Future ISICR Meetings

Oct. 20-25, 2005
Shanghai, China
www.sibcb.ac.cn/ISICR2005.html

Aug. 27-31, 2006
(Joint ISICR/ICS)
Vienna, Austria
www.cytokineresearch.com/2006

ISICR WWW Site

www.ISICR.org

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INTERNATIONAL SOCIETY FOR
INTERFERON AND CYTOKINE RESEARCH
January 2005
Volume 12, No. 1

Interview with 2004 Milstein Awardee Dr. Ernest C. Borden

Hannah Nguyen

Ernest C. Borden, M.D., is Director of the Center for Cancer Drug Discovery and Development at The Cleveland Clinic Taussig Cancer Center and Lerner Research Institute, with a joint appointment in the Department of Cancer Biology at the Cleveland Clinic Foundation. He is also Professor of Molecular Medicine of The Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, a recently formed medical school for the Cleveland Clinic Foundation which offers a 5 year post-Bachelor of Science translational medicine program to now 35 medical students, made possible with a $100 million donation by Mr. Lerner. Dr. Borden received his undergraduate degree from Harvard University and his medical degree from Duke University. He completed an internship at Duke, a residency at the Hospital of the University of Pennsylvania and a postdoctoral fellowship in the oncology division at The Johns Hopkins University School of Medicine. His renowned contribution to interferon and clinical research is complemented with over 236 research publications.

Congratulations on receiving the Milstein Award! What do you consider as your "claim to fame" with respect to your contributions to the interferon field?

I am very honored to be a recipient of the 2004 Milstein Award. I would like to emphasize the important contributions from the Milstein family to the ISICR for these Awards as well as for the Young Investigator Awards. I am very appreciative of all the

*(See **Milstein Awardee**, page 2)*

*(**Milstein Awardee**, cont. from page 1)*

support from the Milstein family to research investigators. They have done a lot to stimulate the interferon field.

In terms of my contributions to the interferon field, it would be in defining the clinical role of interferons and how they function as antitumor modalities. My clinical focus is in melanoma but I have also worked with other tumor types - for example, we showed in one clinical trial the benefits of combining interferons and chemotherapy for one form of lymphoma.

What are your current research interests?

First, I am interested in the role of specific interferon-stimulated genes (ISGs) such as TNF-α related apoptosis inducing ligand (TRAIL/Apo2L) and XIAP associated factor-1 (XAF-1), in the antitumor activity of interferons and how they are related to their anti-angiogenic, anti-apoptotic or other cellular properties. Second, I am interested in augmenting the clinical efficacy of interferons by enhancing the interferon response, using either inhibitors of epigenetic (tumor suppressor) gene silencing or with small molecule inhibitors of SH2 domain-containing protein tyrosine phosphatase (SHP)-1 and -2, phosphatases which turn down interferon signaling (in collaboration with Dr. Taolin Yi, Dept of Cancer Biology, Lerner Research Institute).

How did you become interested in interferons?

I became interested in interferons through an excellent mentor and well-known virologist, Dr. Frederick Murphy, who was working on the pathogenesis of viral infections. It happened 10 years after interferons were discovered. Dr. Murphy asked me to find a project I would be interested in working on in viral pathogenesis. I went to the library and found literature on interferons, and it started from there. And the first time I added a crude interferon preparation to a cell monolayer and saw lytic plaques in the control and an intact monolayer in the treated, I was hooked.

Where do you see interferon research heading?

From a clinical standpoint, interferons still have to reach their full potential. Hopefully combination of interferons with inhibitors of DNA methyltransferase-1 to inhibit epigenetic gene silencing, the development of second generation pegylated or novel interferons, or combination of interferons with peptide inducers of Toll-like receptors-7, -8 and -9 to induce interferons, will contribute in that regard.

What do you consider to be the obstacles to the efficacy of interferons in the clinic?

I think that the first hurdle is to alleviate the unusual side effects of interferons - fatigue and anorexia, which cause interferons to be viewed unfavorably compared to other drugs. I think we need to make molecules with a better therapeutic index. The second hurdle is to understand the mechanism of action of interferons. Is it the anti-apoptotic, anti-angiogenic or the immunostimulatory effect of interferons that is responsible for their antitumorigenic effect? If we knew which biological property was responsible for interferon antitumor activity, we could tailor new molecules accordingly. Some say that interferons are a failure but that is not true. Interferons were the first recombinant proteins to be introduced in clinical medicine, and they proved to reduce morbidity and mortality from cancer, viral disease and from multiple sclerosis. Interferons have a market of approximately 5 billion USD. If one expected a single injection to cure cancer, then they failed, but it is not reasonable to ask that of any drug for life threatening disease.

Do you have any hobbies?

I enjoy spectator sports, and greatly appreciate the Cleveland Orchestra, classical music and opera. We have a woodsy cabin in Algonquin Park, Ontario, which can only be accessed by going across the lake by boat. There is no electricity or plumbing there, so it provides a good disconnect from everyday life.

*(**Milstein Awardee**, cont. from page 1)*

Do you have any mentors or scientists/clinicians that you look up to?

As I mentioned in my speech at the San Juan meeting, I have so many mentors that they are hard to single out. In the scientific community, some researchers don't even realize that they are mentors; some publish great papers that give rise to new insights. Also, there are wonderful people in the lab which give good ideas and they too serve as my mentors.

How much time do you spend in the clinic or in the lab? How do you balance these activities, and is there one that you prefer?

I spend about 25% of my time as a clinical oncologist, primarily with melanoma patients, and then the remaining 75% of my time goes to research. I am extremely busy, but feel fortunate to be able to do both clinical practice and research, as well as to contribute to the education of medical students and research fellows.

As Director of the Center for Cancer Drug Discovery & Development at The Cleveland Clinic Taussig Cancer Center and Lerner Research Institute, what are the highlights of the Center and what do you consider as the important element(s) for a successful institution such as yours?

My primary focus is to augment the movement of discoveries from the lab bench into the clinic. One example is one that I described earlier, involving Dr. Taolin Yi from the Department of Cancer Biology at the Lerner Research Institute and his work with the SHP inhibitors, which was transferred into the clinic as part of an interferon clinical trial.

Are your children in either the medical or scientific fields?

I have two daughters, one is a science writer and the other is a social worker. Six months ago a very unique event happened: one of my daughters delivered identical twin girls, and if you ask me what one of my favorite activities is going to be, it will be as a grandfather to these girls and their 2 year old brother.

How would you describe yourself as a person?

I consider myself very fortunate in my career to pursue what I love and enjoy. I believe that the interferon system is a fascinating and challenging area and opens so many windows in cancer biology, and it will be exciting to be able to understand the 200+ ISGs and their role in the effects of interferons.

What advice would you give to young investigators?

Keep pursuing your ideas and what you believe in.

ISICR Member and former Milstein Awardee Paula Pitha-Rowe Receives Award

The Academy of Sciences of the Czech Republic has awarded Dr. Paula Pitha-Rowe the G.J. Mendel Honorary Medal for Merit in Biological Sciences. The G.J. Mendel Medal, named after the founder of the discipline of genetics, Gregor Johann Mendel, was established by the Czechoslavak Academy of Sciences in 1965. The medal has been awarded by the Academy of Science of the Czech Republic since 1993 in recognition of outstanding contributions in the biological and agricultural sciences. The award is one of the world's top honors in the biological sciences. The ISICR congratulates Dr. Pitha-Rowe on receiving this prestigious award.

ISICR Members win 2 new awards at Annual meeting

New ISICR member Dmitry Liepinsh (National Cancer Institute-Frederick) was the winner of the Friderika Fischer Fellowship, awarded at the meeting and Sujata Balasubramanian (University of Toledo) won a travel Award from the Arthritis National Research Foundation. Congratulations to both ISICR members.

ISICR AWARDS

The Milstein Award
Nominees should be individuals who have made exceptional contributions to research related to interferons and cytokines either in a basic or clinical field. Milstein awards are made possible by the generous gift of Mrs. Seymour Milstein and the Milstein family. This award represents a pinnacle of scientific achievement in our field and is an important landmark of the society.

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

We invite your nominations for eligible candidates for these prestigious symbols of recognition by our society for outstanding achievements. A brief exposition of the reason for your nomination and other supportive documents (such as CV, if available) should be sent to the ISICR President **by March 1**:

Howard A. Young, Ph.D.
Laboratory of Experimental Immunology
Center for Cancer Research
NCI-Frederick
Chandler Street, Bldg. 560/31-23
Frederick, MD 21702-1201
Tel: 301-846-5700
Fax: 301-846-1673
Email: youngh@ncifcrf.gov

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

The Milstein Young Investigator Awards ($1000)

Eligibility: ISICR members and are less than 8 yearsafter receiving a Ph.D or M.D degree. Every year up to five Young Investigator Awards are presented to ISICR members who have made notable contributions to either basic or clinical research within 8 years after receiving their Ph.D or M.D.. This award is provided by a generous gift of the Milstein Family. We urge every eligible individual to apply for the awards. We also ask more senior laboratory advisers to encourage their associates to apply. Send your 2005 Meeting abstract and CV **by June 1** to:

Dr.Paula Pitha-Rowe,
Chair, ISICR Awards Committee
Johns Hopkins University
Dept. of Oncology
1650 Orleans Street
Rm 221
Baltimore, MD 21206
FAX: 410-955-0840,
Email: parowe@jhmi.edu

A brief note describing your accomplishments and a letter of recommendation from your adviser, are strongly encouraged.

The Christina Fleischmann Memorial Award to Young Women Investigators ($1000)
The eligibility rules for this ISICR award are the same as for the Milstein Young Investigator Award (see above) except for gender and that candidates are less than 10 years after receiving a PhD or M.D. degree. Every year the Christina Fleischmann Memorial Award is presented to a young woman ISICR member who has made notable contributions to either basic, translational or clinical research within 10 years after receiving their Ph.D or M.D. This award is made possible through the generosity of the Fleischmann Foundation and is dedicated to the memory of ISICR member and outstanding interferon research scientist Christina Fleischmann.

*(**ISICR Awards**, cont. from page 4)*

Travel Awards
ISICR members who intend to attend the 2005 ISICR meeting in Shanghai, China are eligible for Travel Awards. They are provided primarily through the membership fees, and are based on the scientific merit of the abstract and financial necessity. However, this award does not exempt payment of the registration fee. Please note that there are no age restrictions to this award. However if both senior and junior
members from the same laboratory apply for an award, preference will be given to the junior member. Send your meeting abstract and a note explaining the need for a Travel Award to Dr. Paula Pitha-Rowe, Chair, ISICR Awards Committee (the deadline for ISICR Travel Award applications is June 1). NOTE: THE TRAVEL AWARD DEADLINE WILL NOT BE EXTENDED, EVEN IF THE ABSTRACT DEADLINE IS EXTENDED BEYOND JUNE 1.

Award Recipient Mini-Bios

Hannah Nguyen

Our 2004 Milstein Young Investigator and Christina Fleishmann Memorial Award winners were asked a few questions in order to let ISICR members get to know them a little better:

Chen Dong, Ph.D: 2004 recipient of the Milstein Young Investigator Award
Department of Immunology
MD Anderson Cancer Center
7455 Fannin, Unit 902
Houston, TX 77030-1903

1. What is your current research position?
Associate Professor

2. Description of awarded research: Mitogen-activated protein (MAP) kinases are essential regulators in immune responses, and their activities are modulated by kinases and phosphatases. MAP kinase phosphatase (MKP) is a family of dual-specificity phosphatases whose function is evolutionarily conserved. A number of mammalian MKPs have been identified so far, but their specific physiological functions in negative regulation of MAP kinases have not been genetically identified. Here we examined innate and adaptive immune responses in the absence of MKP5. JNK activity was selectively increased in Mkp5 (also known as Dusp10)-deficient mouse cells. Mkp5-deficient cells produced greatly enhanced levels of pro-inflammatory cytokines during innate immune responses and exhibited greater T-cell activation than their wild-type counterparts. However, Mkp5-deficient T cells proliferated poorly upon activation, which resulted in increased resistance to experimental autoimmune encephalomyelitis. By contrast, Mkp5-deficient CD41 and CD8 effector T cells produced significantly increased levels of cytokines compared with wild-type cells, which led to much more robust and rapidly fatal immune responses to secondary infection with lymphocytic choriomeningitis virus. Therefore, MKP5 has a principal function in both innate and adaptive immune responses, and represents a novel target for therapeutic intervention of immune diseases.

3. What are your research goals? To understand the regulation of immune and autoimmune responses

4. How has this award affected you? I feel privileged and honored to have been selected for this award

Brenda L. Fredericksen, PhD: 2004 Recipient of the Christina Fleischmann Award
University of Texas Southwestern Medical Center
Department of Microbiology
Dallas, TX USA

1. What is your current research position?
Instructor

2. Description of awarded research: Recent outbreaks of West Nile virus (WNV) have been associated with a dramatic increase in both the incidence and severity of human disease. The molecular mechanism for the increase in the pathogenesis of WNV is likely to include novel viral-host interactions that allow the virus to overcome or evade the host innate and/or adaptive immune response. Analysis of the host response to WNV demonstrated that the

*(**ISICR Awards**, cont. from page 5)*

expression of several antiviral genes, including interferon α, did not occur until late in infection and after peak viral production. The delayed induction of the host antiviral response was due the lack of activation of interferon regulatory factor 3 (IRF-3), a transcription factor central to the establishment of the host antiviral state. WNV-induced activation of IRF-3 was not detected until 20 hr post-infection and peak levels of activation did not occur until 24 to 30 hr post-infection. In contrast, IRF-3 has been shown to respond to a broad range of viruses with the kinetics of activation occurring between 2 to 6 hr post-infection. The possibility that WNV actively blocks IRF-3 activation at early times post-infection was examined by co-infecting cultures with WNV and vesicular stomatitis virus (VSV), a virus known to rapidly induce IRF-3. Dual infection of cells with WNV and VSV resulted in the induction of the IRF-3 pathway by 3 hr post-infection, demonstrating that WNV does not block IRF-3 activation. These results suggest that the delayed activation of IRF-3 was due to the accumulation of threshold levels of WNV specific proteins and/or viral RNA required for stimulating the IRF-3 pathway. Alternatively, WNV may sequester the viral stimulus or actively prevent IRF-3 phosphorylation to preclude IRF-3 activation until late in infection. Experiments are underway to identify the viral agonist of the IRF-3 pathway and further define the mechanism by which WNV avoids IRF-3 induction.

3. What are your research goals? My current research focuses on the identification of viral factors responsible for flavivirus induced pathogenesis in order to identify novel targets for treating and preventing infection.

4. How has this award affected you? The attention and exposure that this award has generated for me and my work will be extremely beneficial as I begin the process of obtaining a faculty position and establishing my own laboratory.

5. What are your future career aspirations? My long-term career goal is to establish a productive independent research program focused on defining the role of the host innate intracellular antiviral response in viral paghogenesis.

Albert Mellick, PhD: 2004 recipient of the Milstein Young Investigator Award

Department of Molecular Genetics and Microbiology
130 Life Sciences Bldg.
State University of New York at Stony Brook
Stony Brook, New York 11794-5222

1. What is your current research position? I am a Postdoctoral scientist at New York State University, Stony Brook. I will soon be transferring to the Cold Spring Harbor Laboratories to work in Cancer Angiogenesis in the lab of Dr Vivek Mitall.

2. Description of awarded research: In the last 5 years (and while a post graduate student) I have been interested in the molecular changes that underlie malignancy or metastatic progression in human cancer. I was awarded the prize for investigation of phenotype and genotype changes in a colon cancer population, and characterization of potential interleukin-6 responsive target genes (metalloproteases) in colon cancer. The work has been validated in colon cancer cells in culture using reporter assays.

