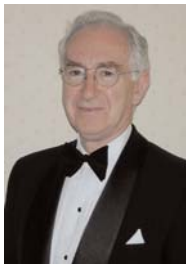
Kathryn C. Zoon, Ph.D

Kathryn C. Zoon, Ph.D. is the Deputy Director for Planning and Development of the Division of Intramural Research of the National Institute of Allergy and Infectious Diseases, NIH since June 2004. Previously she was the Principal Deputy Director of the Center for Cancer Research at the National Cancer Institute (NIH) 2003-2004. She served as the Director of the Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, and was a member of the NIH Scientific Directors, 1992-2003. Dr. Zoon was the Director of the Division of Cytokine Biology in CBER, 1988-1992 where she directed the research and review of cytokines, growth factors, and cellular products. She was at NIH from 1975 to 1980, with Nobel Laureate Christian B. Anfinsen studying the production and purification of human IFNs. She has continued her work in IFN research. She received her B.S. degree, *cum laude*, in chemistry from Rensselaer Polytechnic Institute in 1970 and was granted a Ph.D. in biochemistry from The Johns Hopkins University in 1976. Dr. Zoon is an associate editor of the *Journal of Interferon Research* and the author of over a 100 scientific papers. She was president of the ISICR, 2000-2001. She serves on the Foundation for Advanced Education in the Sciences (FAES) Board of Directors and was the first vice president, 1999-2003. She has received numerous awards, including BioPharm Person of the Year Award 1992, the NIH Lectureship 1994, Sydney Riegelman Lectureship 1994, *Genetic Engineering News* (GEN) Award 1994 for streamlining and improving the regulatory process for biologics and biotechnology products, the Meritorious Executive Rank Award 1994 for sustained superior performance in revitalizing and reorganizing the Center for Biologics Evaluation and Research to meet the challenges of new responsibilities and new technologies, National Cancer Patients "Grateful Patients Award" 1996, Rensselaer Polytechnic Institute Alumni Association Fellows Award 1997, the DHHS Secretary's Award for Distinguished Service 1998 as a member of the FDA Reform Legislation Working Group, the 1999 Johns Hopkins University Delta Omega Alpha Chapter's 75th

*(**Award Recipients**, cont. from page 4)*

Anniversary Outstanding Member Award, the 2001 DHHS Secretary's Award for Distinguished Service for outstanding leadership in positioning FDA as an important contributor to the Nation's capability to respond to bioterrorism. Dr. Zoon was elected to the Institute of Medicine, October 2002. In June of 2003 she received the Johns Hopkins University Distinguished Alumna Award and two Department of Health and Human Service awards for counter-bioterrorism and gene therapy. Finally in May of 2005 Dr. Zoon received the DHHS Secretary's Award for Distinguished Service for the Tissue Action Plan Team.

Philip I. Marcus, Ph.D.



Philip Marcus was born in Springfield, MA in 1927. He attended the Univ. of Connecticut and Univ. of Maine in the Army Specialized Training Program and was stationed in France at the end of WWII. He earned his B.S., M.S., Ph.D. from Univ. Southern Calif. (1950), Univ. of Chicago (1953), and Univ. of Colorado Medical Center [Microbiology/Biophysics](1957), respectively. His Ph.D. thesis involved developing the single-cell cloning procedure (clonogenic assay). This year rep- seminal study.* Science historian Henry Harris has called that discovery "the essential basis for what rapidly became the standard methodology for cloning animal cells." Dr. Marcus entered the interferon field shortly after attending a Cold Spring Harbor Laboratory Symposium in 1962 where he met a fellow who was working with some antiviral substance he had found and called "interferon". His name was Alick Isaacs. In 1963 he taught the first summer course on interferon at the CSHL. A young fellow named Tom Merigan was a participant in that course, as was Charles Weissman. Marcus was a charter member of the Journal of Interferon Research editorial board in 1980, and oversaw its transition to the JICR in 1995, while serving as Editor-in-Chief for 18 years. The first avian type 1 IFN (ChIFN) was cloned in his laboratory in 1994, and many novel aspects of IFN induction by viruses, including a direct demonstration of the quasispecies nature of a virus population with respect to its IFN-inducing, or IFN induction-suppressing phenotypes were elucidated in his laboratory. His recent research involved analysis of the induction of IFN by viruses, a series now numbering to XXV and his current research is designed to control avian influenza virus (AIV) in chickens with ChIFN in order to prevent the evolution of high pathogenicity AIV that may be transmitted to humans. He spent 9 years at the Albert Einstein College of Medicine before joining the University of Connecticut where he's been for 36 years, and he was recently designated a Board of Trustees Distinguished Professor in Molecular and Cell Biology. He shares a Virology/Interferon Research Laboratory there with his long time associate Margaret J. Sekellick.

* You might enjoy the article at www.advance.uconn.edu Vol.24, No. 2, Sept. 7

Joao Marques Ph.D.

Dr. Joao Marques was born in 1976 in Belo Horizonte, in the state of Minas Gerais, Brazil. He received his Ph.D. degree in Microbiology in 2002 from the Federal University of Minas Gerais in Brazil. His thesis work was focused on the characterization of wild poxviruses isolated from several regions in Brazil. After obtaining his degree, he joined Dr. Bryan Williams' laboratory as a postdoctoral fellow in the Department of Cancer Biology, Lerner Research Institute at the Cleveland Clinic Foundation in August of 2002. Dr. Marques' first project at the Cleveland Clinic, recently accepted for publication in the *Journal of Virology*, focused on interactions between p53 and dsRNA signaling and was presented at previous ISICR meetings. Recently he has been studying the activation of dsRNA signaling by siRNAs and has identified structural elements in siRNA, which determine activation of the IFN system and may define self versus non-self cellular recognition of dsRNA structures.

*(**Award Recipients**, cont. from page 5)*

Devanand Sarkar Ph.D.

Dr. Devanand Sarkar obtained his MBBS (equivalent to MD) from Dhaka Medical College, Dhaka, Bangladesh in 1994 and worked as an intern for one year. He then obtained his PhD in Endocrinology and Metabolism from Nagoya University, Japan in 2001. His work there focused on analysis of gene expression between normal adrenal gland versus benign cortisol-producing adrenocortical adenoma and the effect of microgravity on osteoblasts. He joined the laboratory of Prof. Paul B. Fisher in Columbia University in 2001 as a Post-doctoral Research Scientist and was promoted to Associate Research Scientist in 2003. Dr. Sarkar's current research focuses on analyzing the structure and function of IFN-regulated genes, such as human polynucleotide phosphorylase (hPNPase$^{old\text{-}35}$), melanoma differentiation associated gene-9 (mda-9/syntenin) and a novel IFN-regulated gene *mda*-D-74, and cytokines such as melanoma differentiation associated gene-7 (*mda*-7/IL-24). He has also developed adenovirus and lentivirus-based gene therapy approaches using the cancer-specific apoptosis-inducing properties of IFNs and cytokines, such as IFN-γ and *mda*-7/IL-24.

Chunfu Wang MD, Ph.D.

Dr. Chunfu Wang MD, PhD, is a Postdoctoral Researcher, and since 2001 he has been working in the laboratory of Dr. Michael Gale Jr., located in the Department of Microbiology at the University of Texas Southwestern Medical Center, Dallas, Texas. Dr. Wang received his M.D. degree from the Department of Preventive Medicine at China Medical University, Shenyang, China in 1989. He received his Ph.D. in Medical Science from Kanazawa Medical University, Japan in 2001. Dr. Wang is a formally trained molecular virologist and IFN biologist. His research interests are focused on understanding the molecular mechanisms and virus-host interactions that control hepatitis C virus (HCV) replication, viral RNA translation and the host cell response to IFN. Dr. Wang is particularly interested in developing new approaches to improve IFN-based antiviral therapy for the treatment of chronic HCV infection. He holds membership in the ISICR, and the American Society for Virology. Dr. Wang has published several papers on the topic of HCV replication and mechanisms IFN action. He has received Postdoctoral Fellow Travel Awards for participation in society meetings, and is actively involved in student laboratory training within the UT Southwestern Molecular Microbiology training program.

Carole Lynn Galligan Ph.D.

Dr. Carole Galligan is a Postdoctoral Fellow in the Laboratory of Dr. Eleanor Fish at the Toronto General Research Institute and working on the role of IFN-β in experimental autoimmune encephalitis. She previously worked as a postdoctoral fellow at the National Cancer Institute in Frederick MD from 2000-2004 studying the role of chemokines in inflammatory diseases. She obtained her Ph.D. in 2000 from the University of Guelph, Guelph, Ontario in Biomedical Sciences studying the mechanisms of inflammatory diseases.

Youcun Qian Ph.D.

Dr. Youcun Qian received his doctorate in molecular pharmacology from Shanghai Institute of Meteria Medica, Chinese Academy of Sciences, China in 1999. He joined the lab of Dr. Xiaoxia Li in the Department of Immunology in the Cleveland Clinic Foundation in 2000. He has now been promoted to project scientist in the department. He has a very strong interest in the research of both innate and

*(**Award Recipients**, cont. from page 6)*

Dadaptive immunity and has previously worked on IL-1/TLR signaling. His current focus is on the function of a novel molecule, Act1. To investigate the physiological function of Act1, Dr. Qian has generated Act1-deficient mice. Genetic deficiency in Act1 results in a dramatic increase in peripheral B cells, which culminates in lymphadenopathy and splenomegaly, hypergammaglobulinemia and autoantibodies. His findings demonstrate that Act1 plays an important role in the homeostasis of B cells by attenuating CD40 and BAFFR signaling. To further investigate the regulatory role of Act1 in humoral immunity by genetic approach, he generated three kinds of double knockout mice: CD40/Act1, BAFF/Act1 and TACI/Act1. Studies from these double knockout mice showed that CD40 and mainly BAFF are important for the increased peripheral B cells and hypergammaglobulinemia in Act1 deficient mice. Interestingly, Act1-mediated negative regulation of T cell dependent immune responses is CD40 dependant but BAFF independent, while that of T cell independent immune responses is both BAFF and TACI independent, suggesting an unknown pathway for T cell-independent immune responses. His future goal is to discover the mechanism of Act1-mediated negative regulation.

Katja Pokrovskaja, Ph.D.

Katja Pokrovskaja is a research scientist in the Department of Oncology & Pathology at the Karolinska Institute in Stockholm, Sweden. She received her M. Sc. degree from Moscow State

University and received her first PhD degree in molecular biology in 1994 at the Research Center for Hematology in Moscow. From 1991 she continued her research in Sweden in the department of Tumor Biology at the Karolinska Institute where she defended her second PhD thesis in tumor biology in 1999 under supervision of Prof. G. Klein. She did her postdoctoral training in the laboratory of Dan Grandér and Stefan Einhorn at Cancer Center Karolinska. Her research interests include understanding the mechanisms of IFN-α-induced apoptosis of tumor cells and the role of various signal transduction pathways activated by IFN in this process.

