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ISICR
INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH

The History of Interferon: A Contribution to the Interferon Archives by Kawade Yoshimi

Edited by **Paul D. Drew**

(Japanese names are written here in their natural order, i.e., family name first, followed by given name.)

Background and initial phases:

I was not in good shape when I was graduated in 1947 from the University of Tokyo, Chemistry Department. I was born in 1924, and spent my school years in the age of war, against China (1931-45) and against the US and the Allies (1941-45). I had never felt like becoming a scientist and chose science only because science students, unlike literary students, were exempt from being recruited into the army until graduation. Fortunately, the Japanese army was disbanded in 1945 while I was still in the university, but my education was less than minimal not only because of the war but also because of the postwar social chaos. Worst of all, I could not find out what I wanted to do. Luckily I found a young associate professor Watanabe Itaru (1916-), who was striving to start a new style of biology from scratch based on the knowledge he was absorbing from new journals arriving in torrents from the US. I was fascinated by the new biology he depicted, which was to become molecular biology some years later (Watanabe, together with Sibatani Atuhiro, became its principal leader in Japan), and joined his small group to work on the physical chemistry of proteins and nucleic acids. Watanabe himself moved on to bacteriophage, and its mechanisms of replication. I continued to work on the structure-function of nucleic acid molecules. As the double-stranded structure of DNA was being established during the 1950's, I concentrated on RNA. I moved to Kyoto University in 1956, as an associate professor at the Institute for Virus Research, and had a chance to work in the US from 1958 to 1960, one year in New York at the Rockefeller Foundation Virus Laboratories, and one year in Cambridge, MA., at Paul Doty's lab in the Chemistry Department of Harvard University. My work in both places did not go well, but I learned a lot about science and other things. It was a time when molecular biology was firmly establishing itself, and I could witness astounding progress in elucidating the molecular basis of life. Besides, I enjoyed living in the US very much, together with my wife and our little girl. New York then was not very dangerous, and Cambridge was nice and quiet. The living standard in Japan was incomparably lower than in the US, and when I decided to go back to Japan in 1960, it was sheer misery for my wife. But I believed at that time I was obliged to work in Japan to contribute to renovating biology there which was still dominated by the old tradition. In retrospect, I am not sure if my decision to come home was right.

Coming back to Kyoto, I continued working on the structure-function of RNA, and my lab became one of the few places in Japan where one could pursue molecular biological research. Many young people from physics and other non- biology disciplines joined my group and were initiated into molecular

biology. One thing I tried to do then was to study animal cells and viruses with the concepts and techniques of molecular biology that had been established with microbes. I was gradually brought into the IFN field, as briefly described in my article [1] contributed to the Lindenmann festschrift commemorating the thirtieth anniversary of the discovery of IFN. As I wrote there, I had been fascinated by Alick Isaacs' idea that animal cells respond to foreign nucleic acid by production of IFN, just as animals respond to foreign protein by production of antibody. Our research along this line started when my colleague Fukada Tetsuo from Yakult Microbiological Research Institute found that chick embryo cells treated with RNA from bacteriophage MS2 became resistant to virus infection [2]. This research was a byproduct of our futile experiments to test the simplistic idea that, if the genetic code was universal, infectious phage RNA would work in animal cells to produce progeny phage particles. The results were of course negative. Also, our investigations of the RNA-induced interference showed Isaacs's 'foreign nucleic acid' hypothesis to be incorrect. Needless to say, I don't regret it, but I do regret we failed to discover the strong IFN-inducing character of double-stranded RNA then, which was first reported by Hilleman's group at Merck (1967).