3. What are your research goals? I am currently interested in stromal cell biology, and the way that stromal cells and precursors interact with and permit tumor growth and metastatic spread.

4. How has this award affected you? It has allowed me to establish myself as a research scientist in the United States and has increased my profile in the interferon field.

5. What are your future career aspirations? I would like to continue to do research at a high level and establish my own group in cancer research.

Ehssan Sharif-Askari, PhD: 2004 recipient of the Milstein Young Investigator Award

Dept of Molecular Oncology
Lady Davis Institute, McGill University
3755 Cote Ste-Catherine
Montreal, Quebec, H3T 1E2 Canada

*(**ISICR Awards**, cont. from page 6)*

1. What is your current research position? I am a postdoctoral fellow working with Dr. John Hiscott at the Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Canada.

2. Description of awarded research: Cancer, the cause of the highest mortality in the developed world, adopts different forms but always entails serious complications if left untreated. For many years, the effect of anticancer drugs on tumor cells was attributed to their crippling action on rapidly proliferating cancer cells. The lack of specificity of toxic drugs for tumor cells and the resulting toxicity to normal tissue prompted scientists to explore alternative approaches of cancer therapy including oncolytic viruses (OV). Infection with these viruses in humans is usually subclinical due to the protection conferred by a functional interferon antiviral system. However, in most immortalized/transformed cells in which the interferon system is genetically defective, this virus can replicate to high titers leading to rapid cell death through a process known as apoptosis. These studies have paved the way to investigate their therapeutic potential in human cancer. Apoptosis, or programmed cell death, is an orderly and genetically controlled form of cell death. Activation of apoptosis by the host cell in response to virus infection is highly detrimental to the virus. While there is enormous information on the molecular aspects of cellular apoptosis, the field of apoptosis during viral infection is still in its infancy. Therefore, my main objective is to characterize the mechanism of cell death induced by OV, the role of cell death in priming innate immune response against viral infection, and to explore the effect of immune regulators on this process at the molecular level. The outcome of this project will provide us with significant information on how to manipulate resistant cancer cells to be efficiently targeted by OV and induced to die. My contribution to this field will further improve and enhance the use of OV as a potential therapeutic tool in cancer therapy.

3. What are your research goals? The objective of this study is to investigate the interface between virus-induced cell apoptosis and development of the innate antiviral immune response.

4. How has this award affected you? The Milstein Young Investigator award will certainly boost my work toward scientific independence as well as validate the contribution of my research to the improvement of cancer therapy.

5. What are your future career aspirations? To be an independent investigator with a laboratory where I can bring molecular bench work to clinical treatment.

Tomohiko Tamura, MD, PhD: 2004 recipient of the Milstein Young Investigator Award
LMGR/NICHD/NIH
Bldg.6, Rm.2A05
6 Center Drive MSC 2753
Bethesda, MD 20892-2753

1. What is your current research position? I am a Staff Scientist in the laboratory headed by Dr. Keiko Ozato at the National Institute of Child Health and Human Development. I was originally a hematologist specializing in stem cell transplantation in Japan, and learned molecular biology in Dr. Tadatsugu Taniguchi's laboratory.

2. Description of awarded research: I have been working on transcription factors of the IRF family in the differentiation and growth of hematopoietic cells. The work I was awarded for describes the role of two closely related IRFs, IRF-4 and IRF-8, in dendritic cell (DC) development. DCs are a heterogeneous population composed of multiple subsets that have diverse functions. Using mice targeted with IRF-4 and/or IRF-8, we demonstrated that the two IRFs are expressed in distinct DC subsets and are required for the development of respective subsets. IRF-4/8 have common activities to stimulate a basic process of DC differentiation, while they also have specific activities to confer DC's functional diversity. Thus, our findings suggested that these IRFs serve as a backbone of the DC development program.

3. What are your research goals? I would like to investigate the detailed molecular mechanisms by which IRFs control gene transcription to govern immune cell development and function, with a

*(**ISICR Awards**, cont. from page 7)*

particular emphasis on chromatin regulation.

4. How has this award affected you? This award has encouraged me to continue basic research: I needed to make a final decision of whether I would remain in the basic research field or return to be a clinician.

5. What are your future career aspirations? Although I am not sure when it will be possible, I would like to have my own laboratory that seeks novel concepts in understanding gene regulation during hematopoietic cell differentiation. I hope my findings will contribute to clarifying not only normal hematopoiesis but also pathogenesis and therapy of leukemia/lymphoma, since my motivation still comes solely from my 6 years of clinical experience in which I had patients with such diseases, some of whom I could not save.

Finally, I would like to thank the organizers of the excellent meeting and the award committee. I am also grateful to my mentor Dr. Ozato for her strong support, and to my previous mentor, Dr. Taniguchi, for originally letting me know how exciting basic science is as a profession.

Milstein Awardee
Ernie Borden

Milstein
Awardee
Keiko Ozato

Milstein Young
Investigator Awardee
Tomohiko Tamura

Christina Fleischmann
Awardee
Brenda Fredericksen

Milstein Young
Investigator Awardee
Albert Mellick

Milstein Young
Investigator Awardee
Chen Dong

Milstein Young
Investigator Awardee
Ehssan Sharif-Askari

A certain politician looking for supporters surprises ISICR banquet attendees with a visit.

Foot-and-Mouth Disease: A Third Control Alternative

Joseph Cummins*, Steven G. Krakowka*, and David P. Hutcheson*
(Edited by: Dr. Manfred Beilharz*)

The Agro-terrorism Potential

Vaccination and depopulation are the current methods of control for Foot-and-Mouth disease (FMD), but a third alternative is needed to handle agro-terrorism. FMD kills less than 1% of animals affected yet the government kills 100%. A third alternative is needed for managing FMD.

Currently in Amarillo, Texas there are 140 cattle feed yards within a 150 mile radius which have 3 million head of cattle on feed today. Additionally, there are swine production facilities with 2.7 million hogs, and dairies with 137,000 milk cows in the area.

An article in Amarillo's local newspaper on January 23rd 2004, entitled "Area FBI wary of agro-terrorism after September 11," attributes statements to Agent Tim Reid of the Federal Bureau of Investigation (FBI) and focuses on threats of agro-terrorism delivered by crop-dusting aircraft. The article states that the FBI watches domestic groups such as the Environmental Liberation Front, Animal Liberation Front and People for the Ethical Treatment of Animals. Moreover, the article stated; "…Amarillo is no stranger to potential international terrorists." Reid said a medical doctor from Jordan spent 3 years in Amarillo without employment, "but received substantial amounts of money in his bank account." This medical doctor reportedly inquired about crop-dusting aircraft after September 11th. "The individual denied the crop-dusting conversation ever took place, but during the 12-hour questioning, he was deceptive in his answers, Reid said."

In an article by Wes Ishmael entitled "A Soft Underbelly" (July 2004 issue www.beef-mag.com), it was stated that, "When the US invaded Afghanistan, more than 200 US documents were found that had been translated into Arabic, each describing in detail the US planned response capability to the introduction of a foreign animal disease to the livestock industry." Moreover, it was stated that "Documentation verifies that al Qaeda has been talking about agro-terrorism since 1985." The concentrated nature of swine and cattle production makes the Texas Panhandle a prime target for agro-terrorism. There is particular concern about FMD virus because:

i. An outbreak of FMD will cost billions of dollars and cripple US red meat production.
ii. FMD virus is one of the most contagious animal viruses known. Under the right environmental conditions, the virus can be blown by the wind to infect cattle and swine.
iii. FMD virus is a bio-weapon that can be readily acquired by terrorists. In the past 2 years, the FMD virus has caused natural disease in more than 20 countries including Syria, Libya and the Palestinian Autonomous Territories.
iv. Current USDA plans to slaughter and dispose of animals by burial or burning will, we believe, contribute to an economic disaster when FMD arrives. Using FMD virus, terrorists can infect livestock faster than the USDA can slaughter and bury livestock.

We recently reviewed Volume 21(3), December 2002 issue of the Scientific and Technical Review "Foot and mouth disease: facing the new dilemmas," coordinated by G.R.Thomson. That issue dealt thoroughly with vaccination or slaughter as a response to FMD. Scientific evidence supports consideration of a third alternative when faced with FMD. Clearly, a third alternative does not currently fit into the International Health Standards, Part 2, Section 2.1, Chapter 2.11 of the Terrestrial Animal Health Code, 11th Edition, 2003. However, in view of new scientific data and the threat of agro-terrorism, a third alternative for FMD should be developed.

The Type I Interferon Pathway and FMD

Scientists at USDA, Animal Research Service (ARS) have shown that the FMD virus possesses the ability to overcome key host defenses based on interferon (IFN). FMD virus inhibits production of IFNα/β [1] and blocks a key IFN-inducible, antiviral pathway, i.e.- double-stranded RNA (dsRNA) - dependent

protein kinase R (PKR) [2]. Since a FMD viral strategy for control of host cells is to: 1) suppress IFNα/β production, and 2) block the effect of PKR, then treatment with exogenous IFNα or induction of endogenous IFNα will help control FMD.

Indeed, this vulnerability of FMD has led to a novel viral disease control strategy. Scientists at ARS reported that a recombinant replication-defective human adenovirus type 5 vector containing porcine IFNα (Ad5-pIFNα) was constructed [3]. When the Ad5-pIFNα was injected into swine, the resulting IFNα production completely protected 3 swine given virulent FMD virus. Swine with IFNα showed no signs of FMD, did not develop viremia and did not develop antibodies against viral nonstructural proteins. However, when Ad5-pIFNα or this same vector modified to carry bovine IFNα, was injected into cattle, Ad5-pIFNα, but not the bovine version, provided partial in vivo protection by delaying viremia 1 day and decreasing vesicle formulation [4]. ARS scientists reported that Ad5-pIFNα given to pigs 1, 3 or 5 days (but not 7 days) before challenge with FMD virus resulted in complete protection [5]. These scientists reported that pigs were protected even 2 days after IFNα was no longer detected in the blood, presumably because of the induction of IFN stimulated genes (ISG).

Evidence has been accumulating for more than 30 years that FMD virus in vivo is inhibited by IFNα. Straub and Ahl reported that IFN induced in the nasal secretions (NS) by infectious bovine rhinotracheitis (IBR) given intranasally provided protection against FMD viral challenge [6]. One or 2 days after intranasal vaccination with IBR virus, calves were challenged with FMD virus. IFN was detected in the NS within 24 hours of vaccination, and IFN persisted at high levels for 6 additional days and at low levels through the tenth day after IBR virus inoculation. Vaccinated calves had a milder course of FMD and more than a 99% reduction in FMD virus titers in the NS.

In the process of studying FMD virus transmission from carrier to susceptible cattle, carriers of FMD virus were inoculated intranasally with IBR virus in an effort to create a stress which might increase excretion of FMD virus from carrier cattle. However FMD virus disappeared from the esophageal-pharyngeal fluid of the 2 carrier animals 1 day after IBR virus inoculation and was not detected again during the 4-week sampling period [7]. Although IFN was not assayed in this experiment, it would have been induced by IBR virus and probably inhibited the FMD virus in these carrier animals. Clearly, IFN is readily induced in the NS of feedlot calves by modified live intranasal IBR viral vaccine [8,9].

In protection experiments, cattle given coital vesicular exanthema virus (CVEV) and then infected with FMD virus developed a milder form of FMD and developed FMD later than control calves infected with FMD alone [10]. Presumably, the induction of IFN by the CVEV was responsible for the protection noted in this study.

The use of viral inducers of IFN in cattle with FMD is in agreement with the successful use of oral synthetic IFN inducers which protected mice from a subsequent infection with FMD virus [11]. Richmond and Campbell reported that one oral IFN inducer protected mice if given 2, 24 or 48 hours before FMD virus inoculation and another inducer protected mice if given 18 hours or less before FMD virus. A single injection into mice of 150 µg of the synthetic IFN inducer polyriboinosinic: polyribocytidylic acid (PolyI:C) 18 hours before a challenge with 100 LD50 of FMD virus (strain Asia-10) was 100% protective [12]. However, PolyI:C is too toxic in cattle to be used in the control of FMD [13-15].

Cunliffe et al [16] reported that PolyI:C (1 mg/kg weight) was given intraperitoneally to 5 pigs one day before the 5 treated pigs (and 3 untreated control pigs) were placed in a room with 2 pigs with FMD. The controls exhibited signs of FMD on 3, 4, and 4 (mean 3.7) days after FMD virus exposure whereas the PolyI:C-treated pigs exhibited signs of FMD on 4, 7, 7, 7 and 7 (mean 6.4) days after FMD virus exposure. All pigs given PolyI:C exhibited severe but transient adverse effects (pruritus, trembling, urination, defecation and ataxia). Despite the toxicity, treated pigs experienced a delay in development of FMD, compared to controls.

McVicar et al [17] reported that various concentrations of PolyI:C were given intravenously to 11

calves (0.25 - 4 mg/kg weight) and 13 goats (1-4 mg/kg). Two calves given PolyI:C were tested hourly for 6 hours for serum IFN which was detected at each hour. All calves given PolyI:C had a transient temperature increase. Calves were challenged intramuscularly or intradermalingually with 10 million PFU of FMD virus 2-6 hours after PolyI:C was given. Differences were not noted in clinical FMD or viremia between treated and control calves given this challenge of FMD virus.

Goats given PolyI:C had a mean temperature increase of 2.3^{o} F versus 0.5^{o} F in controls given placebo. One goat died within 24 hours and one goat aborted within 48 hours of PolyI:C treatment. Most goats given PolyI:C showed signs of toxicity. Twelve goats given PolyI:C and 7 controls were challenged intranasally with 10,000 PFU of FMD virus. Differences were not noted in clinical FMD, viremia or pharyngeal carriers during the 14 days after challenge.

It appears the chemical inducers of IFNα are too toxic to be useful in the management of FMD [16,17]. This is in contrast to the control of FMD virus reported from viral inducers of IFNα or the administration of the IFNα gene to livestock [4-8].

Orally Administered IFN and FMD

The oral delivery of natural human IFNα (HuIFNα) has been beneficial to cattle undergoing shipping fever, or challenged with virulent IBR virus or Theileria parva [18-21]. In studies involving 7,000 feeder cattle, a single dose of orally administered HuIFNα (0.7 international units [IU]/kg body weight [bw]) at the time of diagnosis of respiratory disease, given with antibiotics, reduced mortality significantly ($p<0.001$), when compared to feeder calves given placebo and antibiotics [18]. Feeder calves were given HuIFNα at 0.0, 0.05, 0.5 or 5.0 IU/kg bw for 4 consecutive days, starting 2 days before a virulent IBR virus challenge. Feeder calves given 0.05 IU/kg bw had significantly ($P<0.05$) greater weight gain after 25 days and fewer days of fever (> 40^{o}C) [19]. In studies of naturally occurring shipping fever, oral HuIFNα given for 3 days before shipping, or once after arrival, improved weight gain or reduced illness [20]. In a challenge study of calves given Theileria parva, the causative agent of East Coast Fever, some calves given oral HuIFNα survived an otherwise fatal challenge [21]. In the 4 studies cited above, the beneficial oral dose of HuIFNα was less than 500 IU per calf.

Orally administered IFNα is beneficial in cats [22], dogs [23], horses [24], swine [25,26], cattle [18-21], mice [27-30] and chickens [31,32]. In humans, oral delivery of HuIFNα is beneficial for the treatment of MS [33-35], Sjögren's syndrome [36-39], fibromyalgia [40], measles [41], aphthous stomatitis [42-44], oral warts in HIV+ patients [45], respiratory syncytial virus [46], lichen planus [47], genital warts [48,49], AIDS [50,51], hepatitis B [52-56], and diabetes [57].