Seymour and Vivian Milstein Travel Awards

2005 ISICR Meeting (alphabetical listing)

Jasper Andersen; Baltimore, MD
Annika Antonsson; Brisbane, Australia
Tracey Baas; Seattle, WA
Chafia Touil Boukoffa; Elalia, Algeria
Daniel Clarke; Brisbane, Australia
Nikhat Contractor; Bethesda, MD
Natalie Dror; Haifa, Israel
Ziyun Du; Memphis, TN
Ashraf El Fiky; Irvin, CA
Tomoaki Hoshino; Kurume, Japan
Vladimir Hurgin; Rehovot, Israel
Lara Izotova; Piscaway, NJ
Thomas Kraus; Chicago, IL
Christopher Krause; Piscataway, NJ
Anna Law; Hong Kong, China
Yeuh-Ming Loo; Dallas, TX
Giorgio Mangino; Rome, Italy
Isabelle Marie; New York, NY
Louis Martinez; New York, NY
Atsuko Masumi; Tokyo, Japan
Karuppiah Mathumani; Philadelphia, PA
Ramtin Rahbar; Toronto, Canada
Sandhya Rani; Cleveland, OH
Mercedes Reboredo; Navarra, Spain
Giovanna Romeo; Rome, Italy
Vijayaprakash Suppiah; Belfast, UK
Jeremy Swann; Melbourne, Australia
Chandra Thakur; Cleveland, OH
Gilles Uze; Montpellier, France
Deborah Vestal; Toledo,OH
Zdenek Zidek; Prague,Czech Republic

ISICR HIRES AN EXECUTIVE DIRECTOR

Debra L. Weinstein (Debbie), the new ISICR Executive Director, will begin working with the society in January of 2006. Debbie earned her undergraduate degree from Tulane University and her Ph.D. in Microbiology and Immunology from the Uniformed Services University of the Health Sciences in Bethesda, MD. Debbie's research interests focused primarily on bacterial pathogenesis and the host response to bacterial infections. In 2002, Debbie moved from the lab to serve as the Executive Director of the Society for Leukocyte Biology (SLB). Since that time, Debbie has worked with the SLB council on several initiatives, including: increasing membership, updating website, print and online materials, planning and producing conferences, providing awards for students and postdoctoral fellows, and improving the financial stability of the society. As a scientist herself and member of scientific societies (SLB, American Society for Microbiology, and Association for Women in Science), Debbie's "insider" knowledge of our membership needs will help her to work with ISICR on membership recruitment and maintenance and continue to plan and then implement successful meetings. Administratively, Debbie plans to use much of the same infrastructure established during her tenure at SLB to benefit ISICR. Debbie looks forward to working with the ISICR leadership and members to see ISICR go from strength to strength.

Debbie resides in Potomac, Maryland with her husband Stafford Goldstein, M.D. and their three daughters. Active in her community, Debbie is the President of her synagogue and is on the board of the Bethesda Chapter of the Association for Women in Science and serves as the chapter's Webmaster.

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Another Road to Interferon: Yasuichi Nagano's Journey

Kazuko Uno[1], Yoichiro Iwakura[2] and Keiko Ozato[3]

Discovery of Interferon

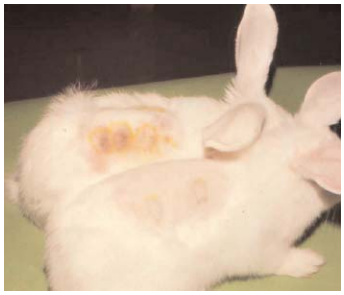
The year 2007 is the 50th anniversary of the discovery of interferons (IFN), the legendary achievement of Isaacs and Lindenmann (1). Their discovery marks the dawn of the IFN/cytokine field. When Isaacs and Lindenmann were looking into their IFN produced in chicken chorioallantoic membranes in response to inactivated influenza virus in England, there was another scientist, named Yasuichi Nagano who was coming very close to and touching IFN on the other side of the globe. In 1954, Nagano and his lifelong collaborator, Yasuhiko Kojima saw an antiviral activity in rabbit skin after injection of inactivated vaccinia virus in their laboratory in Japan (2). During the half century that followed, however, Nagano's work has steadily retreated from the IFN literature, almost to the point of oblivion. In this article we return to Nagano's path and re-examine who he was and what he has done. In this effort Nagano and his work become alive again and we realize that there were multiple roads to the discovery of IFN, the roads built by diverse, pluralistic human endeavor that is worthy of celebration.

Dr. Yasuichi Nagano

Dr. Yasuhiko Kojima

Nagano's scientific work: the 1954 publication on "virus inhibitory factor"

With the aim of developing an improved vaccine for smallpox virus, Nagano began his work at a research institute in The University of Tokyo. He and Kojima established a rabbit skin model to monitor vaccinia virus growth. With this model they tested the effect of UV-inactivated virus administered prior to live virus injection. Rabbit skin was first inoculated with live vaccine virus and tissue homogenates were prepared on various days after inoculation, and homogenates containing live virus were irradiated by ultraviolet for 6 min, completely inactivating the virus. These homogenates were their test materials, and aliquots were injected into 30 independent spots on rabbit back skin. After varying time points, previously inoculated skin regions were challenged with live vaccinia virus. Seven days later viral growth in each spot was measured. Nagano and Kojima found that test homogenates prepared three days and five days after viral inoculation differed in the ability to inhibit viral growth, although they had the same viral titer. The five-day materials contained greater inhibitory activity. They called this activity the virus "inhibitory factor". To further characterize "the inhibitory factor" (referred to hereafter as IF), they fractionated the UV irradiated homogenates in the newly imported ultracentrifuge (Spinco) by centrifugation at 35,000 rpm for 60 min. This centrifugation separated IF from the bulk of virus: the IF activity was in the supernatants, while viral particles were found in the precipitates. The IF activity was resistant to UV irradiation, while the viral fraction was sensitive. A paper describing their findings was published in 1954 in a French journal Comptes rendus des séances de la Société de Biologie *(C.R. Seans. Soc. Biol. Fil)* (2). This journal was renamed later as Journal de la Société de Biologie in 1999, and continues to publish scientific papers at present.



Rabbit skin test

Nagano and Kojima presented these and additional observations in the Annual Meeting of Japan Society for Viral Research held in 1954, recorded in VIRUS, the official journal of the Society (3). Questions from the audience centered on IF and in responding to the question as to whether IF passed through the Seitz filter, and the presenter answered that it did: it was already known that smallpox virus does not pass through the filter, supporting the idea that the IF resided in the soluble fraction. In 1958 Nagano and Kojima published two additional papers on IF again in *C.R. Seans. Soc. Biol. Fil* (4, 5). In the latter

*(**Another Road**, cont. from page 9)*

paper they further characterized IF, and showed that the virus inhibitory activity remained in the supernatants after three rounds of ultra-centrifugation. When the homogenates were injected in the skin the inhibitory activity appeared 24 hours after injection and increased further until day four. This inhibitory activity was not a neutralizing antibody, because the antibody was effective when co-injected with live virus, while IF was effective when injected one day earlier. IF passed through the Seitz filer, but did not pass through cellophane membrane. These properties are consistent with those of IFN. Some of these observations were presented in the 1956 Annual Meeting of The Japan Society for Viral Research (6) as well as in the Meeting of the Japan-France Biology Society held in 1957. At those meetings they reported that IF was produced within 24 hours after injection, the strongest inhibitory activity being seen one to two days after inoculation, followed by another peak on day seven, the latter accounted for by the production of neutralizing antibody. In their later work Nagano and Kojima fractionated their homogenates containing IF: after removing HA and other materials by 60 % ammonium sulfate precipitation, the IF activity was found in the supernatant and could be precipitated by 80 % ammonium sulfate. IF preparations were then dialyzed against cellophane membrane, and some samples were kept in storage. Later, these materials were tested for IFN activity by using the Standard IFN designated by the International Committee and were found to have an IFN titer of ~300,000 IU, an astonishingly high activity (7). Taken together, it is clear that Nagano and Kojima observed in vivo production of IFN in response to inactivated DNA virus in the whole animal model.

Although their system was unique and original, the use of an in vivo model had long plagued their science. Some critiques indicated that the system could not conclusively separate IFN from the antibody. Others argued that the species specificity and antiviral activities against other viruses were not fully clarified in their work. Worse, Nagano and Kojima made en error in mid 1960s, by suggesting that the IF activity resided in the carbohydrate moiety, although they have shown that the IF activity was also sensitive to proteolysis (8). In hindsight, their inconclusive results were an inevitable consequence of the use of an in vivo model and some of the uncertainty was associated with understandable confusions in the pre-purification/pre-cloning era. Furthermore, these problems do not erase the fact that Nagano and Kojima observed IFN production in their animal model, independently of other research on IFN elsewhere.

Nagano and Kojima, scientists of the old school

Yasuichi Nagano (1906-1998) graduated from Hokkaido University, one of seven Imperial Universities in Japan, and then worked in The Institute of Infectious Diseases, Tokyo University, where his work on IF was conducted (the Institute was renamed later as The Institute of Medical Science). Early on, he was send to The Pasteur Institute in Paris to study virology for two years (1936-38), his stipend being supported by the French Government. During his tenure as Professor in Tokyo University, Nagano served as Director of the Institute, until his retirement in 1967. After retirement from Tokyo University, Nagano continued to work first at the Kitasato Institute, then at the Sagamihara National Hospital and finally at the Hayashibara Biochemical Laboratories, Inc., from 1986 until his death.

The early visit to France made Nagano an avid Francophile: he loved all things French for his entire life. In addition to colleagues in The Pasteur Institute, Professor Nakamura of Hokkaido University, who developed the concept of "accompanying substances in viral infection" was an important influence on Nagano's scientific philosophy. His life motto was "Be humble and seek the truth", and this was broadly known among his students and colleagues.

Dr. Yasuhiko Kojima, Nagano's life-long disciple and collaborator, met him as his student and later became his right-hand man, with whom Nagano did all of his work on IF. In his memoir (9), Kojima gives a personal account of how the two scientists came to find IF, pointing out that it was not an accident: in the virology environment then in Japan, the existence of a shadowy activity such as IF was not standard thinking, and he recalls that despite much skepticism

*(**Another Road**, cont. from page 10)*

expressed by others in the Institute, Nagano consistently encouraged Kojima to continue investigating the nature of the inhibitory activity.