While I worked on RNA-induced interference during the '60s, the IFN field was plagued by uncertainties at the very base, because IFN had not been purified and there even were doubts about the reality of IFN as a substance. Clarifying the chemical nature of IFN thus appeared to be the pressing need of the time, and this suited me better than RNA-induced interference. So I started purification and characterization of mouse IFN in 1970, and it eventually turned out to be perhaps my most significant contribution to the IFN field. Earlier, Nagano and Kojima discovered in 1954 that interference with vaccinia virus infection in rabbit skin was induced with a soluble factor from the infected tissue [3]. This is believed to be the discovery of IFN by most Japanese, but I am among those few who don't subscribe to that view [4]. Nagano did not like the name 'interferon' christened by Isaacs and Lindenmann in 1957, and instead used 'virus-inhibiting factor' (IF) for his material, until he changed his mind years later. Under his initiative, the 'Research Association of Virus-Inhibiting Factor' (Uirusu Yokusei-Inshi Kenkyuukai) was formed in Japan. The Association consisted initially of 23 people including those working on animal, plant and insect viruses. They held meetings twice a year starting in December 1961, with about 5 to 10 speakers at each meeting. When I started working on RNA-induced viral interference, I had little contact with other investigators, and rarely attended their meetings, because I was not gregarious and also was arrogant enough to regard their work and meetings rarely interesting. The only person I then had close contact with was Kobayashi Shigeyasu (1935- 1993; called Siggy by western colleagues). Kobayashi was a real biochemist (unlike myself) who did his Ph.D work in Osaka University in the '60s on energy metabolism in cultured cells. He was another fellow dragged into the IFN field by Isaacs' hypothesis, which said that IFN selectively inhibited the energy supply needed for virus growth. Young Kobayashi knew nothing about IFN, but his collaboration with Nagano which started probably in 1962 showed that Isaacs was incorrect. So we owe to Isaacs the recruitment of this powerful guy who was to lead the world in establishing a mass production system of natural human fibroblast IFN.

I don't remember when I first met Kobayashi, but our friendship began while he was at the Kobe Municipal Institute of Hygiene in the late '60s. Our relation was probably the closest during the early '70s, when I began working on purification of mouse IFN and Kobayashi moved to the Toray Research Institute (1971). There, he began large scale cell culture for production of, first mouse, then human IFN. Upon his urging, my group and I gradually joined the Association of Virus- Inhibiting Factor. Our first paper presented there was by Yamamoto Youko in 1973. By that time, the Association had grown to have a few hundred members, and today, it has become a regular 'Society' (Gakkai) with some five hundred members. My friendship and collaboration with Kobayashi, as well as the help of the Association, were vital for the success of the ISIR Kyoto meeting in 1988. His untimely death in 1993 was an immense loss to the IFN community and to me personally.

Several IFN researchers of my generation passed away prematurely:

Nagata Ikuya (1923-77) was the one who I liked and trusted best among the Japanese MDs working on IFN. He died before he could fully demonstrate his potential, and I regret that he did not see the coming of the age of recombinant IFN.

The name of Kurt Paucker (1924-80) will need no introduction here, to whom the first issue of Journal of IFN Research was dedicated. I was happy to get acquainted with him in the early '70s when I was new in the IFN field. He helped me in many ways, and I felt as if we had been old friends. Our collaboration on IFN antibodies was getting under way in '79-'80 to my great delight [5], when I was hit hard in May 1980 by Barbara Dalton's sad letter telling me of his death. From papers sent to me after his funeral, including an obituary written by Jan Vilcek (printed in ASM News, I believe), I learned about the courage he showed through the harsh experiences of his youth

George Svet-Moldavsky (1928-82) is not as widely known as Kurt, but I was impressed by his wide and early visions about IFN and also by his personality. I first met him in Moscow in 1973 (I treasure the Melodia records he gave me then), and later visited his home in New York a few times, where he told me about Bulgakov and other things about Russia. It is a great pity that he died without seeing the collapse of the Soviet Union. Upon his death, his wife Dr. Inna Svet-Moldavsky sent me a deeply moving handwritten letter, with a reprint of an obituary that appeared in Biomedicine & Pharmacotherapy, 37 (1983) 53 (unsigned, but I suspect it was written by Inna). Those who don't know him must at least read this obituary.

Most significant contributions to the IFN field:

Purification of mouse type I IFN:

Purification of IFN from various sources was attempted by a number of investigators in the '60s without much success. However, I found a promising lead in a short note by Kurt Paucker in the July 1969 issue of the Interferon Scientific Memoranda where he described production of high-titered IFN by mouse L cell induced by Newcastle disease virus and its partial purification. My few preliminary experiments in January 1970 indicated that NDV induction in L cells did produce high levels of IFN even in the absence of added serum. This system yielded a starting material already high in specific activity. So I decided to work on this system, even though Paucker already seemed to have advanced far ahead.

Behind my decision of switching to IFN purification was our bitter experience in the final years of the '60s, when student revolts raged everywhere in universities. I was sympathetic to the essence of radical students' criticism of the 'Establishment' and, being unable to find satisfactory counterarguments, I just wanted to seek more 'relevance' in my own work. That is, basic research with more visible connection to the well-being of people. Simple-minded as it may seem, IFN purification as a project appeared good enough to steady my shaky mind.