A critical question is: Does HuIFNα given orally up-regulate ISG in vivo? It has been reported that IFNα or IFNβ given orally up-regulates 1) Mx in mice and humans [58], 2) 2'5' adenylate synthetase (AS) in mice and guinea pigs [59-61] and 3) other genes in humans [62] and mice [63-65]. It is not yet known if PKR is up-regulated after oral administration of HuIFNα to livestock, or if such upregulation is needed to stop FMD virus replication. Perhaps other ISG's upregulated by IFNα will compensate to suppress FMD replication.

ISG are up-regulated within a few hours after oral IFN administration [58,63]. A 15kDa protein called ISG-15 is up-regulated in human buccal epithelial cells in vivo and in vitro with a peak level of ISG-15 detected 2 hours after oral HuIFNα administration [63]. Up-regulation of Mx proteins was detected in the spleen of mice, and in the peripheral blood mononuclear cells of humans, 2-4 hours after murine IFNα or HuIFNα, respectively, were ingested [58]. These data demonstrate that orally administered IFNα has rapid and systemic biological effects in animals and humans.

In light of this accumulated evidence concerning orally administered, low-dose IFNα, the testing of orally administered HuIFNα as a response to FMD virus is recommended. The IFNs are now widely available in purified form as both naturally occurring and as recombinant molecules. An important facet of the IFNs is the fact that the IFNα family is not

species-specific in action, but is better described as somewhat species-restricted. Cells of human origin are protected by IFNα from animal origin and animal cells are protected by IFNα of human origin. Bovine IFNα is active on primate [67], porcine [68] and human cell cultures [68]. Porcine IFNα is active on equine [68], bovine and human cell cultures [68,69]. Human IFNα is active on porcine [68-70], bovine [68-74], and feline [75] cell cultures.

Testing may show that HuIFNα (fed in rations) will supplement production of endogenous IFNα resulting in significant protection against challenge from FMD virus. Funding is being sought to help develop an alternative to slaughter and an adjunct to vaccination. The testing needed is obvious, 1) test liquid or powdered HuIFNα. Different doses of the HuIFNα will be placed in the oral cavity of cattle and swine and blood samples will be drawn to determine by microarrays which doses induce ISG. 2) test the therapy in animals with FMD. Ultimately, the HuIFNα in the ration will be tested in animals undergoing natural FMD outbreaks and/or FMD challenge tests.

The Practical Application of IFNα in Livestock Rations

IFNα is known to be stable in Anhydrous Crystalline Maltose (ACM) at room temperature for 24 months and for 60 months at refrigerated temperatures as long as the moisture content is less than 2%. Some expensive stability testing can be avoided and time saved if ACM is utilized as the stabilizer of the IFNα [76]. Eventually, the ACM/IFNα could be placed in sealed 1/2 pound (0.5 lb.) plastic bags for storage at feedlots or swine production units. Immediately before use, the 0.5 lb. ACM/IFNα can be mixed with 4.5 lbs. of soybean meal (48% protein content). This 5 lbs. of ACM/IFNα soybean meal can then be mixed with 45 lbs. of ration before it is mixed into a ton of ration and fed that day.

The direct cost of 0.5 lb. of ACM is approximately $3.40 and the estimated cost of HuIFNα per ton of ration is less than $1.00 (estimate 1,000 IU per 20 lbs. of feed). Therefore, the direct cost of the ACM/IFNα is approximately $4.40 per ton of feed. There will be additional direct expenses in shipping and packaging but the estimated direct cost of the product (0.5 lb. of ACM/IFNα) delivered to a production unit can probably be held under $6 per ton of ration. Production units will need rat proof storage of the ACM/IFNα. For example, if a feedlot feeds 25,000 head per day, 250 bags of 0.5 lbs. of ACM/IFNα will be needed for a single day's use. If the volume of 0.5 lb. bag is 24 cubic inches (2" X 3" X 4"), then 72 bags of ACM/IFNα can be stored in one cubic foot of space. Therefore, to hold 250 bags will require a space of 3.5 cubic feet. To store a 10 day supply of ACM/IFNα will require 35 cubic feet or a space 6' wide X 18" deep piled 4' high. A secure metal cabinet without refrigeration can be used to store the ACM/IFNα and protect it against moisture and vermin.

If the 10 million cattle currently on feed in the USA will use ACM/IFNα for 10 days, then 1 million bags of ACM/IFNα will be needed. Swine may need a similar amount. If these estimates are correct, the direct cost is only $12 million, far less than the cost of depopulation. These cost estimates do not include the cost of obtaining regulatory approval, or the cost of testing, distribution or any profit.

Conclusions

1. The FMD virus is susceptible to the antiviral effects of IFNα in vivo.

2. The antiviral effect of oral HuIFNα is upported by sound scientific evidence.

3. Natural HuIFNα can be added to animal rations and feed.

4. The dose and relevant schedule of oral HuIFNα which produces maximal up-regulation of host antiviral pathways inhibited by FMD virus can be determined by testing.

5. Oral HuIFNα therapy, with or without FMD vaccination, is an attractive economical alternative to depopulation of livestock with FMD.

It has been a worthy goal of our government to keep a FMD free status. The last outbreak in the US was in 1929. The last outbreak in Canada was 1952 and in Mexico in 1954. It has now been 50 years since FMD occurred in North America. The problem facing the government and the livestock industry is how to deal with FMD if it is introduced by terrorists. When an outbreak of FMD occurs, USDA, APHIS plans to stop all animal transportation, slaughter and dispose of infected and exposed animals, and to clean and disinfect premises in contact with infected animals. No one doubts that the plans of APHIS will successfully eliminate FMD if it is accidentally introduced into a single location in the US. However, if terrorists repeatedly introduce one or more serotypes of FMD virus at multiple sites, how can the eradication plans of APHIS succeed? At what point does the cost of eradication exceed the benefit of eradication? How many of the 97 million cattle and 58 million hogs will be killed in an attempt to eradicate FMD virus repeatedly introduced by terrorists?

Bioterrorists may force the US livestock industry to live with FMD virus. Immuno-modulation using IFN is a tool that may help the livestock industry survive agro-terrorism.

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Note: The article was deemed by the Editor to be of interest to the IFN research community. Comments from the membership are welcome. The Editor-in-Chief of this newsletter (HY) has no financial interests in Amarillo Biosciences or any company involved with oral IFN.

NEW ISICR MEMBERS

The ISICR welcomes these new members and encourages their participation in the annual meeting and in ISICR committees. The membership office can provide contact details.

Alexander N. Dubeykovskiy
New York, NY

Neil Foster
Newcastle, UK

Adolfo Garcia-Sastre
New York, NY

Veijo I. Hukkanen
Turku, Finland

William B. Klimstra
Shreveport, LA

Dmitry Liepinsh
Frederick, MD

Qing Ma
Houston, TX

Stephen G. Maher
Frederick, MD

Jacqueline M. McBride
S San Francisco, CA

Elizabeth Raveche
Newark, NJ

Anuj Sharma
Bethesda, MD

Michael A. Skawinski
Piscataway, NJ

Yu-Ichiro Satoh
Nagoya, Japan

Phillippe A. Tessier
Quebec, Canada

Shulping Tu
New York, NY

Yang Xi
Winnipeg, Canada

New Member Minibios

The newsletter is instituting a new feature designed to introduce new ISICR members to the general membership. Any new members who would like to have their mini-bios included in future issues should contact Thomas Tan at <TAN_SENG-LAI@Lilly.com>

Neil Foster, Ph.D.
Senior Research Associate
Medical School of Newcastle University, UK

Dr. Foster is responsible for the supervision of post-graduate PhD and MRes students. His research interests include many aspects of innate cell biology, particularly early immunological events following host/microbe contact. Currently his group is involved in a number of projects studying the role of novel IL-1 family in myeloid cells (in collaboration with Dr John Sims, Amgen, USA) and the effect of immunomodulators (IL-18 binding protein and vasoactive intestinal peptide, VIP) on proinflammatory circuits. Dr. Foster received his BSc (hons) in parasitology/immunology at the University of Leeds, UK, and his doctorate in the laboratory of Prof Donald Lee (also at Leeds) investigating the effect of intestinal nematodes and VIP on host intestine. Dr. Foster has obtained experience in wide aspect of innate cell biology from his postdoctoral research projects with Prof Barry Hirst (University of Newcastle upon Tyne UK), Prof Paul Barrow (Inst. Animal Research UK) and Dr Gordon MacPherson (Sir William Dunn School of Pathology UK). He is married and has a number of hobbies outside of the laboratory including fishing, playing the guitar and reading (although not at the same time).

Reason for joining the ISICR: "My research of late has focused a lot on the biology of cytokines and although I am a member of the British Society for Immunology, I additionally wanted to join a society which predominantly is concerned with cytokine biology".

(New Member Minibios continued)

Adolfo García-Sastre, Ph.D.
Professor
Department of Microbiology,
Mount Sinai School of Medicine,
New York, USA

Dr. Garcia-Sastre received his doctorate in biochemistry and virology from the University of Salamanca, Spain in 1990. He joined Mount Sinai in 1997 as an assistant professor and was promoted to full professor in 2004. His laboratory has developed several techniques that allow the genetic manipulation of negative strand RNA virus genomes. His lab is currently using this methodology in two major research areas:

1. Generation of negative strand RNA virus vectors, including influenza virus vectors expressing selected antigens from HIV-1, malaria parasites, and tumor cells as a means to induce protective or therapeutic immune responses against these pathogenic agents.
2. Studies on the replication cycle of RNA viruses: The functions of cis- and trans-acting elements in the replication cycle of influenza virus and the interactions of such viral components among themselves and with host components are being investigated.

In addition, Dr. García-Sastre's lab is investigating the ability of different RNA viruses, including influenza, respiratory syncytial, dengue and SARS viruses, to inhibit the induction of innate antiviral immune responses in their hosts. When his lab found that one of the gene products encoded by influenza virus, the NS1 protein, was dedicated to inhibit the induction of the type I interferon response, he suspected and later showed that most, if not all, viruses encode type I interferon antagonists, in order to be able to efficiently replicate within their hosts and to propagate from one host to another.

Reason for joining the ISICR: "I'm very happy to join the ISICR since as a virologist interested in virus-host interactions, I feel that is critical to study the interactions between viruses and the interferon system in order to better understand the ability of viruses to replicate and induce disease".

Veijo Hukkanen, MD., PhD.
Senior Research Fellow
University of Turku, Finland

Dr. Hukkanen received his doctorate in Medical Sciences from the University of Turku, Finland in 1983. He studied the molecular biology and latency of herpes simplex virus (HSV) while he was a postdoc in Dr. Roizman's lab at the University of Chicago in late 1980's (NIH Fogarty postdoctoral fellowship). His research interests include gene therapy of autoimmune diseases of the central nervous system (CNS) using replicative HSV vectors, and the innate and adaptive host responses to HSV infection and to HSV gene therapy vectors. Dr. Hukkanen has described the IL-23 response in HSV infection of the nervous system and studied the effects of immunomodulating chemotherapy on the virus infection of the CNS and on the cytokine responses to viruses. Dr. Hukkanen has held academic positions as Senior Lecturer of Virology at the University of Turku, and as acting Professor of Virology, University of Oulu, and in University of Turku, Finland, where he is presently an Academy Senior Research Fellow. He is the co-organizer of the International Herpesvirus Workshop 2005, to be held in Turku, Finland in summer 2005.

Reason for joining the ISICR: "I am interested in the cytokine responses to virus infections, and also in gene therapy using (herpes) viral transfer of therapeutic cytokines. The ISICR meetings are a great way to get an insight on the advances in the fields of cytokines and the innate host responses."

WWW

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Regards,
David R. Soll, Director,
Developmental Studies Hybridoma Bank

The Genetic Association Database
http://geneticassociationdb.nih.gov/

The Genetic Association Database is an archive of human genetic association studies of complex diseases and disorders. The goal of this database is to allow the user to rapidly identify medically relevant polymorphisms from the large volume of polymorphism and mutational data, in the context of standardized nomenclature.
The data is from published scientific papers. Study data is recorded in the context of official human gene nomenclature with additional molecular reference numbers and links. It is gene centered. That is, each record is a record of a gene or marker. If a study investigated 6 genes for a particular disorder, there will be 6 records.
Anyone may view this database and anyone may submit records. You do not have to be an author on the original study to submit a record. All submitted records will be reviewed before inclusion in the archive. Individual fields are defined here.
Comments and suggestions are very welcome, especially with regard to errors in the data found in the DB. In particular, specific gene comments are useful.

Note: GAD is intended for use primarily by medical scientists and other professionals concerned with genetic disorders, by genetics researchers, and by advanced students in science and medicine. While GAD database is open to the public, users seeking information about a personal medical or genetic condition are urged to consult with a qualified physician for diagnosis and for answers to personal questions.

The Human Protein Reference Database
www.hprd.org

The Human Protein Reference Database represents a centralized platform to visually depict and integrate information pertaining to domain architecture, post-translational modifications, interaction networks and disease association for each protein in the human proteome. All the information in HPRD has been manually extracted from the literature by expert biologists who read, interpret and analyze the published data. HPRD has been created using an object oriented database in Zope, an open source web application server, that provides versatility in query functions and allows data to be displayed dynamically

Interferon Standards: National Institutes of Health NIAID Reference Reagent Repository

Sponsored by the National Institute of Allergy and Infectious Diseases
Operated by Braton Biotech, Inc.
http://www.bratonbiotech.com/braton11.htm

The interferon standard preparations designated by the World Health Organization (WHO) as International Standards or International Reference Preparations are the sole reagents for the international standardization of interferons used for both clinical therapy and experimental research. Reference standards for human and mouse interferons as well as antibodies to the interferons are distributed by the Repository. These materials are not intended for either diagnostic or therapeutic use.

Medical.WebEnds.com
http://medical.webends.com/

Medical.WebEnds.com is a free online medical terminology dictionary with over twenty thousand definitions. It is also an internet index to thousands of other online healthcare resources.

MethDB
http://www.methdb.net/

The purpose of this database is to provide the scientific community with a resource to store DNA methylation data and to make these data readily available to the public. Descriptions of MethDB has been published in the database issues of Nucleic Acids Research in 2001 and 2003 and in the Journal of Nutrition (see PubMed).
The methylation database was supported by a grant from the Klaus Tschira Foundation and is currently supported by a grant from the Genopole Languedoc-Roussillon. The database server is currently maintained at the Institut de Génétique Humaine (CNRS) Montpellier.

Microbiology & Immunology Online
http://pathmicro.med.sc.edu/book/welcome.htm

The chapters of this book are derived from lectures given to our second year Medical Students in the Medical Microbiology course at the University of South Carolina. At present, there are approximately 70 chapters in the book, only a few of which are password-protected. Most chapters will be revised by adding new links to additional web resources and adding questions that will test your knowledge of Microbiology and Immunology.

The National Cancer Institute Biological Resources Branch Preclinical Repository
http://web.ncifcrf.gov/research/brb/preclin/

The BRB Preclinical Repository is an NCI-sponsored facility which contains bulk cytokines, monoclonal antibodies, and cytokine standards that are maintained under carefully controlled storage conditions. The purpose of this facility is to maintain a constant and uniform supply of high quality reagents for scientists at non-profit as well as commercial establishments. There is no charge for this service.