His colleagues describe Nagano as a great teacher and a leader of personal fortitude and charisma (9): he was one of the founders of The Research Association of Virus Inhibitory Factor, the predecessor organization of The Japanese Society for IFN/Cytokine Research (JSICR), the Japanese branch of the ISICR. Currently, the JSICR boasts 430 members (president, Y. Iwakura). The Research Association Nagano organized had directly and indirectly contributed to Japan's IFN research that followed in 1970s and 1980s. For example, Dr. Kobayashi who led a large-scale purification of IFN-b in Toray had worked with Nagano (10). Nagano was awarded The Noguchi Hideyo Memorial Award, The Japan Gakushi-In Award, and The Japan Onshi Award and is an honorary member of the ISICR since 1984.

However, Nagano's research met with complex reactions from Japanese colleagues: while he was influential among some workers, who regarded the publication of IF as the initial IFN discovery, others were not so sanguine about claiming it as an authentic IFN (10) (see below). In his later years Nagano was aware of the fact that his work was not widely recognized and was not fully integrated into the main stream of IFN research that followed. There has been a sense of disappointment and regret about these circumstances among some researchers (9). However, Nagano did not actively seek an adjustment or reevaluation of his status in the field. There is no record on a personal contact between Nagano or Kojima and Isaacs or Lindenmann throughout their scientific career. Some say that Nagano was slow in placing his work in the context of the newly emerging IFN field and rarely presented his work at international settings. Despite these issues, Nagano's standing did not fade in Japan's IFN research community.

Nagano's place in the history: A quest for a new view

As years progressed from 1970s to 1980s, his name gradually disappeared from the IFN literature. The younger generation grew up without knowing about Nagano's work, and this was true even in Japan. Is this because of the limitation of his science? To be sure, his in vivo system was too complex to be decisive in the further characterization and purification of IFN molecules. Or, is it because his papers appeared in French rather than English, the increasingly exclusive language of biology? This may be a contributing factor, however trivial it seems. These factors are, however, mere partial explanations. There were other historical grounds. In the post-war scientific community in Japan there was little sentiment to appreciate endogenous science, as Japanese scientists were too busy catching up with the progress in America and Europe. Their eyes focused strictly on the West. One may assume that Japanese scientists did not feel confident in themselves, and were perhaps reluctant to cite Nagano's work in their papers, for fear of perceived parochialism. Further, there were few Japanese scientists in the field who had sufficient standing to have the opportunity to properly introduce Naganos' work to the international community. It is cleat that his relative obscurity stems from multiple bases.

In spite of these circumstances it is noteworthy that Naganos' standing is making an amazing comeback in Japan. Intense debates among IFN researchers have rekindled the search for Nagano's place in history. These debates have been recorded in the JSICR Newsletters, to which the surviving Kojima (now 77 years old) has been an important contributor. Scholarly investigations of Nagano's contributions have been published by Watanabe (11,12) and Uno, Editor, the JSICR Newsletter (13). The present article is an addition to these efforts. In this effort we view Nagano's historical work with a renewed sense of awe and urgency for re-evaluating his work from a global, multicultural perspective. To be clear, our summation is not an attempt to claim for Nagano the discovery of IFN. Rather, our effort is a quest for a balanced historical understanding of IFN research. These efforts coincide with the globalization of scientific research and the increased awareness that science is universal, contributed by and meant for all of us, regardless of race, gender and nationality. Nagano and Kojima lived in the era when America and Europe dominated science of all fields. At that

*(**Another Road**, cont. from page 11)*

time, research conducted elsewhere on the globe was outside the main orbit and did not attract much attention. Time has changed, and viewing our history in more pluralistic and inclusive ways is now the main stream.

In closing, we would like to point out that the Western literature did not completely ignore Nagano's work. As Watanabe reports (12), Nagano's work is cited by review papers by Pestka (14) and Nathan and Sporn (15). The former introduces the work of Nagano and Kojima as independent research on IFN that supports the finding of Isaacs and Lindenmann. On the other hand, the latter authors, by reviewing the discovery of many cytokines, cite only the Nagano-Kojima paper as the discovery of IFN. In The Interferon System, Stewart II states that "the inhibitory factor by Nagano and Kojima seems to qualify as an interferon" (16). In Interferon and Interferon Inducers (Ed, Finter), Cantel refers to Nagano's IF as one resembling IFN in a number of aspects (17).

Conclusions:

By tracing Nagano's work we find a rich, complex history of the discovery of IFN. IFN was seen by scientists from different corners of the globe, through a different frame of mind, and using different methods, but all converging on the same cytokines. Our progress was multifaceted and nonlinear, and took diverse forms. Our journey to Nagano's paths concludes with reaffirmation of the idea that scientific pursuits are a universal human activity.

Acknowledgements

The authors thank Dr. Y. Kojima for providing us with valuable information, and Dr. I.B. Dawid and J. Robbins for critical reading of the manuscript.

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(***Another Road***, *cont. from page 12)*

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Figure Legend

Rabbit skin test. The rabbit model developed by Nagano and Kojima: a rabbit in the back was inoculated with various IF preparations on the back and then challenged with live vaccine virus.

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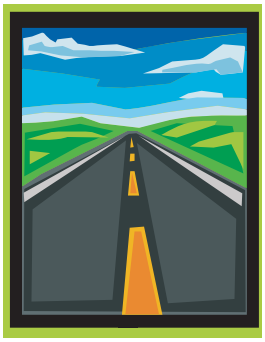

The ISICR needs your help!!!!

The ISICR is still looking for a member to organize a satellite symposium at the 2006 American Association of Immunologists annual meeting in Boston, MA. Please contact Howard Young if you are willing to organize this session.

The ISICR is also looking for someone to take over maintenance of the ISICR website. The website has many new features and the ISICR is looking to continue to upgrade and make the website relevant to the membership. The individual would not need to actually alter the site, just identify new content and work with the Webmaster to make sure the information is up to date. Howard Young has been performing this function for the society for the last few years and would like another member to assume this task. No, this does not have any compensation associated with the task but all members of the society will benefit from your efforts.

Research Scientist Gives $105 Million to N.Y.U.

By RICHARD PÉREZ-PEÑA

A scientist who hid from the Nazis as a child, escaped a Communist regime, did pioneering medical research and made a fortune on a blockbuster drug will give $105 million to the New York University School of Medicine, his professional home for four decades, university officials said yesterday.

The donation by the scientist, Jan T. Vilcek, 72, is one of the four or five largest ever given to a school or health care institution in New York City, and among the biggest in the nation, according to organizations that track such gifts. Dr. Vilcek, an immigrant who has no children, said he was giving most of his fortune to the medical school that has nurtured him and his work, and that cared for his wife, Marica, when she was seriously ill.

"I never expected that I would be in a position to have this kind of wealth," he said yesterday in a telephone interview from Santa Fe, N.M., where he is vacationing. "Immigrants don't usually come with big checkbooks. I came to this country with two suitcases full of useless stuff."

As a longtime employee of the institution receiving the gift, Dr. Vilcek, a professor of microbiology, stands in marked contrast to most major donors to universities and hospitals, who are either charitable foundations or moguls from unrelated businesses, people like Sanford I. Weill, Carl C. Icahn and Maurice R. Greenberg.

"I'm amazed by this gift," said Dr. Robert M. Glickman, dean of the medical school. "For him to put his good fortune back into the medical school, into medical research, is not only wonderful but unusual. It's the largest gift in the history of the medical school, and I think the largest by any faculty member to any school anywhere."

Dr. Vilcek headed a research team whose discoveries led to the development of Remicade, a drug used to treat Crohn's disease, rheumatoid arthritis and psoriatic arthritis. Scientists believe that the work also has implications for treating other diseases, like ulcerative colitis.

More remarkable, perhaps, than Dr. Vilcek's work at N.Y.U. is that he ever got there at all.

His Jewish family survived the long German occupation of Czechoslovakia and the Holocaust. Though they were forced from their comfortable apartment in Bratislava, and into a succession of smaller ones, they were, at first, passed over when many of Czechoslovakia's Jews were deported to concentration camps. When the campaign to round up and exterminate Jews intensified, they fled the city for the countryside.

"I spent the last year of the war with my mother in hiding, and my father somehow made his way through the front lines to the Russian Army," he said. "I was 11 at the time, and it still seemed like an exciting game of some sort. I was aware of the seriousness of the situation, but not completely."

The people who hid him were strangers in a village. "They were among those exceptional people who took great risks for others," he said. It was an experience, he added, that left a powerful impression about the value of helping people.

Years later, when Czechoslovakia was under Communist rule, his parents - his mother was an ophthalmologist and his father worked for a coal mining company - wanted him to become a doctor.

"I resisted it at first," he said. "I would have preferred another profession, but in a Communist country, the law was out of the question and economics was out of the question, because they were both too politicized."

After becoming a doctor and a research scientist, in 1964, when he was 31, Dr. Vilcek and his wife decided to escape..

"In those days you could not really leave, legally, so my wife and I received permission to visit Vienna for a weekend," he said. "We were able to get out that

*(**Research Scientist Gives**, cont. from page 14)*

way, and we did not go back." In 1965, they settled in Manhattan, where they have lived ever since, and he went to work at N.Y.U.

Dr. Vilcek was one of the early researchers on IFN, one of the first immune system proteins discovered and manipulated by scientists. Since the early 1980's, he has worked with another immune protein, TNF-alpha, which is involved in fighting infections. Sometimes the immune system goes awry and produces too much TNF-alpha, causing the severe inflammation that inflicts pain and tissue damage in autoimmune diseases.

Dr. Vilcek and his colleagues developed a chemical that blocked TNF-alpha. Centocor, a pharmaceutical company now part of Johnson & Johnson, and the N.Y.U. scientists turned that discovery into infliximab, which Centocor sells as Remicade.

Remicade hit the market in 1998 and quickly became a major success. The resulting royalties made Dr. Vilcek a very rich man, as well as earning a large amount of money for the university. Sales of Remicade last year were close to $2 billion, according to IMS Health, a consulting company that tracks drug sales, making it one of the 25 best-selling prescription drugs in the country.

N.Y.U. officials said Dr. Vilcek's gift was in three parts - a lump sum of cash, the rights to some future royalties, and a trust. The school declined to state the value of each part, but estimated the combined worth at $105 million.

Most of the money will go toward the sort of basic research on microbes that Dr. Vilcek has done.

Dr. Glickman said it would be used to recruit scientists and upgrade laboratories. A portion of the money will go to the medical school's ear, nose and throat department.

According to the Greater New York Hospital Association, the largest gift to any medical institution in the city was a $130 million bequest to Long Island College Hospital in Brooklyn, from Donald and Mildred Othmer, in 2000.

Dr. Vilcek's may be the single biggest gift to a medical school in the city, according to both the hospital association and The Chronicle of Higher Education. Sanford and Joan Weill gave $100 million to Cornell University's medical school in 1998, and another $100 million in 2002. The school was renamed in their honor.