National Institute for Biological Standards and Control
http://www.nibsc.ac.uk/

NIBSC is a multi-disciplinary scientific establishment whose purpose is to safeguard and enhance public health by standardizing and controlling biological substances used in medicine. NIBSC has a leading international role in preparing, evaluating and distributing International Biological Standards and other biological reference materials. A WHO International Laboratory for Biological Standards.

The Nuclear Protein Database (NPD)
http://npd.hgu.mrc.ac.uk/index.html

What's in the NPD?
The NPD contains information on >1000 vertebrate proteins (mainly those from mouse and human) that are thought to, or known to, be localized to the cell nucleus. Where known, the sub-nuclear compartment where the proteins have been found are reported. Also stored is information on the amino acid

sequence, predicted protein size and isoelectric point, as well as any repeats, motifs or domains within the protein sequence. Biological and molecular functions of the proteins are described using GO terms. Where appropriate, links to other databases are provided (e.g. Entrez, SWISS-PROT, OMIM, PubMed, PubMed Central).

What's not in the NPD?
In general only one isoform of the protein is given (usually the largest). The database contains no information on protein isoforms generated by alternative splicing.

How to use the NPD
You can search the whole database using a protein name, protein motif, nuclear compartment name, or keyword term. Alternatively you can view all of the proteins that have been reported as having a localisation to a particular compartment or that are associated with a particular protein domain, using the nuclear compartment and domain browsers. An introduction to each of the principal sub-nuclear compartments is also provided.

Why was the NPD created?
The NPD is an initiative undertaken by the Bickmore Group of the MRC-Human Genetics Unit (HGU) to organize, and make available data on novel nuclear proteins isolated using gene-trap and other technologies. It quickly became apparent that such a database would be a valuable resource to the entire community, and so data from nuclear proteins reported in the literature has also been added. Thus, this database provides a comprehensive overview of the diversity of many sub-nuclear compartments.

In the future, data from other groups interested in nuclear compartmentalization and function will be included. There are also plans to develop strategic partnerships with other database projects devoted to various aspects of functional genomics, including gene-expression and protein-protein interaction data.

OmniMedicalSearch
www.OmniMedicalSearch.com

OmniMedicalSearch.com is a metasearch engine. It does not operate the same way as search engines like Google or Yahoo. Instead of assembling a unique database of websites to present the search results, the search results from other search engines in various combinations are returned. When you submit a search term, the metasearch software sends that query, simultaneously, to other search engines, websites and databases. When it returns, you are presented with the top results of ALL the search engines and databases you selected. The metasearch engine is designed to search 32 different sources in 3 different categories so you can find everything you need from one convenient website. Each database queried is unbiased and non-commercial in nature and an established authority for delivering responsible medical information.

Oncomine
http://141.214.6.50/oncomine/main/index.jsp

Oncomine 2.0 (O2) is a bioinformatics infrastructure for cancer genomics research. O2 is conceptually similar to Oncomine 1.0 in that it provides simple tools to query and visualize cancer microarray data for a gene or cancer type of interest. O2 includes more cancer microarray data sets and nearly four times more differential expression analyses, including normal tissue analyses and clinical, pathological, and molecular subtype cancer analyses. O2 also includes a correlation module to identify genes that are co-expressed with a gene of interest in a selected cancer type. Furthermore, O2 adds improved gene filters to focus on specific subsets of genes including literature-referenced cancer genes, known therapeutic targets, and genes belonging to particular biological processes, cellular components, and protein families. O2 uses dynamic SVG graphics that can be easily imported and formatted in Adobe Illustrator or Photoshop for figure-making. O2 was developed by the Chinnaiyan Laboratory at the University of Michigan Medical School. Pilot funds were provided by the Dean's Office, the Department of Pathology, and the Comprehensive Cancer Center. As this is the beta version of O2, please forward any questions, comments, or problems to oncomine@umich.edu.

WWW (continued)

Recombineering
www.recombineering.ncifcrf.gov

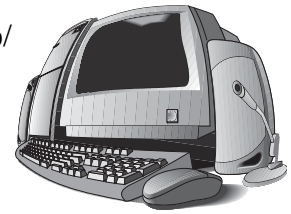
What's Recombineering?
Recombineering (recombination-mediated genetic engineering) is a powerful method for fast and efficient construction of vectors for subsequent manipulation of the mouse genome or for use in cell culture experiments. It is also an efficient way of manipulating the bacterial genome directly. Recombineering is a method based on homologous recombination in *E. coli* using recombination proteins provided from λ phage.

The bacterial strains contain a defective λ prophage inserted into the bacterial genome. The phage genes of interest, exo, bet, and gam, are transcribed from the λPL promoter. This promoter is repressed by the temperature-sensitive repressor *c*I857 at 32°C and derepressed (the repressor is inactive) at 42°C. When bacteria containing this prophage are kept at 32°C no recombination proteins are produced. However, after a brief (15 minutes) heat-shock at 42°C a sufficient amount of recombination proteins are produced. *exo* is a 3'-5' exonuclease that creates single-stranded overhangs on introduced linear DNA. *bet* protects these overhangs and assists in the subsequent recombination process. *gam* prevents degradation of linear DNA by inhibiting *E. coli Rec*BCD protein. Linear DNA (PCR product, oligo, etc.) with sufficient homology in the 5' and 3' ends to a target DNA molecule already present in the bacteria (plasmid, BAC, or the bacterial genome itself) can be introduced into heat-shocked and electrocompetent bacteria using electroporation. The introduced DNA will now be modified by *exo* and *bet* and undergo homologous recombination with the target molecule. The method is so efficient that co-electroporation of a supercoiled plasmid and a linear piece of DNA into heat-shocked, electrocompetent bacteria will work as well.

To Start Recombineering: You can find a number of tested and detailed protocols for doing recombineering on this website. You can also find information about plasmid maps, plasmid sequences, references to recombineering publications, and how to obtain the recombineering reagents.

List of Available Reagents: If you're interested, and are not with a for-profit company, please visit the reagents section for the application procedure and reagents will be shipped at no charge.

Worldmeters
http://www.worldometers.info/
Statistics you probably never knew existed.



STUDENT MEMBERSHIPS NOW FREE!!!

The ISICR International Council recommended and the Board of Directors approved a change in student membership dues. Students joining in 2005 will receive 1 complimentary 3 year membership!!! that means the $10 they were previously required to pay for membership can be used to buy doughnuts for their lab, a pizza or if they really feel generous, chocolate that can be sent to a certain ISICR officer (hint: last name is opposite of "old').

Featured Clinical Trial

THE CLEVELAND CLINIC FOUNDATION
Phase II Trial of Interferon-β In Patients with Metastatic Cutaneous Melanoma and Metastatic Ocular Melanoma

Principal Investigator	
Ernest C. Borden, M.D	Medical Oncologist
Co-Investigators	
R. Bukowski, M.D.	Medical Oncologist
S. Thakkar, M.D.	Medical Oncologist
J.Brell, M.D.	Medical Oncologist
J.Kim, M.D.	Surgical Oncologist
P. Elson, Sc.D.	Biostatistician
B. Williams, Ph.D	Cancer Biologist

FAST FACTS
Patients with histologically proven metastatic melanoma are eligible for this trial. The eligibility criteria are outlined on the pretreatment checklist, which must be completed prior to registration and must be submitted with the pre-study form and initial flow sheets at the time of registration.

Registration:

1. Provide patient's name, hospital number, eligibility checklist, and pre-study form.

2. Register patient at (216) 444-7921.

Questions regarding this protocol and patient eligibility should be directed to the following individuals:

Ernest C. Borden, M.D.
(216) 444-8183
The Cleveland Clinic Foundation, Desk R40
Taussig Cancer Center
9500 Euclid Avenue
Cleveland, OH 44195

Barb Denk
(216) 444-7926
The Cleveland Clinic Foundation, Desk R33
Taussig Cancer Center
9500 Euclid Avenue
Cleveland, OH 44195

Objectives
Assess objective clinical response rate to IFN-β in patients with metastatic melanoma at a maximally tolerated dose (MTD). Determine the frequency and degree of apoptosis induction in metastatic melanoma by the TUNEL assay. Assess safety and tolerance of IFN-β at MTD

Rationale for Present Trial
Induction of apoptosis and mouse antitumor effects suggest activity in melanoma. A phase II trial of the IFN-β at MTD is required to establish clinical response frequency and impact on progression free survival.

Experimental Design
Patient Population
Patients (n=30) with a diagnosis of metastatic melanoma with objectively measurable tumors will be eligible.

Treatment Plan
An open label design will be used. Patients will be treated with an initial schedule of IFN-β at 12 x 10^6 units/m^2 SQ daily for 2 weeks. If the dose is tolerated without the presence of a Grade III or Grade IV toxicity as measured by the NCI Common Toxicity Criteria (version 2.0), the dose will be escalated to 18 x 10^6 units/m^2 SQ daily. Patients will continue to receive IFN-β unless disease progression or a dose-limiting toxicity (DLT) supervenes.

Patients enrolled in this trial who have cutaneous or subcutaneous metastatic disease will be asked to undergo biopsy of the largest lesion (minimum > 1cm in diameter) at three time points in order to assess molecular response to treatment. Biopsies will be performed pretreatment, day 8 and day 29. Two standard 3-mm punch biopsies will be done on cutaneous lesions and incisional biopsy will be done for those patients with subcutaneous lesions. One biopsy specimen from each time point will be processed for routine H&E staining immunohistochemistry for

(featured clinical trial continued from page 25)

proteins related to apoptosis induction; the second biopsy will be placed in Trizol and snap frozen at -700 or-800 for further analysis of cellular RNA.

Patients with biopsy accessible lesions may decline the procedure prior to enrollment and at any time during the study without affecting their participation in the trial protocol.

Patient Eligibility
Inclusion Criteria. All patients must meet all of the following criteria:

Patients must have measurable disease as defined by the NCI's new Response Evaluation Criteria in Solid Tumors (RECIST) Guidelines.

Patients must have a life expectancy of 3 months. Performance status (ECOG) of < 2 (< 3 for patients with cutaneous metastases).

Patients must have recovered from the toxicity of any previously administered radiation therapy given > 28 days from the start of treatment and must not have had general anesthesia in the prior 28 days from the start of treatment.

Patients must have the following pretreatment laboratory findings:
ANC $\geq$ 1.2 x 10^9/L
Platelets $\geq$ 100 x 10^9/L
Hemoglobin $\geq$ 9.5 gm/100 ml
Creatinine $\leq$ or = 1.5 mg/dl
Bilirubin (total) $\leq$ 1.5 ml/dl

Patients must not have received any adjuvant IFN-α2 therapy $\leq$12 months prior or have received IFN-α2 therapy for metastatic disease $\leq$30 days prior to enrollment on trial or <6 months for patients with cutaneous metastases.

Patients must have received $\leq$1 prior systemic regimen (chemotherapeutic or biological) for metastatic disease. Patients with cutaneous metastases may have had $\leq$3 prior regimens.

All patients must be informed of the investigational nature of this study and must provide written informed consent in accordance with institutional and federal guidelines. A copy of the informed consent document signed by the patient must be given to the patient.

Exclusion Criteria. Any of the following makes a patient ineligible for this trial:

Patients with a history of serious cardiac arrhythmia or cardiac arrhythmia requiring treatment, congestive heart failure, angina pectoris, or other severe cardiovascular disease, i.e., New York Heart Association Class III or IV.

Patients with local and systemic infections requiring antibiotics within the past 28 days.
Pregnant or lactating women, and fertile women or men unless surgically sterile or using effective contraception.

Patients with CNS metastases or unknown seizure disorder. Stable brain metastases must be confirmed by a normal neurologic exam and CT or MRI scans.

Patients who have received radiation and/or resection to the brain will be eligible if their head MRI or CT is without evidence of disease for > 6 months from surgery and/or radiation (patients with cutaneous metastases and previously radiated and/or resected CNS metastases that are controlled and not requiring dexamethasone may be enrolled).
Pre-admission medication or other treatment exclusions:

Patients requiring ongoing replacement therapy with physiologic doses of corticosteroids will be eligible. Radiotherapy - must have been completed >28 days from the start of treatment. Surgery - no major surgery requiring general anesthesia within the previous 28 days from the start of treatment.

Patients who are known to be positive for HIV or HBsAg.

No patient may have had a malignancy other than a malignant cutaneous melanoma and ocular melanoma (vulvar, anal or other mucosal melanomas), with the following exceptions:
Basal or squamous cell carcinomas of the skin.
Carcinoma in-situ of the uterine cervix.
Any malignancy treated with curative intent and in complete remission for >3 years.

Patients with organ allografts.

Patients under the age of 18

Patients with a history of severe psychiatric disorders

(featured clinical trial continued from page 26)

Clinical Trials

More information on this list can be obtained at **http://clinicaltrials.gov** [CT], **http://www.centerwatch.com/search.asp** [CW], or **http://clinicalstudies.info.nih.gov** [CCNIH].

1. Recombinant Human **Interferon Beta-1a** in Acute Ischemic Stroke. *Contact*: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754. Toll Free: 1-800-411-1222; TTY: 1-800-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, Email: prpl@mail.cc.nih.gov. Study Number: 05-N-0036

2. A Pilot Open-Label Study of **Interleukin-1 Trap** in Adult Subjects with Autoinflammatory Disease. *Contact*: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754. Toll Free: 1-800-411-1222; TTY: 1-800-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, Email: prpl@mail.cc.nih.gov. Study Number: 05-AR-0014

3. Immunization of Patients with Renal Cancer Using HLA-A2 and HLA-A3-Binding Peptides from **Fibroblast Growth Factors 5 (FGF-5)**. *Contact*: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754. Toll Free: 1-800-411-1222; TTY: 1-800-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, Email: prpl@mail.cc.nih.gov. Study Number: 04-C-0259

4. A Study of Subcutaneous "**Cyt 99 007**" (**interleukin-7**) in Conjunction with Peptide Immunization in Patients with Metastatic Melanoma. *Contact*: Recruitment Center - Surgery Branch, CRC, Room 3-5581, National Institutes of Health, Bethesda, MD 20892-4754, Phone: (866) 820-4505; Fax: (301) 451-1927; E-mail: june_kryk@nih.gov. Study Number: 04-C-0235

5. **Interferon** and Octreotide to Treat Zollinger-Ellison Syndrome and Advanced Non-B Islet Cell Cancer. *Contact*: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 9000 Rockville Pike, Bethesda, Maryland, 20892; Patient Recruitment and Public Liaison Office 1-800-411-1222; TTY 1-866-411-1010; E-mail: prpl@mail.cc.nih.gov. Study ID Numbers: 880194; 88-DK-0194

6. **Consensus Interferon** (**CIFN**) and **IFN γ-1b** with or without Ribavirin for treatment of Chronic Hepatitis C (nonresponders). *Contact*: Medical Information, Tel: 1-888-486-6411; InterMune, Inc., Brisbane, California, 94005. Study ID Number: AGHC-002

7. **Interferon alfa**, Isotretinoin, and Paclitaxel in Treating Patients With Recurrent Small Cell Lung Cancer. Contacts in 30 US States, Australia, New South Wales, Peru, Puerto Rico and South Africa. Study chair: Joseph Aisner, MD, Cancer Institute of New Jersey. Study ID Numbers: CDR0000304430; ECOG-E6501

8. Merimepodib (MMPD) in Triple Combination (with **pegylated interferon** and ribavirin) for the Treatment of Chronic Hepatitis C. Contacts in 19 US States. More information at http://www.metrotrial.com. Study ID Numbers: VX03-497-205

9. SU011248 versus **Interferon-alfa** as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma. More information at SU011248 Clinical Trial Information Service, Tel: 877-416-6248. Contacts in 10 US States. Study ID Number: A6181034

10. A Study of **Albuferon** with Ribavirin in Interferon Treatment Experienced Subjects with Chronic Hepatitis C. Contact: Thomas Platek, Tel: 1-866-447-9749; for Arizona, Florida, Maryland, Minnesota, North Carolina, Texas and Virginia. Study ID Numbers: Clinical Protocol ALFR-HC-05

11. **hu14.18-Interleukin-2** Fusion Protein in Treating Young Patients With Recurrent or Refractory Neuroblastoma. Study chairs or principal investigators: Paul M. Sondel, MD, PhD, Study Chair, University of Wisconsin Comprehensive Cancer Center; Suzanne Shusterman, MD, Children's Hospital of Philadelphia. Study ID Numbers: CDR0000360723; COG-

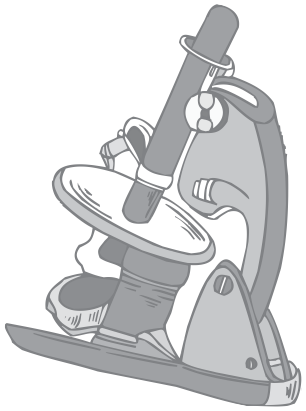
(featured clinical trial continued from page 27)

ANBL0322Shusterman, MD, Children's Hospital of Philadelphia. Study ID Numbers: CDR0000360723; COG-ANBL0322

12. Study of **Interleukin-21** for Metastatic Malignant Melanoma and Metastatic Kidney Cancer. *Contacts*: University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan, 48109, Research Information, Tel: 800-865-1125, Bruce Redman, DO, Principal Investigator; and University of Washington/Seattle Cancer Care Alliance, Seattle, Washington, 98109, Jennifer Revall, Tel: 206-288-2041, Linda Kirsch, Tel: 206-288-1195 and John Thompson, MD, Principal Investigator. Study ID Numbers: 494C10

13. Study of **TRM-1**(**TRAIL-R1 monoclonal antibody**) in Subjects with Relapsed or Refractory Non-Small Cell Lung Cancer (NSCLC). Contact: Thomas Platek, Tel: 1-866-447-9749, E-mail: Thomas_Platek@hgsi.com, for Colorado, Illinois, North Carolina, Tennessee and Texas. Study ID Numbers: TRM1-ST03

14. Study of **TRM-1** (**TRAIL-R1 monoclonal antibody**) in Subjects with Relapsed or Refractory Non-Hodgkin's Lymphoma (NHL). Contact: Thomas Platek, Tel: 1-866-447-9749, E-mail: Thomas_Platek@hgsi.com, for Minnesota, Nebraska, New York, Pennsylvania and Tennessee. Study ID Numbers: TRM1-HM01



American Association of Immunologists 2005 Annual Meeting International Society for Interferon and Cytokine Research Guest Symposium

Chairs: Xiaojing Ma & Pat Fitzgerald Bocarsly

Xiaojing Ma, Ph.D.
Weill Medical College of Cornell University
"Regulation of Cytokine Production During Phagocytosis of Apoptotic Cells".

Sergei Kotenko, Ph.D.
UMDNJ - New Jersey Medical School
"IFN-lambdas: new kids on the block of antiviral protection, their friends and relatives"

Brian R. G. Williams, Ph.D.
Lerner Research Instititute,
Cleveland Clinic Foundation
"Activation of innate immunity signaling by double stranded RNA and CpG oligonucleotides; virus associated molecular patterns"

Patricia Fitzgerald-Bocarsly, Ph.D.
UMDNJ- New Jersey Medical School
"Plasmacytoid dendritic cells: key players in antiviral immunity"

Anyone interested in organizing the Guest Symposium for the 2006 AAI meeting should contact ISICR president, Howard Young. Due to limited funds, ISICR cannot provide travel/housing support but will reimburse registration upon request.

Reviews of Interest

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Science is the belief
in the ignorance of the experts.
~ Richard Feynman, *American Physicist*

If you're not part of the solution,
you're part of the precipitate.
~ Henry J. Tillman

Did You know...????

If a statue in the park of a person on a horse has both front legs in the air, the person died in battle; if the horse has one front leg in the air, the person died as a result of wounds received in battle; if the horse has all four legs on the ground, the person died of natural causes.

The reason firehouses have circular stairways is from the days of yore when the engines were pulled by horses. The horses were stabled on the ground floor and figured out how to walk up straight staircases.

Each king in a deck of playing cards represents a great king from history Spades - King David; Clubs - Alexander the Great; Hearts - Charlemagne; and Diamonds - Julius Caesar.

In Shakespeare's time, mattresses were secured on bed frames by ropes. When you pulled on the ropes the mattress tightened, making the bed firmer to sleep on. Hence the phrase "goodnight, sleep tight".

It was the accepted practice in Babylon 4,000 years ago that for a month after the wedding, the bride's father would supply his son-in-law with all the mead he could drink. Mead is a honey beer and because their calendar was lunar based, this period was called the honey month we know today as the honeymoon.

In English pubs, ale is ordered by pints and quarts. So in old England, when customers got unruly, the bartender would yell at them mind their own pints and quarts and settle down. It's where we get the phrase "mind your P's and Q's"

Many years ago in England, pub frequenters had a whistle baked into the rim or handle of their ceramic cups. When they needed a refill, they used the whistle to get some service. "Wet your whistle" is the phrase inspired by this practice.

In Scotland, a new game was invented. It was entitled Gentlemen Only Ladies Forbidden.... and thus the word GOLF entered into the English language.

A duck's quack doesn't echo, and no one knows why.

Clans of long ago that wanted to get rid of their unwanted people without killing them used to burn their houses down - hence the expression "to get fired."

The term "the whole 9 yards" came from WWII fighter pilots in the Pacific. When arming their airplanes on the ground, the .50 caliber machine gun ammo belts measured exactly 27 feet, before being loaded into the fuselage. If the pilots fired all their ammo at a target, it got "the whole 9 yards."

Hershey's Kisses are called that because the machine that makes them looks like it's kissing the conveyor belt.

The phrase "rule of thumb" is derived from an old English law which stated that you couldn't beat your wife with anything wider than your thumb.

The name Jeep came from the abbreviation used in the army for the "General Purpose" vehicle, G.P.

When Heinz ketchup leaves the bottle, it travels at a rate of 25 miles per year.

It's possible to lead a cow upstairs...but not downstairs.

Humans are the only primates that don't have pigment in the palms of their hands.

In 10 minutes, a hurricane releases more energy than all the world's nuclear weapons combined.

Cytokines 2004 Meeting Summary

Matt Fenton

The 5th joint meeting of the International Society for Interferon and Cytokine Research (ISICR) and the International Cytokine Society (ICS), was held at the Caribe Hilton Hotel in San Juan, Puerto Rico, on October 21-25, 2004. The meeting was entitled "*Cytokines in Cancer and Immunity*," and it was focused on recent discoveries relating to the role of cytokines in immunity, tumor immunology, and inflammation. Organization of the meeting was provided by Drs. Matthew Fenton, Nancy Ruddle, John Hiscott, and Nancy Reich who comprised the Executive Organizing Committee. The Scientific Organizing Committee included the members of the Executive Organizing Committee plus Drs. Eleanor Fish, Amanda Proudfoot, David Wallach, Giorgio Trinchieri, and Tadamitsu Kishimoto. The invited speakers included Drs. Tak Mak and Michael Karin as the keynote speakers, as well as a long list of outstanding plenary and symposium speakers. The program consisted of 22 invited plenary presentations, 21 symposium presentations, 108 oral workshop presentations (selected from submitted abstracts), plus three poster sessions. A complete collection of submitted abstracts is still available on the conference web site (**www.cytokines2004.org**).

During the past several years, a plethora of cytokines involved in oncogenesis, inflammation, innate immunity, and tumor immunity has been identified and the relevant regulatory mechanisms studied. The research areas focusing on these cytokines extend over several fields, including immunology, oncology, hematology, virology, and molecular biology. Many meetings focus on cytokines, or on cancer, as central themes, but few bring information from diverse faculties to tie the information together. This year's 2004 joint ISICR-ISC meeting concentrated on the complex cytokine-receptor interactions and regulatory mechanisms involved in cancer and immunity. In addition to these themes, the meeting also covered topics that are perennially presented at each of the societies annual meetings (e.g. gene regulation, receptor biology, signal transduction, host defense, new cytokines, and inflammation). We were particularly proud to provide a forum for the presentation of the 2004 ICS Lifetime Membership Award to Dr. Joost Oppenheim, who is a co-founder of the ICS an a pioneer investigator in the field of cytokine biology. The ISICR awarded their prestigious Milstein Awards to Drs. Keiko Ozato and Ernie Borden.

In his keynote address at the opening evening, Tak Mak reported data generated using a variety of elegant knockout mouse models to explain how dysregulation of programmed cell death can lead to degenerative diseases, autoimmune diseases, and cancer. Both the first plenary talk by Frances Balkwill, and the second keynote address by Michael Karin, discussed the causative roles of cytokines in carcinogenesis. Dr. Balkwill presented evidence that the inflammatory cytokine tumor necrosis factor (TNF-α), which was originally identified by anti-tumor activities that it mediates (wherefore its name), actually acts in epithelial malignancies as a major endogenous tumor-promoting agent. She reported that TNF-α serves as an endogenous tumor promoter in epithelial malignancies. Mice lacking the TNF-α or TNF receptor genes were resistant to tumors. IL-1β appears to have a similar tumorigenic activity. Michael Karin, in discussing one of the principal signaling mechanisms by which inflammatory cytokines act, activation of the transcription factors of the NF-κB family, showed that these transcription factors contribute in a number of ways to carcinogenesis. The two speakers discussed the mechanisms for these tumor-promoting functions as well the potential therapeutic uses of TNF-α and NF-κB-blockers in cancer.

Robert Silverman (Cleveland) identified RNA activators of the interferon-induced enzyme, 2', 5'-oligoadenylate synthetase, in prostate cancer cells but not in normal cells, that may have a role in tumor suppression. The activators include two cellular mRNA species. Raymond Kaempfer (Jerusalem) showed that interferon-γ mRNA is a potent activator of the interferon-induced enzyme, PKR, causing interferon-γ protein synthesis to be inhibited, and thereby autoregulates the production of this inflammatory cytokine. The mRNA structure that activates PKR has been resolved; it is composed of several precisely aligned short helices stabilized by an RNA pseudo

knot, and extends from the 5' end well into the open reading frame. Christophe Caux (Dardilly) reported that type I and type II IFNs are distinctly regulated by engagement of toll-like receptors TLR3 and TLR8. On TLR stimulation, interferon-γ is induced in innate immune lymphocytes (NK and γδT cells) but not in regular T cells. Induction through TLR3 is dependent on interferon-β. Takashi Fujita (Tokyo) cloned a novel cytoplasmic receptor for double-stranded RNA. It is an RNA helicase that has a role in innate immunity. Double-stranded RNA unmasks a domain in the helicase that allows the protein to active IRF-3, required for interferon induction. Richard Flavell (New Haven) presented a TGF-β-centric view of the immune system. The inhibitory signal from TGF-β is caused both by its direct immunosuppressive action and by the induction of expansion of regulatory T cells.

Richard Jove presented in his plenary talk evidence that the STATs, another group of transcription factors that mediate many of the functions of cytokines, also contribute to the growth and survival of both solid tumors and blood malignancies as well as to the induction of tumor angiogenesis. Additional lessons that can be gained from the EGF receptor family as to ways by which receptor signaling mechanisms can contribute to cancer and to approaches for cancer therapy based on this knowledge, were presented by Yosef Yarden (Rehovot).

Overall, papers focusing on the increasing linkage between inflammation and cancer highlighted the meeting. Presentations demonstrated how numerous pro-inflammatory signals were parts of the tumor environment and these signals promoted tumor growth and inhibited the innate and adaptive immune responses by the host. Other papers demonstrated the role of STATs, particularly STAT3, in promoting tumorigenesis. The clinical use of interferons, including genetically modified "super interferons" against cancer and viral infections was also reported on at the meeting. In addition the use of anti-cytokine therapies, including anti-IL-6 receptor, soluble IL-21 receptor, anti-IFN-γ and IL-1 receptor antagonist were shown to have dramatic effects in animal models and upon patients, thus indicating that these therapies will become part of mainstream medicine in the near future.

In addition to the practical applications of cytokines and anti-cytokine therapies, a great deal of molecular biology was presented on cytokine and cytokine-receptor structure-function, cytokine signaling, downstream activation of specific signaling pathways and activation of nuclear proteins. These studies provided attendees with a clearer picture of how cytokines, chemokines and interferons exert their affects at the biochemical and molecular levels.

ISICR Election Results

Secretary 2006-2008
Sidney Pestka

Treasurer 2006-2008
Robert Friedman

Board of Directors 2005-2006
John Hiscott (Canada)
Ara Hovanessian (France)
Menachem Rubinstein (Israel)

ISICR Committee Reports 2005

Board of Directors Meeting
Sunday, October 24, 2004
Members in Attendance: Howard Young, Bryan Williams, Otto Haller, Kathy Zoon, Ernie Borden, Eleanor Fish, Keiko Ozato, Robert Friedman, Sam Baron, Nando Dianzani, Sidney Pestka

The Board of Directors meeting was opened at 12:30 PM by Howard Young. The attendees are listed above. The discussion first summarized what was presented at the International Council Meeting by Howard Young. The Board endorsed giving students who have not obtained their advanced degree a free 3 year membership. In addition, the Board approved the concept of a patient booklet on Interferons and authorized Howard Young to procede with the development of such a publication.

The next topic of discussion was the status of the Annual meetings. The meeting in Australia showed a loss of $15,000 (US) and the Board of Directors approved paying $15,000 to cover the shortage. Considering all the funds supplied by the Society as seed money for this meeting, this sum represented a large loss for the ISICR. The major reasons for the shortfall were poor attendance by ISICR members and a dramatic change in the currency exchange from the time the meeting was planned to the time of the actual meeting. The meeting next year, 2005, in Shanghai organized by Xin Yuan Liu was discussed. Xin Yuan Liu was not able to get a visa and so the brochures for the 2005 meeting were not available to the attendees at the Puerto Rico Meetings. Furthermore Dr. Liu could not be at the Membership Committee Meeting because of his inability to obtain a visa. Nevertheless, the meeting planning appears to be going well and Dr. Liu has had success in fundraising. This meeting will be held immediately before the International Cytokine Society meeting, that will be held in Seoul, Korea.

Next, the 2006 meeting in Austria was discussed by Howard Young. There has not been good communication with the organizing committee for the 2006 meeting and during the current meeting, one of the organizers, Josef Schwarzmeier proposed dates at the end of August. This was initially not looked upon favorably by the ISICR Board but it was explained that if the meeting was held prior to Sept. 1: 1) the Austrian government would provided 30,000-40,000 euros for the banquet, 2) the city of Vienna would provided 15-17,000 euros for the meeting and 3) student housing would be available for 60-70 euros/night. Given the significant financial advantages in having the meeting at the proposed time (the same dates were also proposed in 2002), the Board voted to accept those dates. Eleanor Fish mentioned that there has been some difficult communication between various organizers that has made it difficult for the Meetings Committee members and Chair to communicate with the organizers. This has been a problem for many of the meetings.