The donation by Dr. Vilcek ranks among the 30 largest ever given to a single college or university anywhere in the country, of which only a handful were specifically for medical work, according to a ranking maintained by The Chronicle of Higher Education.

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Adipokines

By Jianping Ye

Pennington Biomedical Research Center, Louisiana State University System

Adipokines are proteins secreted from adipocytes that are involved in the regulation of fat and glucose metabolism. On the basis of function, adipokines can be either cytokines or secreted enzymes. Some of them are exclusively produced by adipocytes including Leptin, Adiponectin and Adipsin. Production is not restricted to adipocytes as some family members are produced by other type of cells and a subset have been extensively studied in the immunology or cancer fields, including TNF-α, IL-1, IL-6, and TGF-β. With the increased prevalence of obesity over the world, adipokine analysis has been a very active and cutting-edge area in the fields of obesity, diabetes and metabolism. Presented here is a table summarizing the adipokines.

(*Adipokines* *continued from page 15*)

	Adipokine/protein	Effect on insulin sensitivity	Adipocyte-specific secretion	Receptor	Expression in obese condition	Reference
1	Leptin	Positive	Yes	Cloned	Increased	1, 2, 3
2	Adiponectin	Positive	Yes	Cloned	Decreased	1, 2, 3
3	Visfatin/PBEF	Positive	No	Not known	Increased	3
4	Vaspin	Positive	Yes	Serine protease inhibitor	Increased	4
5	Adipsin/ASP	Negative	No		Increased	1, 2, 3
6	TNF-α	Negative	No	Cloned	Increased	1, 2, 3
7	Resistin	Negative	No	Cloned	Increased	1, 2, 3
8	IL-6	Negative	No	Cloned	Increased	1, 2, 3
9	MCP-1	Negative	No	Cloned	Increased	1, 3
10	PAI-1	Negative	No	Serine protease inhibitor	Increased	1, 3
11	RBP-4	Negative	No		Increased	5
12	Angiotensin	Negative	No	Cloned	Increased	1, 3
13	Serum amyloid A	Unknown	No			1, 3
14	Alpha 1-acid glycoprotein	Unknown	No			3

Abbreviation: ASP, acylation stimulatory protein; MCP-1, Monocyte Chemoattractant Protein-1; PAI-1, Plasminogen Activator Inhibitor-1; IL-6, Interleukin 6; PBEF, Pre-B cell colony Enhancing Factor; RBP-4, Retinol Binding Protein 4; TGF-b, Transforming Growth Factor-beta; TNF-a, Tumor Necrosis factor-alpha.

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FROM THE EDITORS OF JICR

JICR is planning a special issue to commemorate the 50th anniversary of the discovery of IFN.

One idea is to take advantage of the occasion from an historical perspective and request pioneers in the field to write a series of personal accounts of their experiences in research and clinical use of IFNs. We invite suggestions from the ISICR membership regarding names of individuals who should be asked to write such "Reflections". In addition, if you have alternate or additional ideas about how to celebrate this anniversary, please share that with us as well. Please send your suggestions to Ganes Sen at seng@ccf.org

NEW ISICR MEMBERS

The ISICR welcomes these new members and urges them to become involved with ISICR committees and the ISICR International Council. For complete contact information, please contact the ISICR web-site and go into the Membership site or contact the ISICR office.

Anbu K. Adikesavan
Uttar Pradesh, India

Sefik Alkan
St. Paul, MN

Tracey L. Baas
Seattle, WA

Josef Bodor
New York, NY

Ling Cao
Farmington, NY

Benny K. W. Cheung
Hong Kong, China

Daniele Decanine
Bahia, Brazil

Ziyun Du
Memphis, TN

Sherief Z. El-Shazly
Salmiyah, Kuwait

Ashraf E. Fiky
Irvine, CA

Feng Guo
Jena, Germany

Nhan Ho
Ho Chi Minh, Vietnam

Chad A. Hudson
Syracuse, NY

Yoshi-Hiro Ide
Shizuoka, Japan

Pasi Kaukinen
Helsinki, Finland

Ramasamy R. Kavitha
Uttar Pradesh, India

Anna H. Y. Law
Hong Kong, China

Davy C. W. Lee
Hong Kong, China

Giovanna Lombardi
London, UK

Hong-Tao Lu
Richmond, CA

Guangxiang G. Luo
Lexington, KY

Luis Martinez-Sobrido
New York, NY

Stephen S. Morse
New York, NY

Karuppiah Muthumani
Philadelphia, PA

Cecil Pickett
Kenilworth, NJ

Mercedes Reboredo
Pamplona, Spain

Rajesh K. Roy
Maharashtra, India

Bonnie J. Sacarny
Armonk, NY

Masahiro Sakai
Miyazaki, Japan

Lin S. San
Chapel Hill, NC

Devanand Sarkar
New York, NY

(*New Members* *continued from page 17*)

Ram Savan
Miyazaki, Japan

J. P. N. Singh
Uttar Pradesh, India

Jiannan Song
Chapel Hill, NC

Dongxu Sun
New York, NY

Qiang Sun
Montreal, Canada

Jeremy Swann
Melbourne, Australia

Nelson Tang
Hong Kong, China

Ajay Wanchu
Chandigarh, India

Xueyan Zhao
Birmingham, AL

Haoyang Zhuang
Gainesville, FL

New Member Minibios

Thomas Tan

Tracey Baas Ph.D.
Senior Fellow
Department of Microbiology
University of Washington
Seattle, WA

Dr. Baas received her Ph.D. in the field of organic chemistry. Since joining the Katze laboratory in early 2003, her work has focused on using DNA micorarrays to study virus-host interactions. Her current interests include viral respiratory diseases, presently SARS and influenza, and gleaning gene expression data from both pulmonary clinical autopsy samples (formalin-fixed or snap-frozen) and non-human primate animal models. She is also interested in the implementation of pulmonary cytobronchial brushings as a way to further elucidate the time course effect of virus-host interactions at primary sites of infection. More recently, Dr. Baas and members in the Katze lab used custom-designed macaque oligonucleotide microarrays to probe Pigtailed macaques (Macaca nemestrina) infected with a reconstructed strain of Texas influenza virus (A/Texas/36/91) for molecular events that take place as a result of the local and systemic response to infection. Dr. Baas and her colleagues found that among tissues showing pathology, those with viral RNA present had a unique transcriptional signature compared to those with viral RNA absent and was exemplified by regulation of many IFN-induced and chemokine genes that contribute to the progression of the innate immune response, such as CXCL11, G1P2, ISG20, CCL18, and CCL2, as well regulation of genes involved in apoptotic and pulmonary pathways. A subset of these IFN-induced signature genes was successfully investigated using cytology brushings to evaluate the potential for future diagnostics. It is hoped that the comparison of direct and indirect transcriptional regulation at the cellular level in the host will aid in understanding more fully how molecular events contribute to the localized pathological changes observed in lung tissue and to disease progression in humans.

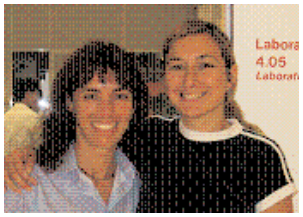
Reasons for joining ISICR: "I decided to join ISICR

(***Mini Bios*** *continued from page 18*)

because as a scientist interested in host response to pulmonary pathogens, I feel that it is important to understand how cytokines can initiate and amplify the inflammatory response that can lead to either resolution of pulmonary infiltrates or progression of lung injury and acute respiratory distress syndrome."

Reason to join the ISICR: "Our work involves developing strategies aimed at stimulating the immune system with cytokines like IL-12 to treat mouse models of liver cancer. Thus the ISICR constitutes an excellent scientific environment to share results of studies involving cytokines and interferons-mediated pathways and to learn more about the interrelated net of responses trigger by IL-12 expressed in the liver."

M. Gabriela Kramer, Ph.D.
Staff Investigator
Mercedes Reboredo, Ph.D.
Postdoctoral Fellow
University of Navarra
Pamplona, Spain



M. Gabriela Kramer (left), originally from Uruguay, received her PhD with honors in the field of molecular biology and biochemistry at the University Complutense of Madrid-CSIC, 1997. In her thesis work, she investigated the mechanism of rolling-circle plasmids replication in Streptococcus pneumoniae and Staphylococcus aureus. After two years of postdoctoral work at the University of Pittsburgh, PA (USA) she joined the group of Dr. Jesus Prieto (University of Navarra, Pamplona, Spain) to develop gene therapy vectors for specific and controlled gene expression in the liver. In 2001 Dr. Kramer became a staff Investigator at the Center of Applied Medical Research (CIMA), Pamplona, where she is conducting projects aimed at improving gene therapy protocols based on the expression of IL-12 in the liver for the treatment of hepatocellular carcinoma.

Mercedes Reboredo (right) obtained her PhD in biological sciences in 2000 and worked for one year at the Imperial College (London, UK) on cell apoptosis mediated by cytomegalovirus infection. In 2004 she joined Dr. Kramer's lab as a postdoctoral fellow. Dr. Reboredo is focused on determining the in vivo kinetics of IL-12 expression when it is controlled by a doxycycline(dox)-inducible system. She is also involved in analyzing the effects of the constitutive expression of a dox-dependent transactivator using-microarray technology.

Dr. Guangxiang (George) Luo
Associate Professor
Departments of Microbiology, Immunology, and Molecular Genetics
University of Kentucky College of Medicine
Lexington, KY

Dr. George Luo obtained a medical degree from Xiang-Ya School of Medicine, Central South University of China in 1983 and Master of Public Health from Capital University of Medical Sciences in Beijing, China in 1986. He worked as a visiting scientist and research associate at Fox Chase Cancer Center in Philadelphia and Mount Sinai School of Medicine in New York from 1988 to 1992. He then moved to Bristol-Myers Squibb Pharmaceutical Research Institute as an Investigator and then became a senior investigator working on antiviral drug discovery. In 2000, He joined the Department of Microbiology, Immunology, and Molecular Genetics at the University of Kentucky College of Medicine. The current research in his lab is centered on the molecular mechanisms of hepatitis C virus (HCV) replication, HCV and host interaction, antiviral drug discovery, and viral carcinogenesis. Recently, he has developed stable cell lines that robustly produce and secrete infectious HCV into the culture media. Additionally, he demonstrated the establishment of a culture system of HCV RNA replication in the mouse embryo fibroblasts, providing a powerful system to study HCV and host interactions using diverse gene-knockout mouse cells. He becomes increasingly interested in the molecular mechanisms of IFN - induced antiviral response against HCV replication. He believes that the innate immunity is critical to recovery of an acute HCV infection. His research programs are currently supported by National Cancer

(***Mini Bios*** *continued from page 19*)

Institute (NCI) and National Institutes of Allergy and Infectious Diseases (NIAID) of NIH. He has served on several NIH study sections and as an ad hoc reviewer for China National Natural Science foundation and Swiss Science Foundation and couple of other state funding agents. Currently, he is a member of the editorial board of Journal of Virology.

Reasons to join ISICR:
"Becoming a member of the ISICR, I would like to interact and collaborate with colleagues in the IFN and cytokine research community in order to determine the role of innate immunity in the control of HCV replication and the underlying mechanism of chronic HCV infection."

Dr. Karuppiah Muthumani
Dept. of Pathology and Lab. Medicine
University of Pennsylvania,
Philadelphia, PA

Dr. Karuppiah Muthumani received his Ph.D. in Molecular Biology from the School of Biological Sciences, Madurai Kamaraj University, Madurai, India in 1995. He completed his postdoctoral research at the University of Pennsylvania School of Medicine, PA, USA. Dr. Muthumani became a Senior Research Investigator, Dept. of Pathology and Lab. Medicine, University of Pennsylvania, Philadelphia, PA in 2004. Currently, his research is aimed at studying the molecular pathogenesis of HIV-1 infection, focusing on the role of the HIV-1 accessory gene Vpr. Specifically, he is investigating the role of the Vpr gene product in modulation of host cell immune responses during HIV infection.

Reasons to join ISICR: "I have been working on HIV research since 1998, mainly focusing on cytokine immune regulation in HIV-1 pathogenesis. I think joining the ISICR society will benefit my research by interacting with scientists in the area of immune signaling and building a network of researchers who share common research interests and in establishing new connections and broader communications with colleagues in the research community."

ISICR Members in the News

Dr. Patrick Matthys

The Royal Academy of Medicine of Belgium has recognized ISICR member Patrick Matthys with an award for his contribution to the elucidation of a disease mechanism utilizing in vivo animal models. Dr. Matthys is a postdoctoral research fellow of the Fund for Scientific Research Flanders and is an associate professor at the Rega Institute, University of Leuven in Belgium. Using IFN-γ receptor knockout mice, he elucidated a new mechanism of extramedullarly myelopoiesis and expansion of a pathogenic Mac-1+ cell population in the pathogenesis of collagen-induced arthritis, an animal model for rheumatoid arthritis.

Dr. Larry Pfeffer

Tennessee Governor Phil Bredesen has appointed ISICR member Dr. Larry Pfeffer to the University of Tennessee Board of Trustees for a one year term. Upon making the appointments to fill vacancies on the Tennessee Board of Regents, University of Tennessee Board of Trustees and the Tennessee Student Assistance Corporation, the Governor stated "These Tennesseans each share great knowledge in the areas of teaching and learning, and I'm confident they'll offer valuable perspectives about how to build on and improve our efforts in higher education across the state. said. I appreciate their contributions to education in the State of Tennessee."

The UT Board of Trustees governs the entire UT system, including campuses in Knoxville, Chattanooga and Martin. The system serves more than 42,500 students across the state. Dr. Pfeffer is currently Muirhead Professor and Vice-Chair, Department of Pathology; President of the Faculty Senate, University of Tennessee Health Science Center, Memphis and Interim Deputy Director and Director for Basic Research, University of Tennessee Cancer Institute.

ZEN FOR THOSE WHO TAKE LIFE TOO SERIOUSLY

1. SAVE THE WHALES...COLLECT THE WHOLE SET.
2. A DAY WITHOUT SUNSHINE IS LIKE...NIGHT.
3. ON THE OTHER HAND, YOU HAVE DIFFERENT ...FINGERS.
4. I JUST GOT LOST IN THOUGHT. IT WASN'T FAMILIAR TERRITORY.
5. 42.7 PERCENT OF ALL STATISTICS ARE MADE UP ON THE SPOT.
6. 99 PERCENT OF LAWYERS GIVE THE REST A BAD NAME.
7. I FEEL LIKE I'M DIAGONALLY PARKED IN A PARALLEL UNIVERSE.
8. HONK IF YOU LOVE PEACE AND QUIET.
9. REMEMBER, HALF THE PEOPLE YOU KNOW ARE BELOW AVERAGE.
10. HE WHO LAUGHS LAST THINKS SLOWEST.
11. DEPRESSION IS MERELY ANGER WITHOUT ENTHUSIASM.
12. THE EARLY BIRD MAY GET THE WORM, BUT THE SECOND MOUSE GETS THE CHEESE.
13. I DRIVE WAY TOO FAST TO WORRY ABOUT CHOLESTEROL.
14. SUPPORT BACTERIA. THEY'RE THE ONLY CULTURE SOME PEOPLE HAVE.
15. MONDAY IS AN AWFUL WAY TO SPEND 1/7 OF YOUR WEEK.
16. A CLEAR CONSCIENCE IS USUALLY THE SIGN OF A BAD MEMORY.

17. CHANGE IS INEVITABLE, EXCEPT FROM VENDING MACHINES.
18. GET A NEW CAR FOR YOUR SPOUSE. IT'LL BE A GREAT TRADE!
19. PLAN TO BE SPONTANEOUS TOMORROW.
20. ALWAYS TRY TO BE MODEST, AND BE PROUD OF IT!
21. IF YOU THINK NOBODY CARES, TRY MISSING A COUPLE OF PAYMENTS.
22. HOW MANY OF YOU BELIEVE IN PSYCHO-KINESIS? RAISE MY HAND.
23. OK, SO WHAT'S THE SPEED OF DARK?
24. HOW DO YOU TELL WHEN YOU'RE OUT OF INVISIBLE INK?
25. IF EVERYTHING SEEMS TO BE GOING WELL, YOU HAVE OBVIOUSLY OVERLOOKED SOMETHING.
26. WHEN EVERYTHING IS COMING YOUR WAY, YOU'RE IN THE WRONG LANE.
27. HARD WORK PAYS OFF IN THE FUTURE. LAZINESS PAYS OFF NOW.
28. EVERYONE HAS A PHOTOGRAPHIC MEMORY. SOME JUST DO NOT HAVE FILM.
29. IF BARBIE IS SO POPULAR, WHY DO YOU HAVE TO BUY HER FRIENDS?
30. HOW MUCH DEEPER WOULD THE OCEAN BE WITHOUT SPONGES?
31. EAGLES MAY SOAR, BUT WEASELS DO NOT GET SUCKED INTO JET ENGINES.
32. WHAT HAPPENS IF YOU GET SCARED HALF TO DEATH TWICE?
33. I USED TO HAVE AN OPEN MIND BUT MY BRAINS KEPT FALLING OUT.
34. I COULDN'T REPAIR YOUR BRAKES, SO I MADE YOUR HORN LOUDER.
35. WHY DO PSYCHICS HAVE TO ASK YOU FOR YOUR NAME?
36. INSIDE EVERY OLDER PERSON IS A YOUNGER PERSON WONDERING-WHAT HAPPENED?
37. LIGHT TRAVELS FASTER THAN SOUND, WHICH IS WHY SOME PEOPLE APPEAR BRIGHT UNTIL YOU HEAR THEM SPEAK...

Clinical Trials

Hannah Nguyen

http://www.centerwatch.com/search.asp [CW], or http://clinicalstudies.info.nih.gov [CCNIH].

AFR10 - Combination Therapy of Imatinib Mesylate (IM) + **Alpha-2A Interferon** for Chronic Phase CML Patients Resistant or Refractory to IM Used as Single Therapy for at Least One Year. Contacts: Franck Nicolini, MD, Lyon, 69437, France, 33 472 110 180, franck.nicolini@chu-lyon.fr; Mauricette MICHALLET, MD, Principal Investigator, Hospices Civils de Lyon. Study ID Numbers: 2003.317. ClinicalTrials.gov Identifier: NCT00146913

A Study to Evaluate the Combination of **Pegylated Interferon Alfa** Plus Valopicitabine in Patients with Hepatitis C. Contact: Kristin Kleber, 617-995-9807, kleber.kristin@idenix.com. Contacts in 17 US States. Study ID Numbers: NV-08A-006. ClinicalTrials.gov identifier: NCT00118768

BAY 43-9006 (Sorafenib) Versus **Interferon Alpha-2a** in Patients with Unresectable and/or Metastatic Renal Cell Carcinoma. Contacts: Texas Oncology, PA, Dallas, Texas, 75246; Anita Duncan, 214-370-1807, anita.duncan@usoncology.com. Study ID Numbers: 11848. ClinicalTrials.gov identifier: NCT00117637

BEYOND Study - **Betaferon/Betaseron** Efficacy Yielding Outcomes of a New Dose in Multiple Sclerosis (MS) Patients. Contacts: BEYOND Study Information 800-788-1467. Contacts in 34 US States. Study ID Numbers: 306440. ClinicalTrials.gov identifier: NCT00099502

S-Citalopram for the Prevention of **PEGASYS**-Induced Depression. Contacts: Thomas Berg, PD Dr. Principal Investigator, Charité Campus Virchow-Klinikum, Hepatology and Gastroenterology, Berlin, 13353, Germany; +4930450553072 thomas.berg@charite.de Study ID Numbers: ML18075; ClinicalTrials.gov identifier: NCT00136318

EARLY **IFNB-1a** and Simvastatin Combination Therapy in Clinically IsolateSyndrome Suggestive of Multiple Sclerosis. Contacts: Cynthia Kenan, 919 843-7641, kenanc@neurology.unc.edu; Jennifer Smrtka, 919 966-8043, smrtkaj@neurology.unc.edu; Silva Markovic-Plese, Principal Investigator, University of North Carolina-Chapel Hill MS clinic within the Neuroscience Hospital, Chapel Hill, North Carolina, 27599, United States. Study ID Numbers: 04-NEUR-387. ClinicalTrials.gov identifier: NCT00146068

SB497115 (Oral **Thrombopoietin Receptor** Agonist) Versus Placebo In Adults With Thrombocytopenia Due To Hepatitis C (this study is examining several different doses of SB497115 as a treatment for patients with chronic hepatitis C-related thrombocytopenia who are potential candidates for antiviral treatment with **pegylated interferon** and ribavirin). Contacts: GSK Clinical Trials, Study Director, GlaxoSmithKline. Contacts in 9 US States and in the United Kingdom. Study ID Numbers: TPL102357. ClinicalTrials.gov Identifier: NCT00110799

Bevacizumab and **Interleukin-2** in Treating Patients With Metastatic Kidney Cancer. Contacts: Mayer Fishman, MD, PhD, Principal Investigator, H. Lee Moffitt Cancer Center and Research Institute. Study ID Numbers: CDR0000434852; MCC-13921; MCC-IRB-102782; NCI-6438. ClinicalTrials.gov identifier: NCT00126490