Sidney Pestka and Sam Baron had indicated that centralization of the organization of the meetings will be necessary. There was much discussion about this by all members present and a general feeling that over the long term there should be a centralized organization to help arrange all the meetings of the ISICR. It was suggested by Howard Young and some others that a Memorandum of Understanding between the Society and the meeting organizers should be a written document that is signed by the organizers so that they recognize that the responsibility for the full funding of the meetings is the responsibility of the organizers. To centralize the meeting organization we would need to have a coordinator or an executive director responsible to the officers and the Board of Directors. There was also a general consensus that we need to have earlier planning and development of all the meetings. Several of the meetings have not been planned far enough in advance. In addition it was also a general consensus that there be a broad scientific overview of the meetings so that not only the Meetings Committee but the Publications Committee should have an understanding of what will be presented and evaluate the scheduled sessions to be presented prior to finalization. The Board approved naming the Meetings Committtee chair as an ad hoc member of the Board so that they will be fully informed of all decisions regarding meeting planning and organization.

There was discussion of the venue for the 2007 meeting. Washington, D.C. is under consideration, as well as New York City. David Levy has indicated that he would consider taking the responsibility to organize a meeting in NYC. In Washington it was felt that a number of people would be willing to take on the responsibility. Furthermore, the NCI and NIAID might be interested in supporting this meeting. Another potential venue is London since it will be the 50th anniversary of the discovery of interferon. Frances Balkwill indicated that she might help organize such a meeting if London was chosen. In addition, prior to the Board meeting, George Stark indicated that he would contact George Foster about the 2007 meeting as well. The Welcome Trust was mentioned as one organization that might be approached for funding. The International Cytokine Society has indicated that they would like to have joint meetings with us every year rather than every other year. No decision was made by the Board of Directors as it was felt that further discussion was needed. The registration at this year's meeting in Puerto Rico was 508.

The Board endorsed the idea that newsletters will be sent in the future as Acrobat PDF files, unless a member requests a hard copy. However the newsletter published prior to the meeting will be continued to be supplied to meeting organizers for inclusion in the meeting welcome material.

The Board of Directors approved to continue the relationship with George Galasso. George interacts with FASEB and provides a report of the FASEB responsibilities/actions four times a year.

Next, the issue of officer meeting expenses was discussed. In most annual meetings the hotel costs for the officers were covered by the meeting organizers. This was not done at this meeting in Puerto Rico. The Board voted to cover only the hotel room of the officers if requested by the officers.

The election of officers was next discussed. Howard indicated that Robert Friedman and Dhan Kalvakolanu both volunteered to serve as treasurer, if elected. The Board indicated that each should provide a brief statement to be included with the ballot. Sidney Pestka was asked if he would reconsider running for secretary. He indicated that part of the problem was that the ISICR was no longer providing sufficient funds to cover the administrative assistant and that much of the Secretary's efforts are devoted to fundraising for the society. The Board then voted to increase the support to the secretary from $10,000 to $18,000. Next, Sam Baron indicated that his office had been providing service gratis to the ISICR and he estimated that the costs were $5000/year. The Board then voted to provide the Treasurer's office with $5000/year to cover expenses, beginning in 2005. It is anticipated that these sums will eventually be provided to an Executive Director for the services being carried out in the Secretary and Treasurer's offices.

International Council Meeting
Saturday, October 23, 2004

Members in Attendance: Ihdalis Flores, Erik Lundgren, BenZion Levy, Christine Czarniecki, Patrick Matthys, Kathy Zoon, Antonina Dolei, Michael Tovey, David Levy, Bob Silverman, George Stark, Anthony Meager, Lawrence Pfeffer, Samuel Baron, Steve Ralph, Nigel McMillan, Sidney Pestka, Howard Young

The meeting was opened at 7:45 AM by President Howard Young. The attendee list appears above. Howard Young discussed the changes in the By-Laws and Constitution that were approved by the membership. The International Council members can serve more than one term. In addition, all the awardees of the Society now must be members as officially noted in the By-Laws. Howard Young noted that he prepared award plaques for the Milstein Awards that could be used every year since the general template was already prepared by Mac Mannes Inc. There was discussion about the newsletters that are published three times a year. The general consensus was that the issues could be sent electronically to save printing and mailing costs. There was consensus that Howard Young, with his associate editors, has been doing an excellent job in preparing these newsletters. A new feature in future issues will be a mini-bio of three new full members of the society.

Howard Young suggested developing a pamphlet for patients about interferons. Hoffmann-LaRoche publishes their own pamphlet for patients but this one would be a general pamphlet for interferons that all patients could utilize. Howard will ask the NCI to help print and prepare the document and it will have the input from many physicians and nurses. The International Council endorsed this idea.

The issue of getting new members and retaining existing members was brought up for discussion. Howard Young emphasized that the International Council has a responsibility to help recruit new members and that the small pamphlet about the ISICR (distributed to all International Council members present) should be used by International Council members when they attend meetings. In addition, Howard recommended sending prospective members an e-copy of the latest newsletter. Antonina Dolei (Italy) recommended that students be given a free 3 year membership, rather than charging them $10 US/year and the International Council endorsed this proposal.

There was a brief Treasurer's and Secretary's report by Sam Baron and Sidney Pestka. The detailed reports can be seen in the Treasurer's and the Secretary's report in the January newsletter. Howard Young noted that there were four levels, $500, $800, $1,000 and $1,200 for the travel awards this year. This year Keiko Ozato and Ernie Borden were honored as recipients of the Milstein Awards in addition to four Milstein Young Investigator awardees and the Christina Fleishman awardee.

General Membership Meeting
Sunday, October 24, 2004

Members in Attendance: Howard Young , Nando Dianzani, Sam Baron, Keiko Ozato, Otto Haller, Dhan Kalvakolanu, Phil Marcus, Margaret Marcus, Ganes Sen, Ernie Borden, Tadamitsu Kishimoto, Peter Staeheli, Joseph Sekelilk, Antonia Dolei, Nancy Reich, Vivian Barak, Yuichiro Satoh, Takashi Fujita, Jacques Theze, Dan Carr

The General Membership Meeting was opened up by Howard Young at 8:15 AM. The attendees are listed above. President Young outlined the information provided to the International Council Meeting to the general membership (see report of International Council Meeting).

ISICR Archives Committee
October 21, 2004

The meeting was attended by Sam Baron, Nando Dianzani, Phil Marcus, Sid Grossberg, Jan Vilcek, and Robert Friedman. The discussion was devoted to how we can persuade members to contribute pictures from meetings and other events from the 1960s and 70s for the Archive. This is the one element in which the Wellcome Trust feels the Archive is most deficient, as reported by Norman Finter. The members of the committee on their own will try to obtain these individually, and I as co-chair will go through the ISICR membership list in order to email directly to those who may posses such material in order to ask for their contribution of it to the Archive.

Respectfully submitted,
Robert M. Friedman, MD
Co-chair, Archives Committee

ISICR Awards Committee
October 21,2004

Attending: T.Fujita, D.Novick , P.Pitha , R.Silverman H.Young, and K.Zoon

1. The meeting addressed the issue of nomination of Milstein Awardees and Honorary Members. It was agreed that the nomination and selection process has to be done well in advance so the nominees could be selected by the committee by May 1st. Therefore the deadline for these two nominations will be March 1, 2005. This deadline will be also advertised in the ISICR Newsletter.

2. The selection of the travel awardees, Milstein Young Investigators and Christine Fleischman award were also discussed. It was suggested and agreed that the deadline for these nominations should be June 1, 2005 and this deadline will be not extended even if the abstract deadline is extended beyond June 1.

3. The committee felt that the number of strong applicants for the Milstein Young Investigator Award could be increased. One possibility to increase applicants would be to urge the International Council to nominate suitable members for the awards.

4. It was also agreed that the abstract and CV of the applicants should be sent electronically to the chair of the awards committee. Travel award applicants would no longer be required to submit a letter of recommendation or a CV. Rather a brief letter describing their current position in addition to their abstract would be sufficient.

5. Due to the difficulty of some committee members in opening the applications electronically, it was suggested that the meeting organizers have an internal site where the travel award abstracts could be posted. Such a site would be accessible by only the committee members via a password. Howard Young indicated he would communicate this suggestion to Dr. Liu, organizer of the 2005 meeting.

6. The committee decided that no more than 2 awards will be given per Principal Investigator's Laboratory, depending upon funding availability and # of applications. In addition, while applicants may in fact apply for multiple awards (e.g. Milstein Young Investigator, Christina Fleischmann and Travel Award), only 1 award will be given to any single individual.

Respectfully submitted,
Paula Pitha-Rowe
Chair, ISICR Awards Committee

ISICR Finance Committee
October 21, 2004

The Finance Committee met on October 21, 2004 and the following individuals participated: Samuel Baron (Treasurer and Chair), Howard Young (President), Sidney Pestka (Secretary), Otto Haller (President-elect), Bryan Williams (Board of Directors), Eleanor Fish (Board of Directors), and Ferdinando Dianzani (Past President and Committee Member).The treasurer presented the current budget, the projected budgets, the certified public accountant filing for the IRS, and projections for the future. It was noted that even though the last meeting balance was negative, the Society remains in good financial condition based on reasonable but diminishing sponsorships and reserves from previous years. This year's travel awards were continued at the level of about $45,000.

It was agreed that future priorities would continue to be sponsorship contributions, increasing other revenue, and selection of meeting locations that are likely to be well attended and have a positive financial return for the Society.

Discussed briefly was the option of centralizing part or all of the activities of the Society under single and, perhaps, professional management. These functions might include the meetings organization, treasurer's duties, secretary's duties, FASEB functions, and fundraising. Full discussion of centralization was deferred to the Board of Directors meeting (see Board minutes).

A full budget report will appear in the Spring newsletter.

Respectfully submitted,
Sam Baron
Chair ISICR Finance Committee

ISICR Meetings Committee
October 21, 2004

The meeting was called to order on Sunday, October 21, 2004. Present for all or part of the meeting were members and Ad hoc members (Nancy Reich, Yuichiro Satoh, Michael Tovey, Paul Hertzog); representatives from the ISICR Board of Directors (Howard Young and Kathy Zoon) and guest David Levy. The meeting was chaired by Christine Czarniecki.

Opening remarks
Christine Czarniecki reviewed the current member list of the ISICR Meetings Committee
Members:
Yoichiro Iwakura (Jan 2002-Jan 2005)
Allan Lau (Jan 2004-Jan 2007)
Leonidas Platanias (Jan 2004-Jan 2007)
Nancy Reich (Jan 2004-2007)
Yuichiro Satoh (Jan 2004-Jan 2007)
Michael Tovey (Jan 2004-Jan 2007)
Giorgio Trinchieri (Jan 2002-Jan 2005)

Ad hoc Members:
Paul Hertzog (2000-2004) - Cairns Meeting 2003
Xin-yuan Liu (2002-2006) - Shanghai Meeting 2005
Josef Schwarzmeier (2003-2007) - Vienna Meeting 2006

Terms
Terms of full members run for 3 years, starting and ending in January. Organizers of the annual ISICR Meeting (who are also ISICR members) serve as Ad hoc members from the time of the ISICR meeting at which their meeting proposal is approved until one year after the annual meeting of which they are an organizer.

2003 - Cairns, Australia
Paul Hertzog provided a detailed final report for the 2003 ISICR meeting in Cairns, Australia. The Committee thanked Paul and his colleagues for their efforts for the meeting organization and final report.

The meeting was attended by 289 delegates with approximately equal distribution from ISICR Members (84); Non-members (67) and students (68). The general feedback received by the organizers was positive about the general organization of the meeting, the topics covered in the sessions and the quality and breadth of invited speakers.

Several new initiatives were undertaken at this meeting:
1. Student breakfast with the invited speakers
2. Afternoon break on day 2 for Social activity (and networking)
3. Evening specific poster viewing session with refreshments
These were considered great successes and contributed to opportunities for scientific interaction and networking for all participants.
Unfortunately this meeting ran at a loss. The financial summary indicated a "bottom line" deficit of AUD $21,048 (exchange rate at time of this committee meeting: approx USD $14,032) after return of the ISICR seeding funds (AUD $11,000).

Factors contributing to the deficit:
- Exchange rate fluctuation (>20% since initial estimates meant >AUD $22,000 deficit in income)
- Sponsorship of AUD$114,000 was lower than expected
- Poor attendance by ISICR members. Only 84 ISICR full members and 45 student members attended. - This lack of patronage included office bearers of the Society, resulting in many Committee meetings either being poorly attended or cancelled.

The Organizers have requested that the ISICR Board cover the deficit.

2004 - San Juan, Puerto Rico

Nancy Reich provided a detailed report on the current meeting in San Juan. The organizers reported that 427 people had preregistered and these included: Members (167); Non-members (90); Industry (75) and students (95). Total conference income was estimated at $273,000 with the following breakdown: Income from registration was approximately $150,000; thirteen exhibitors registered and paid for exhibition space which raised $20,000; external fundraising raised $101,000 ($89,000 received at time of this committee meeting) including a small ($3000) R13 NIH Conference grant submitted by Matt Fenton. No seed funds were provided by ISICR. Fundraising was difficult. Contributions from Asian companies were almost nonexistent and the contributions from companies that had contributed generously in previous years (e.g. Centocor, Biogen) were small for this conference.

Meeting expenses are estimated at $253,000 with the largest expenses for food and beverages; audiovisual support ($30,000); and speaker travel ($46,000). Thus the organizers expect to end up with a profit that will be divided equally between the ISICR and the ICS.

The committee discussed problems that had come to our attention prior to the meeting. One of significance dealt with abstracts being "lost" and thus not able to be reviewed for potential speaker slots. The Meetings Committee strongly recommends that for future meetings, a receipt system be established that will allow all those who submit an abstract to receive a dated receipt. If the submitter does not receive a receipt by a certain time the individual can contact the Organizers for corrective action.

With regards to fundraising, the Meetings Committee strongly recommends that future organizers consider applying to NIH as Matt Fenton did. Christine Czarniecki agreed to contact Matt and request a copy of the NIH grant application that was submitted.

2005 - Shanghai, China

Xin-yuan Liu, the Chair of the 2005 Meeting was not able to attend due to visa difficulties. However, he did provide the Meetings Committee Chair with the following update prior to the meeting.

The meeting will take place October 20-24, 2005. The venue will be in the Shanghai International Everbright Convention Center (IECC), which is the second largest convention center in Shanghai. There are 44 members on the International Advisory Committee and 35 members on the National Advisory Committee. More than 80 scientists have been invited to participate as speakers including: Nobel Prize laureate Dr. Ferid Muard; US National Medal of Technology laureate, Dr. Sidney Pestka; present, future and past ISICR presidents (Howard Young, Otto Haller, Keiko Ozato and Kathryn Zoon) and also the US youngest academician of the National Academy of Science, Dr. Xiao Dong Wang. Financial support is good. A website has been set up for this meeting. It can be accessed at www.sibcb.ac.cn/ISICR2005.html.

The Meetings Committee recommends that the organizers provide financial updates to ISICR President Howard Young and the ISICR Meetings Committee throughout the year.

2006 - Vienna, Austria

Josef Schwarzmeier, the Chair of the Organizing Committee of the 2006 Joint ISICR/ICS/ECS Meeting was not able to attend our committee meeting. However, he did provide an update subsequently. This meeting which will be the 6th joint meeting of the two societies will take place August 27 - 31, 2006 in Vienna, Austria. The meeting will take place in the Hilton-Stadpark, Austria's largest Congress Hotel. The completely renovated Hilton, Vienna is centrally located adjacent to the popular "Stadpark" and St. Stephen's Cathedral. There is direct access to the airport by the City-Airport train (CAT). The reasons for the earlier than normal dates were numerous: significant financial contributions from the city and state government for a meeting held before Sept. 1 and availability of student housing before Sept. 1 for 80 euros or less.