An Open-Label, Randomized Study Comparing the Uptake of **rIL-2** in HIV-1 Infected Individuals Receiving Different Combinations of Antiemetics and Analgesic Agents During **rIL-2** Dosing in ESPRIT: Toxicity Substudy of ESPRIT: TOXIL-2 Substudy. Contacts: David A Cooper, M.D, +61 2 9385 0900; Sarah L Pett, M.D, Principal Investigator, National Centre in HIV Epidemiology and Clinical Research, Faculty of Medicine, University of New South Wales, Sydney, Australia, +61 2 9385 0900 Ext. 50909, spett@nchecr.unsw.edu.au. Contacts in Argentina, Australia and Israel. Study ID Numbers: ESPRIT TOXIL-2 UNSW PSO 6361. ClinicalTrials.gov identifier: NCT00147355

(***Clinical Trials*** *continued from page 22*)

TNFalfa Blocking Treatment of Spondylarthropathies. Contacts: Mikkel Oestergaard, Professor, MD, Ph.D, +4521603865, mo@dadlnet.dk; inge juul soerensen, MD, Ph.D, Principal Investigator, Hvidovre University Hospital, Dept. of Rheumatology, Denmark, +4536322278 i.juuls@dadlnet.dk. Study ID Numbers: 232-001; KF 02-050/04. ClinicalTrials.gov identifier NCT00133315

Azacitidine and **Etanercept** in Treating Patients With Myelodysplastic Syndromes. Contacts: Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109-1024, United States; Bart L. Scott, MD, Principal Investigator, 206-667-1990 bscott@fhcrc.org. Study ID Numbers: CDR0000432957; FHCRC-1926.00; NCT00118287. ClinicalTrials.gov identifier: NCT00118287

Study of Intra-Articular Delivery of **tgAAC94** in Inflammatory Arthritis Subjects. Contacts: Alison Heald, M.D., 206-623-7612 Ext. 7350, healda@targen.com; Gregory Pate, B.S, 206-623-7612 Ext. 7827, pateg@targen.com. Contacts in Colorado and Washington. Study ID Numbers: 13G01; NIH Protocol Number: 0504-705. ClinicalTrials.gov identifier: NCT00126724

Screening Protocol to Determine Eligibility for Studies of the **Chemokine Coreceptor 5 (CCR5) Antagonist GW873140**. Contacts: GSK Clinical Trial, Ph.D., Study Director, GlaxoSmithKline. Contacts in 32 US States, Canada and Puerto Rico. Study ID Numbers: CCR104627. ClinicalTrials.gov identifier: NCT00123890.

Phase II Study of **IL-11 (Neumega)** in Von Willebrand Disease. Contacts: Margaret V. Ragni, MD, MPH, Principal Investigator, University of Pittsburgh; Holly Chapman, RN, 412-209-7411 Ext. 7384, hchapman@itxm.org; Dana McDermot, BSN, RN, 412-209-7411 Ext. 7425, dmcdermo@itxm.org, Hemophilia Center of Western Pennsylvania and General Clinical Research Center, Pittsburgh, Pennsylvania, 15213-4306, United States.Study ID Numbers: 0403006. ClinicalTrials.gov identifier: NCT00151125

Interleukin-13 PE38QQR Immunotoxin and Radiation Therapy With or Without Temozolomide in Treating Patients Who Have Undergone Surgery for Newly Diagnosed Malignant Glioma. Cleveland Clinic Taussig Cancer Center, Cleveland, Ohio, 44195, United States; Michael A. Vogelbaum, MD, PhD, 216-444-8564, Study Chair. Study ID Numbers: CDR0000398182; CCF-IRB-7161; NEOPHARM-IL13PEI-106. ClinicalTrials.gov identifier: NCT00105014

YOUR AGE BY CHOCOLATE MATH

This is pretty neat. 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 have chocolate (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 --I'll wait while you get the calculator.

5. If you have already had your birthday this year add 1755... If you haven't, add 1754

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 have chocolate this week)

The next two numbers are YOUR AGE! (Oh YES, it is!!!) THIS IS THE ONLY YEAR (2005) IT WILL EVER WORK. WHILE IT LASTS.

Reviews of Interest

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REVIEW OF: *INTERFERON: THE SCIENCE AND SELLING OF A MIRACLE DRUG*

Author: Toine Pieters

Perhaps each period of great scientific advance had its own unique ideas and unique scientists. Examples of periods of great scientific advance include those surrounding the biological discoveries of contagion, vaccines, sanitation, antibiotics, immunity, and genetics. Such a unique period seemed to follow the discovery of IFN as one of the most important natural host defenses against viruses and as a major immunomodulator during tumorigenesis, bacterial infections, and autoimmune diseases. During this period, the study of IFN as a prototype intercellular messenger (cytokine) led to effective therapy of some important medical problems including:

- Viral infections such as chronic hepatitis C virus infection;
- Bacterial infections such as those occurring during chronic granulomatous disease;
- Tumors ranging from benign warts to Kaposi's sarcoma in AIDS patients;
- Multiple sclerosis, an autoimmune disease.

The book entitled, Interferon: *The Science and Selling of a Miracle Drug*, carefully documents and details the events surrounding the discovery and elucidation of the IFN system, including most of the scientists, institutions, pharmaceutical companies, government agencies and their multifaceted motivations. The book carefully identifies discovery of the main scientific principles. It does not present the specifics of the science since they have been thoroughly reviewed elsewhere by scientists themselves, including in a textbook chapter available on the internet (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books).

My perspective on Interferon: The Science and Selling of a Miracle Drug may be influenced by having spent one year working with Alick Isaacs, one of the insightful discoverers of IFN, at the British National Institute for Medical Research. Also, I know and admire the co-discoverer, Jean Lindenmann. For me, reading this book was like reliving the powerful emotional and intellectual excitement of this major scientific advance.

I believe the book presents a number of important and humbling lessons for all, including:

- The time required for acceptance of a paradigm shift varies markedly, as illustrated by the delayed acceptance of the IFN system in contrast to the almost immediate acceptance of the discovery of the molecular structure of DNA.
- The time for development of a medically useful product, like IFN, is probably measured better in decades rather than in years.
- Motivations of scientists and institutions are many and varied.
- Paradigm change has come to rely heavily on randomized control trials.

This book, *Interferon: The Science and Selling of a Miracle Drug*, is compelling reading for those interested in the IFN story, including the historical background and the scientists behind the discovery. The book is a thorough and readable account that is unique for IFN and has parallels with other major discoveries. I believe that this book will appeal to basic and clinical scientists, physicians, patients, policy makers, and historians.

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INDO-US COLLABORATIONS: PROGRESS, OPPORTUNITIES & AN INTERFERON/CYTOKINE CONNECTION

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Dr. Nitya Nand, then the Director of the Central Drug Research Institute (CDRI), a premier national laboratory of the Council of Scientific and Industrial Research (CSIR) dedicated to the multidisciplinary field of drug research in India, visited the Uniformed Services University of the Health Sciences (USUHS) in 1981 and discussed with Drs. Robert M. Friedman, and Radha Maheshwari, the possibility for organization of an Indo-US workshop on IFN at CDRI and for pursuing the research collaboration on the use of IFN in parasitic infections, especially malaria. Upon the invitation of Dr. Nitya Nand, Drs. Friedman and Maheshwari from USUHS visited CDRI, Lucknow in November 1982. Over the years, contacts have been established with several institutions, including CDRI; Industrial Toxicology Research Centre (ITRC) and King George's Medical College (KGMC), Lucknow, Institute of Pathology, and All India Institute of Medical Sciences, (AIIMS) New Delhi; Cancer Research Institute, Bombay; Birla Institute of Technology and Science, (BITS), Pilani; Owasi Hospital and Research Centre, Hyderabad; National Institute of Pharmaceutical Education and Research (NIPER); Institute of Microbial Technology; and Post Graduate Institute (PGI), Chandigarh; National Institute of Oceanography, Goa; National Institute of Immunology; and Malaria Research Centre, Delhi; Amala Cancer Hospital, Trichur, Kerala; and Armed Forces Medical College (AFMC), Pune; and Arogyadham, Deendayal Research Institute, Chitrakoot. An important aspect of these collaborations is the exchange of scientists and other experts between the U.S. and India. Several U.S. and Indian scientists travel to the other country to collaborate on projects or for participation and planning in one of the many workshops and conferences.

ORGANIZATION OF WORKSHOPS/SYMPOSIA

A mini-symposium on IFN was organized in 1981 at USUHS for a CSIR delegation that included Drs. M.L. Dhar, B.K. Bacchawat, M.R. Das and V.C. Vora from India and Dr. Deshpande, the Science Counselor from the Indian Embassy. Drs. Friedman and myself, USUHS; Dr. Leonard Kohn, NIAMDD, NIH; and Dr. T. Sreevalsan, Georgetown University Medical Center made presentations and presented an overview of the various aspects of IFN research.

We have been actively involved in the organization of four teaching courses in India on behalf of NIH. These teaching courses included extensive state of the art lectures and hands-on demonstration of laboratory techniques. In each of these courses, 10-15 outstanding U.S. faculty and approximately 30-40 young scientists from all over India participated. The first course was conducted in 1985 on *"Interferon in Biomedical Research"* at the Center Drug Research Institute (CDRI) Lucknow, India. The U.S. faculty included: Radha K. Maheshwari, Robert Silverman, and Robert Friedman (USUHS); Samuel Baron (University of Texas at Galveston); Thomas Merigan (Stanford University, CA); T. Sreevalsan (Georgetown University); John Ortaldo (NCI, NIH); and Christine Czarniecki (at that time at Genetech, Inc.).

We have participated in the International Meeting on *"Frontiers in Pharmacology and Therapeutics in the 21st Century"*, New Delhi and organized a symposia on the *"Role of Cytokines in Human Health and Diseases"*. The symposia was chaired by Dr. Val Hemming, Dean, USUHS, who in his opening remarks reviewed the importance of cytokines, the most potent mediators of the immune system in various diseases. Other speakers of the symposia included Drs. Maheshwari and Pankaj Seth of Department of Pathology, USUHS, Dr. Gregory Prince, President, Virion Systems Inc, Rockville, and Dr. Mohammed Sayeed, Professor, Department of Surgery and Physiology, Loyola University School of Medicine, Maywood. Speakers addressed the

(***Indo-US Collaborations*** *continued from page 26*)

importance of cytokines in infectious diseases and attracted a large interactive audience.

RESEARCH ACTIVITIES

Our contact with CDRI led to the development of a major collaborative effort, resulting in a seminal discovery on the potent inhibitory effort of human IFN (IFN) gamma against malaria in rhesus monkeys and Genentech supplied the large quantities of cloned human IFN-g for monkey experiments. We have jointly pursued the role of cytokines in the following areas:

a. ROLE OF CYTOKINES IN VIRAL, MALARIAL, LEISHMANIAL AND FUNGAL INFECTIONS

b. ROLE OF CYTOKINES/GROWTH FACTORS AND NATURAL PRODUCTS IN WOUND HEALING, CANCER AND ANGIOGENESIS

c. ROLE OF CYTOKINES AND PHARMACOLOGICAL AGENTS IN ISCHEMIA/REPERFUSION AND HYPOXIA/REOXYGENATION INDUCED-INJURY

d. PREVENTIVE EFFICACY OF IMMUNOMODULATORS AND CYTOKINES AGAINST HEALTH EFFECTS OF ENVIRONMENTAL POLLUTANTS AND CARCINOGENS

Today, when we look back, there is a lot to be proud of, since much has been achieved. The accomplishments in the collaborative projects have been impressive. Many scientific papers have been published in refereed journals, a large number of Masters and Ph.D. theses have been completed, new capabilities and facilities were created, several research presentations were made in National and International meetings. Many new scientific concepts and methods have been developed and several workshops with hands on training were organized and two books from these workshops were published. These collaborative research efforts have also helped USUHS to fulfill its primary mission of helping to care for members of the Uniformed Services. One of the most important aspects of these partnerships has been the creation of a series of personal relationships, indeed close friendships, between both junior and senior Indian and US scientists and administrators. Such ties have been instrumental in constantly establishing new areas of collaboration that are likely to prove fruitful venues of future scientific cooperation. The lives of many people in both countries have been enriched through out joint endeavors. We are justly proud of our joint endeavors and trust the future years will prove to be as fruitful as the past twenty.

Addgene Plasmid Repository for Life Science

http:///www.addgene.org

Addgene is a non-profit organization dedicated to promoting sharing of plasmid constructs described in published literature. Addgene stores original plasmid samples submitted by scientists and distributes them for use in advancing life science research.

Addgene accepts plasmids in either DNA or bacterial form and stores them as bacterial glycerol stocks both on-site and at a backup facility off-site. Addgene staff assists the contributing laboratory with compiling vector map and plasmid construction information. Plasmids are shipped to requestors within two working days of approval from the recipient university's technology transfer office.

We encourage you to submit your plasmids to this community resource. Addgene will save time for your laboratory. Instead of answering plasmid requests, your laboratory can focus on research. In addition, your plasmids will be archived so that turnover of students and post-doctoral fellows will not result in plasmid loss.

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WWW

Send us websites that help your research so ISICR members can benefit from your experience.

Bioteach (recommended by Kevin Ahern in Biotechniques)
Bioteach.ubc.ca

What is BioTeach?
The goal of this project is to provide a broad range of information and teaching resources on subjects in biotechnology. Specifically, this site will present one, three, and five page treatments of interesting and important biotechnology issues and topics. Most articles will be written for the educated layman (Grade 12 to 1st year undergraduate level) and will be associated with references that high school teachers may find useful in presenting this information to their classes.

The articles will explain issues and techniques that we find important and exciting. ... What is cancer? How does one sequence DNA? What are local BioTech companies in Vancouver working on? What's the big deal about stem cells? What does 'genetic engineering' really mean? ... The list goes on.

Articles and information within the BioTeach website will be arranged around nine different subject areas: molecular biology, bioethics, bioengineering, cell biology, bioinformatics, biocareers, biodiversity, biomedicine, biopersonality.

Center for Science and the Media
http://scienceandmedia.org/

Established in 1997 by scientist and media expert Dr. Eliene Augenbraun and others, the Center for Science and the Media (CSM) is dedicated to improving the ability of scientists and engineers to communicate with the public. By doing so, CSM ultimately seeks to help shape a more informed public, better prepared to address science and technology issues in an increasingly complex world.

Through a partnership with **ScienCentral, Inc**., CSM sponsors news desks at ScienCentral News, covering science, health and technology. ScienCentral News reports are broadcast across the country through ABC and NBC local TV affiliates. CSM has also supported research on the impact of commercial television on the general public, the interest level of television news producers in carrying science and technology content in their newscasts, and professional development for scientists and engineers. The Center for Science and the Media is a non-profit 501(c) (3) organization.

International HapMap Project
http://www.hapmap.org/cgi-perl/gbrowse/gbrowse/hapmap

The International HapMap Project is a multi-country effort to identify and catalog genetic similarities and differences in human beings. Using the information in the HapMap, researchers will be able to find genes that affect health, disease, and individual responses to medications and environmental factors. The Project is a collaboration among scientists and funding agencies from Japan, the United Kingdom, Canada, China, Nigeria, and the United States. All of the information generated by the Project will be released into the public domain.

The goal of the International HapMap Project is to compare the genetic sequences of different individuals to identify chromosomal regions where genetic variants are shared. By making this information freely available, the Project will help biomedical researchers find genes involved in disease and responses to therapeutic drugs. In the initial phase of the Project, genetic data are being gathered from four populations with African, Asian, and European ancestry. Ongoing interactions with members of these populations are addressing potential ethical issues and providing valuable experience in conducting research with identified populations.

Public and private organizations in six countries areparticipating in the International HapMap Project. Data generated by the Project can be downloaded

with minimal constraints. The Project officially started with a meeting in October 2002 (http://genome.gov/10005336) and is expected to take about three years.

IPath
http://www.invitrogen.com/content.cfm?pageid=10878&CID=NLC-NATUREAfCS&ATT=IPATH

The iPath™ biological pathways tool is a FREE, user-friendly, web-based research tool containing 225 interactive maps of human metabolic and signaling pathways that you navigate through to learn about the function of your gene or protein of interest. These maps have been created for Invitrogen by GeneGo, a company that develops analytical tools, data content, and algorithms for understanding complex biological system pathways.

National Cancer Institute Cancer Bulletin
http://www.cancer.gov/ncicancerbulletin

A weekly newsletter from the Director of the U.S. National Cancer Institute.

NucleaRDB
http://receptors.ucsf.edu/NR/

An Information System for Nuclear Receptors

Primary and secondary data on Nuclear Receptors:
Sequence information
List of Swiss-Prot & TrEMBL entries (sorted by ID, family or organism)
Database cross-references for sequences and fragments
Multiple sequence alignments and other sequence-derived data sorted per family
cDNAs and protein-cDNA pairwise alignments
Phylogenetic trees
List of the potential Nuclear Localization Signals for the nuclear receptors

Structural information
2D structure data
Structural alignment of the LBDs
Description of 3D structures with useful annotations (data collected by Simon Folkertsma, CMBI)
List of PDB files available (data mainly extracted from the Swiss-Prot entries)
NRSAS: Nuclear Receptor Structure Analysis Servers

Mutation data
Mutation data extracted from the literature by text mining
The Nuclear Receptor Mutation Database (NRMD)

Genetic information
Chromosomal location of nuclear receptor genes

Information on binding partners:
Data on dimers
Data on ligands
Data on co-modulators
Data on DNA targets

Useful tools and links:
Blast your sequence against the NucleaRDB at the CMBI (Select the NucleaRDB in the list of protein databases)
Flo's query system to easily find your favorite entry.
NucleaRDB Query system (Under development).
Useful information resources
Other information:
Articles written by the NucleaRDB participants
Other information relevant to nuclear receptors (meetings, links, addresses, ...)
Information about the data (DB content, Updates, FTP access, ...)
How to cite the NucleaRDB

Paralign
www.paralign.org

This site provides a service for searching public sequence databases for sequences similar to a given query sequence. Searches can provide valuable information about gene relationships, functions and structure. Very accurate and rapid searches can be carried out because this service is based on very sensitive

comparison methods and is powered by a large computer cluster.

The two comparison algorithms used are called Smith-Waterman (SW) and ParAlign. The first algorithm was published by Smith and Waterman (1981) and is a well established method that finds the optimal local alignment of two sequences. It is generally regarded as the "gold standard" for sequence comparison and gives the best results. However, in ordinary implementations, it is very time-consuming. By exploiting parallel computing technology, we have made the Smith-Waterman method run about 8 times faster than normal. It is therefore called accelerated Smith-Waterman. This site features the fastest implementation published of the SW-algorithm on any general-purpose microprocessor. For more information about the new implementation see Rognes and Seeberg (2000).

The other algorithm, ParAlign, is a heuristic method for sequence alignment. In almost all cases ParAlign finds exactly the same alignments as the SW-algorithm, but it is not guaranteed. However the speed of ParAlign is much higher. In essence, ParAlign is about as sensitive as Smith-Waterman but runs at the speed of BLAST. For more details, please see the publication by Rognes (2001). The parallel computing technology used is also known as multimedia technology or Single-Instruction Multiple-Data (SIMD) technology and is embedded in most modern processors including the Pentium, PowerPC, Itanium, Alpha and similar microprocessors.

The software is also adapted to computers with several processors and to clusters of several computers. The online searches are now powered by a cluster of 33 computers with 2 Intel Xeon 2.4 GHz processors each. PARALIGN is designed to identify weak similarities. For identification of nearly identical nucleotide sequences, BLASTN and similar tools are faster and more appropriate. More information about PARALIGN may be found on Sencel's website and in the PARALIGN User's guide.

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Saebo PE, Andersen SM, Myrseth J, Laerdahl JK, Rognes T (2005). PARALIGN: rapid and sensitive sequence similarity searches powered by parallel computing technology. Nucleic Acids Research, 33(Web Server issue):W535-9, 2005.

Rognes and Andersen (2005). PARALIGN User's guide. Sencel Bioinformatics AS, Oslo, Norway.

Smith T.F. and Waterman M.S. (1981). Identification of common molecular sub-sequences. Journal of Molecular Biology, 147 (1) 195-197.

Availability

Stand-alone executables for several different computer systems are available from Sencel Bioinformatics. Free software licenses are available for non-commercial academic use. Free evaluation licenses for commercial users are also available. Contact Sencel for more information.

Development and Funding

The software and service is developed by Sencel Bioinformatics and the Bioinformatics group at the Centre for Molecular Biology and Neuroscience (CMBN) and the Institute of Medical Microbiology, Rikshospitalet-Radiumhospitalet and University of Oslo, Norway. The service is supported by the National Programme for Research in Functional Genomics in Norway (FUGE), in the Research Council of Norway. The computers are hosted by the Centre for Information Technology Services at the University of Oslo.

WWW (continued)

Peptide Antigen Database
http://www.proteinlounge.com/peptide_database.asp

The most important aspect in the production of antibodies or drugs is the design of the peptide-antigen. A peptide-antigen is a small segment (15-18 amino acids) of the protein sequence of interest. These peptide-antigens can be used for immunization in order to produce antibodies against the protein or they can be used as a basis for small-molecule/drug targeting. Protein Lounge has created the first complete Peptide Antigen database.