The Congress Secretariat is Austropa Interconvention. The preliminary Program and Call for Abstracts will be available in summer 2005. Deadline for abstract submission is March 31, 2006. A website has been set up and can be accessed at www.cytokineresearch.com/2006.

The Local Organizing Committee and International Advisory Committee have been established and the organizers are planning a scientific program that will bring together leading investigators in molecular biology of cytokines, cancer research and immunology. The themes to be covered include new cytokines, cytokine functions and structures, gene regulation, signal transduction, cell cycle control, role of cytokines in immunology, inflammation, angiogenesis and host defense. A significant part of the conference will be devoted to therapeutic effects of cytokines in the management of malignant and non-malignant disorders.

In addition, since this conference will be held during Vienna's 250th anniversary of Mozart, many musical events will take place at this time and an impressive social and sightseeing program will be planned.

New Proposals: 2007

The ISICR Meetings Committee currently has no proposals to consider for meetings beyond 2006.

David Levy attended the meeting to propose New York City as a possible location for 2007. There was general enthusiasm for this location especially considering that: (i) 2007 will be the 50th Anniversary of the discovery of interferon and New York City has a special significance to the ISICR; and (ii) there is a strong scientific presence of cytokine research in that city. In addition, it is a desirable location to travel to from other countries in terms of ease of getting there, cost and time-wise and offers hotels in a wide range of prices. The Meetings Committee encouraged David to prepare and submit a formal proposal as per the ISICR Meeting Guidelines.

Howard Young proposed Washington DC as a location for 2007 and said that he had approached NCI with a request for funding. Kathy Zoon also suggested approaching NIAID for additional funds. The advantages of this location were similar to New York City in terms of strong scientific presence of cytokine research, desirable city to travel to from outside US. In discussions it was clear that the ability to raise funds would be an important aspect for this location. (post-meeting note: Howard Young learned that NCI would not provide funding for this meeting).

A third possibility for 2007 was London or somewhere in the UK - also considering the 50th anniversary of interferon. The discussion centered upon costs and the problem with the current exchange rate. (post-meeting note: through the efforts of George Stark, Howard Young, Norman Finter and others, Graham Foster has agreed to take the lead and prepare a formal proposal for 2007 in the UK).

Proposals for beyond 2007

The committee discussed possible locations for future meetings. If 2007 is in New York then 2008 should be in Europe and possibilities in order of interest were: (i) Athens (to take advantage of the infrastructure established for the recent Olympics) with Leon Platanias to look into this possibility; (ii) Nice (due to the success of our previous meeting there) with Michael Tovey to look into this possibility; and (iii) Lisbon or Madrid if we can identify a cytokine investigator to take the lead.

Other Business

The committee discussed the pros and cons of having one cytokine society instead of the ISICR and ICS. The opinions are still split and Kathy Zoon informed us that the financial organization of each of the societies is very different and that any merger of the two would be difficult/complicated in that regard.

However it should be noted that the incoming ICS President, Matt Fenton, has indicated that the ICS has a strong desire to hold joint meetings with the ISICR every year. He felt it did not make sense for the two societies to compete with each other with respect to finding and attendees since the interests of both societies significantly overlapped, as was evident from the current meeting. Howard Young will continue discussions with ICS and the ISICR Board and keep this committee updated.

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

Respectfully submitted,
Christine Czarniecki
Chair, ISICR Meetings Committee

ISICR Membership Committee
October 21, 2004

Members present: Eleanor Fish (acting Chair), Ana Gamero, Larry Pfeffer, Howard Young (attended part of the meeting).

The committee noted that membership has remained relatively flat over the years (see below), despite a number of different strategies to increase membership. The committee did find that the new ISICR pamphlet was useful and a value in promoting the society. In addition, Howard Young informed the committee that PBL Biomedical had included the ISICR newsletter with a number of their product shipments at no cost (other than printing the newsletter and shipping to the company) to the ISICR. To increase membership the following recommendations were made:

1. Assign members of the Membership Committee to conduct PubMed searches (every 3 months?) for recent publications in which 'IFN' is mentioned. Ascertain whether authors are ISICR members and if not, send out information and invitation to join. One particular focus should be on authors who publish in the *J. of Interferon and Cytokine Research*.

2. Contact FASEB office and request that announcements for the ISICR go out with mailings to other societies.

3. Distribute ISICR flyer, Newsletters and Meeting Announcements at other scientific meetings, e.g. ASH, AACR, Hepatology mtgs. Specifically, identify ISICR members that would attend these larger meetings and provide them with the relevant literature for posting or placement on appropriate tables. In particular members should be encouraged to provide the ISICR flyer to appropriate companies that might be willing to put them in their booths when they participate in commercial exhibitions.

4. Consider some type on "incentive" for new members. Post meeting note: The IC recommended and the Board approved a free 3 year membership for students beginning in 2005.

ISICR Membership Statistics as of September 15, 2003

A. Current Members:

1. Paid Members	- 624
Breakdown of membership:	
a) Members who renewed	- 532
b) New Members	- 92
c) Members who renewed with bad addresses	- 0
Status:	
a) Regular members	- 487
b) Student Members	- 114
c) Corporate Members	- 12
d) Emeritus Members	- 11
2. Honary Members	- 22
Total Paid and Honary members	**646**

B. For Follow-up:

1. Active Members paid in 2002 who have not renewed	- 142
2. Active members paid in 2001 who have not renewed	- 100

C. Marked for Deletion:

1. members whose last dues payments were in 2000	- 77
Total members Listed in the dbase	**965**

D. Members Paid in Advance:

For 2004	- 115
For 2005	- 41

Respectfully submitted,
Eleanor Fish
Acting Chair, ISICR Membership committee

ISICR Nomenclature committee
October 21, 2004

The meeting was called to order at 2:00 pm on Thursday, October 21, 2004 at the joint meeting of the ISICR and the ICS, San Juan, Puerto Rico.

Members present. A. Dolei, R. Pines, S. Kotenko, E. Lundgren, I. Marie. The meeting was adjourned until 4.30 pm, October 22, when G. Schreiber joined the committee.AD was chosen to write the minutes.

1. The minutes from the previous meeting in Cairns (Oct. 26, 2003) have been distributed and were not further discussed.

2. EL introduced the proposal from IUPHAR (International Union of Pharmacology) to make a systematic classification of receptors. More than 30 working groups have been established and a database exists that includes chemokine receptors, but so far not cytokines. IUPHAR welcomes input. A decision was made that EL should contact IUPHAR for discussion, that available information should be distributed to the committee members and that the issue will be further discussed during the meeting next year.

3. Definition of interferons
After discussion of previous decisions and the criteria used, the committee concluded that each case has to be decided on its own merits. It is not possible to set up a generalized profile of criteria. However, some of the following criteria have to be fulfilled to qualify as an interferon:

1) A secreted polypeptide which acts through cell surface receptors and activates a signaling cascade, which directly promotes the induction of genes which confer an antiviral state on cells.
2) Interferon types are divided according to the sequence homology between them and utilization of common receptors.

Respectfully submitted,
Antonina Dolei
Erik Lundgren
Chair, ISICR Nomenclature Committee

ISICR Publications Committee
October 21, 2004

The Meeting of the Publications Committee was called to order at 3:30 p.m. on October 21, 2004. Committee members present included: Jerry Tilles, Deborah Vestal, Manfred Beilharz, Ganes Sen (ex officio) and Tom Hamilton (guest). Bob Fleishmann was regrettably not in attendance because of a conflict and requested Jerry Tilles to Chair the meeting. The new business centered on a decline in the number of pages in the Journal.

Ganes Sen distributed a hard copy report entitled, "JICR Status Report for 2004". The report began with a table showing the Journal's Impact Factor (I.F.) over the last eight years. It was clear that the journal has maintained high quality with an increased I.F. to 2.120 from 1.885 last year. This year's I.F. is near the top in the eight-year survey. The next table gave a ten-year listing of manuscripts received, papers published and pages published. The critical comparisons shows that a ten-year average of 183 manuscripts received and 989 pages published compare with 106 (54%) manuscripts submitted, and 636 (64%) pages published for the comparable first nine months of 2004. It was quite clear that the underlying problem is the decrease in the number of manuscripts submitted. The next table summarized the 106 manuscripts submitted in 2004. Of the 70 that had been completed, 30% were in the two-week guaranteed category. Both the latter and the regular submissions had a 29% rejection rate. There followed tables on the distribution of manuscripts among the Associate Editors, names of the 32 members of the Editorial Board who reviewed in 2004, and names of the 54 Ad Hoc reviewers in 2004. A final table listed the 20 members of the Editorial Board who personally authored manuscripts in 2003-2004.

Discussion by the committee focused on ways to increase the number of manuscripts submitted. It was noted that steps recommended and initiated in the past included specific theme-issues, occasional review articles, and a request to the members of the Editorial Board to submit manuscripts. A suggestion to have a section of the Journal for junior faculty manuscripts was considered to potentially lower the quality and I.F. of the Journal. It was noted that the Editorial Board has 92 members, 18 Associate Editors, and two Editors. If each submitted a manuscript every two years, the problem would be eliminated. Ganes Sen pointed out that, as a come-on, page charges had been waived for members of the Editorial Board last year. If the members of the Board take pride in their Society and its Journal they should be willing to contribute manuscripts of the appropriate caliber. It was the unanimous recommendation of the committee that the President of the Society should send a letter co-signed by the renowned senior members of the Society to the members of the Editorial Board stating that if they take pride in the Society and its Journal, they should submit articles personally. In addition, they should encourage other members to do the same. It was noted that PBL, Inc. has agreed to continue underwriting the cost of on-line access to the JICR for all members of the ISICR. There being no further business, the Publications Committee adjourned at 4:30 p.m.

Respectfully submitted,
Jerry Tilles
Acting Chair, ISICR Publications Committee

ISICR Standards Committee
October 21, 2004

Attendees: Ronald Bordens, Wendy Jones, Tony Meager, Sidney Grossberg (Chairman)

Dr. Grossberg opened the meeting at 1500 hours and distributed drafts of documents from World Health Organization (WHO) meetings held during the past year as well as copies of the minutes of the previous ISICR Standards Committee meeting in Torino. The current minutes deal with matters relevant to a new interferon (IFN)-β standard, lymphoblastoid IFN-α n1 potency assignment, IFN neutralizing antibody reporting, a new tumor necrosis factor-α standard, new WHO recommendations for standards, and candidate cytokine standards in preparation.

I. Old Business

During the previous year, three major topics of concern that have been the subjects of discussions at earlier ISICR Standards Committee meetings have led to the Committee sending recommendations to the WHO, Geneva, and the WHO laboratory at the National Institute of Biological Standards and Control (NIBSC) near London, regarding: (1) The urgent need to complete the analysis of data from the International Collaborative Studies on candidate IFN-β reference standard preparations in order to establish a highly purified replacement IFN-β standard; (2) Issues concerning the international standard for lymphoblastoid interferon (HuIFN-α n1); and (3) Recommendation for WHO to endorse the Kawade approach as the standard method for the calculation and reporting of results of interferon neutralization antibody tests. These matters were subsequently addressed in a WHO Informal Consultation held at NIBSC 20-21 October 2003, the formal report of which was then forwarded to the Expert Committee on Biological Standardization (ECBS), the WHO final authority on biological materials; pertinent parts of that report are summarized below.

II. Pertinent portions of the Report on the 7th WHO Informal Consultation on Standards for Cytokines, Growth Factors, and Endocrinological Substances (20-21 October 2003, Potters Bar, U.K.).

II.A. Recommendation of a replacement interferon-β International Standard (IS) Preparation. Based on the data analysis of the WHO International Collaborative Study and the desirability to replace the 2nd WHO International Standard (IS) of IFN-β, Gb23-902-531, it was recommended that candidate IS 00/572 containing highly purified, CHO cell-derived, glycosylated recombinant human IFN-β be established as the 3rd WHO IS with an assigned potency of 40,000 International Units (IU) per ampoule to replace the second IS Gb23-902-531 that contained a less-pure, human fibroblast-derived IFN-β preparation. Whereas 00/572 is suitable for the standardization of all glycosylated human IFN-β preparations, it was further recommended that the 1st WHO IS of interferon-β, serine-17, Gxb02-901-535, should continue to serve as the IS for standardization of interferon-β, serine 17 (Betaseron, Betaferon) and other non-glycosylated IFN-β preparations the dose-response curves of which have the same slope as this IS. At its meeting in November, 2003, the ECBS accepted these recommendations.

II.B. Review of the issue of possible potency reassignment of the second IS of human lymphoblastoid interferon-α n1 95/568. The previous minutes of the ISICR Standards Committee have detailed the problem that the four Japanese manufacturers of lymphoblastoid interferon have found in two collaborative studies, namely, a discrepancy of approximately 30% between the units defined by the 1st WHO IS for HuIFN-α n1, Ga23-901-532, established in 1983, and the 2nd WHO IS, 95/568 established in 1999, in relation to the Japanese national standard. Based on recommendations by Drs. Norman Finter and Masayoshi Kohase as well as the Japanese manufacturers, the ISICR Standards Committee had proposed to WHO two possible resolutions, either (1) to carry out further collaborative assay studies, with the four Japanese comp-anies included, to establish a new value for 95/568, or (2) to withdraw the second IS 95/568 and reinstate the 1st WHO IS, Ga23-901-532. Dr. Norman Finter presented the results of the Japanese collaborative studies to the WHO Consultative Group meeting in London that felt there was no scientific basis to propose that the potency of the 2nd WHO IS, 95/568, be reassigned to 50,000 IU instead of its currently assigned potency of 38,000 IU, while recognizing the adverse implications on the use of IFN-α n1 produced and used in Japan. It was stated, however, that potential solutions should be explored with consideration of the problem that other users or any existing or new potential manufacturers outside Japan may face. This issue was accordingly not referred to ECBS. International inquiries have since been circulated by WHO as to whether there are other manufacturers outside Japan, and to date none has been reported. The issue remains to be resolved.

II.C. Standard method for calculation and reporting of results of interferon neutralization antibody tests. A formal proposal was submitted to WHO for presentation to the ECBS on behalf of the ISICR Standards Committee, recommending that the WHO endorse the approach developed by Dr. Yoshimi Kawade for the computation and the reporting of IFN neutralizing antibody results as Ten-fold Reduction Units (TRU) per ml. The WHO Consultative Group agreed that there was a pressing need to harmonize the calculation and reporting of results not only of IFN neutralizing tests but other therapeutic protein neutralizing antibody tests and that a variety of other methods and means of calculating results were currently in use and that it was important to collect more data using different bioassays and means of calculating results. The WHO Consultative Group recommended that (1) the Kawade approach for the calculation and reporting of results of IFN neutralizing antibody tests is to be encouraged, (2) investigators are encouraged to use WHO homologous interferon IS to monitor and report the sensitivity of their bioassays, as stated in the ISICR Standards Committee proposal, (3) investigators should use both the Kawade and in-house approaches to calculate and express anti-IFN NAb titers and report them side by side, as recommended by the ISICR Standards Committee, and (4) more data should be collected from either new collaborative studies or manufacturers using alternative neutralizing antibody tests todetermine whether the Kawade approach is superior in practice for reducing inter-laboratory variability of results and/or confirm its assay independence.

The ISICR Committee has been informed that three manufacturers of IFN-β products have conducted a collaborative neutralizing antibody study with a number of human sera. Data obtained with the viral cytopathic bioassay as well as with one based upon the induction of the IFN-inducible protein MxA to quantify neutralizing activity, have been submitted, using the Kawade method to calculate and report results. The results are now being analyzed at NIBSC.

II.D. Replacement tumor necrosis factor (TNF)-alpha. The 1st WHO IS for human tumor necrosis factor-α, 87/650, the stocks of which were close to exhaustion, was recommended to be replaced by the candidate IS, 88/786, which contains 1.0 microgram of full-length, purified, BALL-1 cell-derived, human TNF-α. The ECBS at its November 2003 meeting approved 88/786 as the 2nd WHO IS of hTNF-α with an assigned potency of 46,500 IU per ampoule.

III. Draft Summary Report on the WHO Informal Consultation on "Recommendations for the Preparation, Characterization, and Establishment of International and Other Biological Reference Standards" (30 September-1 October 2004, Geneva, Switzerland).

III.A. Introduction: The primary function of the WHO is to develop, establish, and promote international standards with respect to food, biological, pharmaceutical, and similar products and to standardize diagnostic procedures as necessary. The guidance document resulting from this meeting is intended to be scientific and advisory in nature and builds on earlier WHO guidelines published in 1978 (1) and revised in 1986 (2) and 1990 (3). This updated document is being pre-

pared for presentation to the WHO ECBS as a result of recent developments, including scientific and technical advances, an increase in the number and range of materials classified as biological substances, and the discontinuation of WHO Biological Reference Materials that now can be fully characterized by chemical and physical means.

These recommendations are in three parts: (1) the General Considerations section addresses the scientific basis of biological standardization; (2) Part A addresses the background to the need for an international biological reference material, general considerations about procurement and characterization of suitable material, factors to be taken into account in the preparation of a batch of a candidate reference material and assessing its suitability, the testing and collaborative assay of the batch, quality assurance, and the information to be provided to WHO so that appropriate reference materials can be established by the WHO ECBS; and (3) Part B provides advice and guidance to regional and national control authorities as well as individual laboratories on the preparation and establishment of secondary biological reference materials. Such materials may be assigned values in International Units (IU) by assay against the corresponding WHO reference material.

III.B. Definitions: WHO biological reference standards are comprised of complex composition that require biological or immunological assay for appropriate characterization. They include incompletely characterized proteins, antigens, vaccines, antisera, blood products, nucleic acid standards, as well as small, well-characterized proteins. Thus, a *biological substance* is a material of biological, biotechnological, or synthetic origin that cannot be characterized fully by chemical and/or physical means alone.

An *International biological measurement Standard (IS)* is defined as a preparation of a substance of biological, biotechnological, or synthetic origin, the activity of which is defined by the WHO in terms of an International Unit (IU) or another suitable unit of activity. Provided the candidate standard has been shown to be suitable for its purpose, its unitage is attributed to the first International Standard in an arbitrary manner after an international collaborative study has been completed. Biological activity in International Units are assigned to replacement International Standards, where appropriate, by comparing them with the previous standard.

A *Reference Reagent* is defined as a preparation of a substance of biological, biotechnological, or synthetic origin, the activity of which is defined by WHO in terms of a unit, and is intended to be an interim reference material, and thus not to be expressed in IU. The published catalog of WHO biological reference materials numbers more than 300, and is updated each time preparations are added or removed from the list (4).

The concept of *commutability* in the *in vitro* diagnostics field attempts to evaluate the way different systems are affected by samples, e.g., sera from patients. Commutability is considered a desirable characteristic to be determined for the reference material by an evaluation built into the collaborative study, that is, by a comparison of the ratio between the results of two procedures for the reference material and for other samples included in the collaborative study. Thus, a commutable biological reference material should show similar behavior with routine samples when different measurement procedures are applied.

Along with developments in other fields involving the characterization of reference materials, a requirement to define what the biological reference material measures is included in this guideline. In other fields this is refereed to as a definition of the so-called *measurand*, which for biological materials may be a protein structure, biological activity, or an immunological activity, but not necessarily the same as the routine assay methods that the biological reference supports.

III.C. Biological Standardization Principles: The set of principles used by WHO for biological standardization include the following: (1) The reference preparation should be assigned a value in arbitrary rather than absolute units; (2) The unit is directly traceable to a reference preparation with a physical existence; (3) The characterization of the reference preparation, and therefore the unit, is unrelated to a specific method of determination; and (4) The properties of the reference standard must resemble as closely as possible those of the preparations that are to be assayed against it, with the key property the biological or immunological activity(ies) for which the reference preparation will serve as a standard. Biological materials may be shown to have different types of biological activity such that separate reference preparations may be established for bioassay and for immunoassay standards; also, assignment of different types of biological activity to the same reference preparation may occur. Some international standards may be used for qualitative rather than quantitative purposes.

The extent to which the general metrological topic of uncertainty, as defined by the International Organization for Standardization in its publication ISO 17511 (5), might apply to biological reference standards has been discussed in the light of new regulations from the European Union concerning *in vitro* diagnostic devices; where biological reference standards are assigned a value in arbitrary International Units, an uncertainty value has not been given. However, it has been recommended that the memoranda accompanying reference materials should contain a statement of the coefficient of variation (CV) of the fill of the preparation to reflect ampoule-to-ampoule variation. The ECBS has concluded that the choice of a unit should reflect, and be based on, the biological and medical as well as the physiochemical information available determined on a case-by-case basis for each reference material; many biologicals exist in both active and inactive states, and the activity (IU) rather than the content (SI) (Système Internationale) reflects biological activity and thus is more clearly relevant to the clinical situation in a patient. Where a measurement of total content (biologically active plus biologically inactive molecules) may be more clinically relevant than biological activity alone, measurement of structure and expression of results in SI would be more appropriate. Thus, it was considered that WHO biological reference materials that have assigned values in arbitrary IU rather than SI units can be included with the category of so-called higher-order reference materials in *in vitro* diagnostic devices in instances where the matter has arisen. Where a WHO biological reference material is to be calibrated in SI units, the principles outlined in ISO 17511 (5) should be fol-

lowed, necessitating the existence and use of an appropriate single reference method and an assignment of uncertainty derived from calibration data. Such a reference method should not be a bioassay since the factors that affect their results cannot be fully described. It is important that the decision on the route of characterization to be followed for a WHO biological reference material must be clearly made at the outset of the study.

The remainder of the report is made up of the following components, which are relatively detailed and technical, and the outline is listed here for future guidance to members or agencies needing to learn about these matters, when the document is finalized by WHO.

General Considerations

Part A. Recommendations for the preparation, characterization, and establishment of
international biological reference materials.

1. Introduction
2. Quality assurance
3. Assessment of need and procurement of materials
4. Distribution into final containers
5. Processing filled ampoules
6. International collaborative studies
7. Detailed information to be provided to WHO
8. Establishment of an international biological reference material

Part B. Recommendations for the preparation, characterization, and calibration of regional, national, or laboratory biological reference materials

1. Introduction
2. Assessment of need and procurement of material
3. Distribution into and processing of final containers
4. Calibration

Acknowledgements

Appendix 1: Considerations for setting priorities in developing WHO International Biological Measurement Standards or WHO Reference Reagents

Appendix 2: Information to be included in instruction leaflets and safety data sheets for users of international or other biological reference materials

The complete report will be submitted to the ECBS for final review and acceptance for publication.

III.D. References: Some references are listed here but are not meant to substitute for the more than 30 references in the current draft document:

1. WHO Technical Report Series, No. 626, 1978
2. WHO Technical Report Series, No. 760, 1987
3. WHO Technical Report Series, No. 800, 1990
4. WHO Technical Report Series, No. 897, 2000 and updates at ww.who.int/biologicals
5. In vitro diagnostic devices - measurement of quantities in biological samples - metrological traceability of values assigned to calibrators and control materials. ISO 17511 (2003).

IV. New candidate reference preparations in progress at NIBSC:

Thrombopoietin - definitive fill completed and under evaluation
Interleukin-17 - definitive fill completed and under evaluation
Interleukin-18 - definitive fill completed and under evaluation
TNF-related Apoptosis-Inducing Ligand (TRAIL)- definitive fill completed and under evaluation
B-Lymphocyte Stimulator (BLyS) - trial fill completed and under evaluation
IL-21, IL-23, IL-28, and IL-29 have been proposed for development of reference preparations, but are subject to donation of suitable materials.

The Committee recognized the growing number of therapeutic biologically similar IFN and cytokine products that are increasingly available for clinical application. Knowledge of the activity and other properties of such products in comparison with those of fully characterized, licensed products, however, remains sparse. It was felt, therefore, that evaluation of these new products would benefit from international discussions and consideration at WHO; action to stage appropriate meetings was endorsed.

Respectfully submitted,
Sidney E. Grossberg
Chair, ISICR Standards Committee

The 2005 Annual Meeting of theInternational Society for Interferon and Cytokine Research (ISICR)

20-24 October, Shanghai, China
http://www.sibcb.ac.cn/ISICR2005.html

Scientific sessions

Interferon/Cytokine/Chemokine Signal Transduction Pathways & their Regulation

Interferons/Cytokines/Chemokines and receptors Regulation of Interferon/Cytokine/Chemokine Expression

Interferon/Cytokine/Chemokine induced genes and their functions

New Interferons/Cytokines/Chemokines
Interferons/Cytokines/Chemokines and Immunology (including T cell/B cell/NK cell/Dendritic cell biology)

Interferons/Cytokines/Chemokines and Cancer

Interferons/Cytokines/Chemokines and Apoptosis, Anti-angiogenesis, Gene Therapy

Interferons/Cytokines/Chemokines and infection/inflammation/related disorders

Interferons/Cytokines/Chemokines and Autoimmune/Neurological Diseases

Clinical use of Interferons/Cytokines/Chemokines
Interferons/Cytokines/Chemokines and the Biotech Industry

Organized by:

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Interferon and Cytokine Research Committee of the Chinese Society of Microbiology

The Secretariat of Shanghai 2005 ISICR Annual Meeting is Prof. Zuxun Gong. The Head of secretariat office is Ms. Hua Xu. All communications to the secretariat should be sent directly to her.
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Website: www.sibcb.ac.cn/ISICR2005.html

Important dates:

Deadline for early registration	May 20, 2005
Deadline for abstract submission	May 20, 2005
Deadline for fellowship application	June 1, 2005
Date for cancellation refund 80% registration fee refund 60% registration fee no refund of registration fee	 Before Aug. 30, 2005 Before Sept. 30, 2005 After Oct.1, 2005

Registration

Registrations should be submitted only online (http://www.conference.ac.cn/isicr.html). All participants are kindly requested to complete the online registration form and to send their payment at the time of registration. **No registrations will be accepted without evidence of payment.**

	Before May 20, 2005	**After May 20, 2005**	**On site registration**
Member	US$ 450	US$ 500	US$550
Non member	US$ 500	US$ 550	US$600
Students	US$ 250	US$ 280	US$320
Accompanying persons	US$ 150	US$ 200	US$250

The Registration fee includes conference bag, program and abstract book, lunch and coffee breaks during the conference, welcome reception, farewell dinner and complimentary tour.

Registration fee for accompanying persons:

Welcome reception and farewell dinner.
Complimentary tour in Shanghai.

Visas and Invitation Letter

We will issue an official invitation letter to those who have paid the registration fee and completed the online registration. You should go to the nearest Chinese Embassy or Consulate with this invitation letter to apply for an entry visa(s). If any problem arises, please contact the Secretariat of the Conference

Payment

All payments must be in US dollars without bank charges.

▶ Bank cheques payable to: Shanghai Institutes for Biological Sciences,CAS

The bank draft of the registration fees should be sent to Institute of Biochemistry and Cell Biology, SIBS, CAS. Mail to: 320 Yue Yang Road, Shanghai, China Zipcode: 200031

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1. Make sure to indicate the name of " The 2005 Annual Meeting of the International Society for Interferon and Cytokine Research" and your full name on the money transfer.
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HOTEL ACCOMMODATIONS

Hua Ting Hotel *****	US$ 140	15 mins by taxi to conference venue
Everbright Converntion Center****	US$ 85	Conference venue
Hua Xia Hotel***	US$ 50	Next to conference venue
	US$ 20	

All hotel rooms are standard room with one breakfast. To confirm your choice, **a first night deposit** is required for each hotel room reserved.

Hotel reservation deadline: August 10, 2005.
After this date, the hotel accommodation cannot be assured. No reservation will be accepted without receipt of the payment for the first night.

Written cancellations must be submitted to the organizing secretariat not later than September 30, 2005. In this case, the first day deposit will be refunded. No cancellation requests will be accepted after the above mentioned deadline

Abstract

You are invited to submit your best scientific work in any area of the program sessions. Accepted abstracts will be organized into sessions based on topic area and type of presentation. All abstracts should be on A4 paper in Rich Text Format (Windows XP or below). Use this only if you cannot save the document in the above formats, Abstracts should be no longer than 300 words and use Times New Roman font (12 points) in the text and 14 points and bold in the title.

Please submit the abstract by e-mail to hxu@sibs.ac.cn together with your abstract form. The deadline for abstracts is May 20, 2005.

Oral presentation

Oral presentations will be scheduled on each day of the congress. Authors will be notified if their paper has been selected for oral or poster presentation before September 30, 2005.

Beer and Ice Cream Diet

(Author unknown)

As we all know, it takes 1 calorie to heat 1 gram of water 1 degree centigrade. Translated into meaningful terms, this means that if you eat a very cold dessert (generally consisting of water in large part), the natural processes which raise the consumed dessert to body temperature during the digestive cycle literally sucks the calories out of the only available source, your body fat. For example, a dessert served and eaten at near 0 degrees C (32.2^{o} F) will in a short time be raised to the normal body temperature of 37^{o}C (98.6^{o} F). For each gram of dessert eaten, that process takes approximately 37 calories as stated above. The average dessert portion is 6 oz, or 168 grams. Therefore, by operation of thermodynamic law, 6,216 calories (1 cal./gm/deg. x 37 deg. x 168 gms) are extracted from body fat as the dessert's temperature is normalized.

Allowing for the 1,200 latent calories in the dessert, the net calorie loss is approximately 5,000 calories. Obviously, the more cold dessert you eat, the better off you are and the faster you will lose weight, if that is your goal.

This process works equally well when drinking very cold beer in frosted glasses. Each ounce of beer contains 16 latent calories, but extracts 1,036 calories (6,216 cal. per 6 oz. portion) in the temperature normalizing process. Thus the net calorie loss per ounce of beer is 1,020 calories. It doesn't take a rocket scientist to calculate that 12, 240 calories (12 oz. x 1,020 cal./oz.) are extracted from the body in the process of drinking a can of beer.

Frozen desserts, e.g., ice cream, are even more beneficial, since it takes 83 cal./gm to melt them (i.e., raise them to 0 deg. C) and an additional 37 cal./gm to further raise them to body temperature. The results here are really remarkable, and it beats running hands down.

Unfortunately, for those who eat pizza as an excuse to drink beer, pizza (loaded with latent calories and served above body temperature) induces an opposite effect. But, thankfully, as the astute reader should have already reasoned, the obvious solution is to drink a lot of beer with pizza and follow up immediately with large bowls of ice cream.

We could all be thin if we were to adhere religiously to a pizza, beer, and ice cream diet.

Bon Appetit!

IMPORTANT NOTICE REGARDING THE ISICR NEWSLETTER

In order to save the society printing and mailing costs, beginning with this issue the newsletter will be distributed electronically as a pdf file. If you still would like a printed copy, you must request one directly from the ISICR membership office. We urge you to forward the newsletter to anyone you think might be interested in becoming an ISICR member.

Remember: you must be an ISICR member in good standing (that means you've paid your dues for 2005) to receive further issues of the newsletter and to be eligible for ISICR awards.

Renew your membership today! The ISICR needs your continued support and participation.

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