The Peptide Antigen database contains antigenic peptide targets against all known protein sequences throughout a variety of organisms. All peptide targets are linked to Protein Lounge's online hydroplotting tool, which allows you to view an interactive version of the protein sequence on a hydrophilicity/phobicity plot. This is a necessary database for anyone working with antibody or drug development.

Primer Bank
http://pga.mgh.harvard.edu/primerbank/

PrimerBank is a public resource for PCR primers. These primers are designed for gene expression detection or quantification (real-time PCR). PrimerBank contains about 180,000 primers covering most known human and mouse genes. There are several ways to search for primers: GenBank Accession, NCBI protein accession, LocusLink ID, PrimerBank ID or Keyword (gene description).

The primer design algorithm has been extensively tested by real-time PCR experiments for PCR specificity and efficiency. Up to now, we have tested over a thousand primers and the design success rate is > 99%.

Reference:
Xiaowei Wang and Brian Seed (2003) A PCR primer bank for quantitative gene expression analysis. Nucleic Acids Research 31(24): e154; pp.1-8.

SeattleSNPs
http://pga.gs.washington.edu/

SeattleSNPs is funded as part of the National Heart Lung and Blood Institute's (NHLBI) Programs for Genomic Applications (PGA). The SeattleSNPs PGA is focused on identifying, genotyping, and modeling the associations between single nucleotide polymorphisms (SNPs) in candidate genes and pathways that underlie inflammatory responses in humans. Investigator Opportunities SeattleSNPs offers investigators several opportunities to make use of the project's resources:

- Nominate Genes for Re-sequencing
  As part of its mission, SeattleSNPs is soliciting requests from individual investigators for candidate genes to be re-sequenced for SNP discovery

- Traveling Workshops
  SeattleSNPs is now accepting applications from potential host sites for One- and Two-Day Traveling Workshops

- Genotyping
  SeattleSNPs is providing genotyping support for research related to heart, lung, blood, and sleep

The ISICR expresses its sincere gratitude to Dr. Xin-Yuan Liu, his staff and the local organizing committee for planning and organizing the 2005 ISICR meeting

Information for the 2005 ISICR meeting

What is the Chinese currency?

The Chinese currency is RMB. RMB (Renminbi) means "People's Currency".
$100 USD = ABOUT 815 yuan RMB. For pictures of Chinese currency, go to http://www.chinatoday.com/fin/mon/

How do I get to the Everbright Convention Centre from the PuDong International Airport?

1. The secretariat has arranged a shuttle bus from the airport to the Everbright Convention Centre from 9:00am to 8:00pm, Oct. 20, 2005. One bus leaves every hour on the hour. Please look for a Welcoming sign to the 2005 ISICR meeting.

2. You may take Mag-Lev train from the airport to the Long Yang Road No. 2 Subway Station (50 RMB or ~6 USD) then directly transfer to the No.1 Subway at the People Square Subway Station and get off at Cao Bao Road Subway Station. The Everbright Convention Centre is a 5 minutes walk from the subway station. Cost of the subway is 2-5 RMB.

3. You may take the airport shuttle bus Line 3 to the Xu Jia Hui Subway Station and then take a taxi to the Everbright Convention Centre. It should only cost about 2 USD or 15RMB. Note: Taxis do not accept USD or Euros and limit the number of passengers to 4 people. Currency exchange booths can be found at the airport or at hotels or banks.

4. A taxi from the airport to the convention center will cost approximately 20 USD or 150 RMB. Again, USD or Euros are not accepted.

Meeting Sponsors

Organizers

Chinese Academy of Sciences (CAS)
National Natural Science Foundation of China
Shanghai Institutes for Biological Sciences, SIBS, CAS
Zhejiang Sci-Tech. University, School of Life Science
Second Military Medical University

Sponsors

Hongfang Song (daughter of Xin-yuan Liu)
Becton Dickinson (BD)
Huaxin High Biotech. Inc.
Guangzhou Baike Med. Drug Develop. CO. LTD.
Huiyang Life Sciences and Tech. Corp.
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Haerbin Bioproducts CO. LTD

Shanghai Guoyuang Biotech. Inc.

Fujian Fuzhou Kaihua Drug Inc.

Organizing Committee

International Society for Interferon and Cytokine Research (ISICR)
Inst. of Biochemistry and Cell Biology, Shanghai Inst. for Biological Sciences, CAS
Zhejiang Sci-Tech University, School of Life Science
Second Military Medical University

Co-organized by
The Chinese Society of Biochemistry and Molecular Biology
Shanghai Society for Biochemistry and Molecular Biology
The Chinese Society of Biotechnology
Shanghai Society for Biotechnology
Interferon and Cytokine Research, the Chinese Society of Microbiology

Local Organizing and Program Committee
Liu, Xin-Yuan, Academician of the Chinese Academy of Sciences (CAS) Zhejiang Sci-Tech University, School of Life Science
Lin, Qishui, Academician of the Chinese Academy of Sciences (CAS)
Cao, Xuetao, Vice-principal of the Second Military Medical University
Gong, Zuxun, Former vice director of the Institute of Biochemistry and Cell Biology, SIBS, CAS
Qi, Guorong, Former vice director of the Institute of Biochemistry and Cell Biology, SIBS, CAS
Qi, Zhongtian, Professor of the Second Military Medical University, International Council Member of ISICR
Jiao, Binghua, Professor, Chairman of the Chinese Society for Interferon and Cytokine Research
Ma, Dalong, Beijing University, School of Medicine
Tong, Kuitang, Shanghai Institute of Biological Products
Fan, Zhongshan, Secretariat of the Chinese Society for Interferon and Cytokine Research
Ma, Kuimeng, Secretariat of the Shanghai Society of Biotechnology
Wang, Tongxi, Head of office for the Society of Biochemistry and Molecular Biology
Xu, Hua, Head of Secretariat office of the 2005 ISICR Meeting

Secretariat
Email: hxu@sibs.ac.cn
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320 Yue Yang Road, Shanghai, China
Postcode: 200031
Website: www.sibcb.ac.cn/ISICR2005.html

Rooms
The plenary sessions will be held in the Grand Ballroom, (Banquet Hall).
Concurrent symposiums sessions will be in Guang Da No. 9, 11 and audio-visual Hall.
Workshops session will be held in Guang Yun No. 3, 6 and Guang Da No. 7.
The trade exhibition will be located in Guang Da No. 8.
Poster display boards will be located in Guang Da No. 16.
Reception and Banquet will be in the Grand Ballroom. (Banquet Hall)
Computers are available in the exhibition room for speakers to check their presentations.
For internet access, please inquire at your hotel reception desk.

Organization Officer and Registration Desk
1. Registration desks are located at the main entrance (i.e. the lobby) of the Everbright convention center and will be open from 10:00-23:00 on Oct.20 and from 8:00-18:00 on Oct.21. Registrations after those times will be handled by the organizing officer.
2. The organizing office is located beside the registration desk; ask at the registration desk for directions. This office will be open every day from 8:00-23:00.
3. Delegates should collect their meeting bag, name tag and other conference material at registration and then proceed to the reception desk of their hotel to get their room assignment and key.
4. A message board will be located beside the registration desk.

Registration

Delegates will receive the following upon their registration:

- A meeting bag with a copy of the delegate handbook and scientific program proceedings.
- Coupons for Lunches on Friday through Monday.
- Coupons for the Welcome Reception and Banquet.

Important Delegate Information

Name Tags

Delegates are required to wear their nametags to all scientific and catered sessions.

Insurance

The hosts and organizers are not responsible for personal accidents, any travel costs, or the loss of private property and hence are not liable for any claims. Delegates requiring insurance should make their own arrangements.

Smoking policy

Smoking is not permitted in the venue.

Mobile Phones

Please ensure your mobile phone is turned off during all sessions.

Social Program

The Welcome Reception will be held in Everbright Convention Center on Oct. 20 Thursday evening from 7:30-9:00 pm. Participants in the evening tour on Oct.21 should be signup at the reception entrance. For participants staying at the Convention center, breakfast is included in your room charges. If you are staying at other hotels, please inquire at your hotel reception desk.

Lunch will be in the Everbright Convention Center for those meeting participants that are staying at the Convention center and the Hua Ting Hotel. Lunch for others will be in the Hua Xia Hotel.

The Huangpu River night tour will be on Friday Oct. 21. Buses will be available to transport participants to and from the Huangpu River.

The Banquet will be held on Oct. 23, Sunday 7:00-9:00pm, beginning with the best workshop and poster presentation awards. An evening tour may be possible if there is sufficient interest from participants. Interested attendees and guests should sign up for this tour at the entrance of the Banquet Hall during the Banquet. A limited number of tickets will be available and can be purchased from the organizer office for the dinner, reception or banquet.

The Satellite Meeting will be chaired by Dr. Xue-Tao Cao, the Second Military Medical University and Dr. Xiao-Jing Ma, Cornell University. Communication with Dr. Cao can be made via mobile phone (13901694481) or with his assistant in Shanghai (Ms. Qing-Qing Wang: 13606640030) or in Hangzhou (Prof. Li-Huang Zhang: 13606644729). For the Satellite meeting, buses will be provided for transportation to Zhejiang University in Hangzhou. All arrangements have been handled by Prof. Zhang of the Institute of Immunology, Zhejiang University. Satellite meeting participants will stay at the Zhijiang Hotel (four star) in Hangzhou, located at Mogan Shan Road 180-200, Hangzhou 310005, China, Tel (86 571) 88066888, Fax: (86 571) 88064966. Website: www.zj-hotel.com.cn

Special Awards for 6 outstanding workshop speakers and 6 outstanding posters will be presented before the Banquet.

Opening Ceremony of 2005 Shanghai ISICR Meeting

Thursday, 20 Oct. 2005 (5:00PM-7:30PM)

Grand Ballroom (Banquet Hall)

Opening Ceremony and Welcome Address

Xin-Yuan Liu (Chairperson 2005 ISICR Meeting)
Welcome Speech by City Mayor 5:00-5:20
Translator Ms. Hongfang Song

Awards Ceremony

Howard A. Young (President ISICR) 5:20-5:40
Milstein Award Lectures
Dr. Nancy Reich 5:40-6:05
Dr. Menachem Rubinstein/Dr. Daniela Novick 6:05-6:30

Keynote Speech

Ferid Murad, Nobel Prize Winner 6:30-7:10

Introduction to Chinese Life Science and Biotechnology Research

Vice President of the Chinese Academy of Sciences, Dr. Zhu Chen 7:10-7:30

Welcome Reception

Oct. 20, Thursday, 7:30-9:30

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