Uncertain about the feasibility of the project, I dared not recruit other people in its initial phase. Since we could not afford to hire helpers, I did everything from dish washing, preparation of culture medium, growing L cells in many Roux bottles to purification trials and assay of IFN (I had an amiable notion then that scientists should not be privileged to be exempt from simple physical labor). Despite these hardships, I presented my initial results at the national virology meeting in the fall of 1970. After that, several people joined the project, including Yamamoto Youko, Ohwaki Makoto, Tsukui Kazuo, and Matsuzawa Tetsuro. The final stage was carried out by Iwakura Yoichiro and Yonehara Shin [6]. Fujisawa Jun-ichi also contributed greatly.

Interestingly, several groups succeeded in complete purification of human and mouse type I IFN at about the same time (the late '70s). Roughly speaking, purification could be achieved by careful application of the available biochemical techniques, such as affinity chromatography of various sorts. No fundamental difficulties were encountered necessitating radical innovations. The essential thing was to start with as much crude material as possible (because the IFN protein is of such a high specific activity), and to monitor the purification processes by microanalytical methods using samples as small as possible. The former point meant for our lab a lot of muscular labor by the investigators involved, which was the highest hurdle to overcome.

Antibody to IFN was first obtained by Paucker in the early '60s, and the antigenicity became an important, almost the only, handle to the molecule before pure materials were available. In the early '70s, human leukocyte and fibroblast IFNs were recognized to be antigenically distinct. Concerning mouse IFNs, Yamamoto in my group demonstrated that the two molecular species of L cell IFN, 24K and 35K, were antigenically distinct. She further found mouse type I IFNs from various sources, including lymphoid cells consisted of the same two antigenic species as those of L cell IFN. We also found that the 24K IFN cross-reacted with human leucocyte IFN, using antisera donated by Jan Vilcek. So, what we did was recognize the two molecular species of mouse type I IFN, and show their basic resemblance to the human counter parts. This contributed significantly to establishing the concept of the α and β types of IFN [7]. I reported on this in the fall of 1979 at the New York Academy Symposium and the data were warmly received. The most exciting news from that meeting consisted of three reports describing N-terminal amino acid sequence of IFNs, obtained by the use of the newly established microsequencing technique of Hunkapillar. These included human fibroblast IFN by Ernest Knight (13 residues); a component of human lymphoblastoid IFN by Kathy Zoon's group (20 residues); and a component of mouse Ehrlich ascites tumor IFN by Peter Lengyel's group (24 residues). These developments lead to a proposal the next year (1980) concerning the unified nomenclature of IFN α, β, and γ, thus replacing old names such as leukocyte and fibroblast IFNs. This may appear a simple concept, but I think it actually represents an extremely important milestone in the history of IFN, as it is a condensed expression of the achievements of many investigators and clearly marks the change of IFN from being merely a poorly defined 'factor' to respectable chemical molecules. This provided a firm foundation for IFN research, on which to build biological and medical research.

Cloning of the mouse IFN-β gene:

The late '70s and the early '80s were hectic times with the cloning of multiple IFN genes. These studies transformed the entire IFN field. We cloned mouse IFN-β cDNA in collaboration with Taniguchi Tadatsugu in Tokyo [8]. The principal worker on this project was a then graduate student Higashi Yujiro, supported by several people including Sokawa Yoshihiro and Watanabe Yoshihiko in my group. I am glad this clone has been distributed to many labs around the world, with the help of Dr. Howard Young.

Quantitative method of neutralization of IFN activity by antibody:

Neutralization of IFN activity by antibody is a common procedure in IFN laboratories, and is conceptually so simple that there may well seem to be no theoretical or practical problems that need be considered. But when I began neutralization assays in the late '70s, I was frustrated by the lack of reproducibility in the values of antibody titer obtained, and felt there was something wrong in the way to express the titer. I first thought, like others in the field, that a given quantity of antibody would neutralize a corresponding fixed quantity of IFN, but my results indicated that antibody neutralized IFN in a fixed ratio; i.e., if it neutralizes 10 units to 1 unit, it will

neutralize 20 units to 2 units, rather than to 11 units. Seeking the explanation I searched the literature, but to my surprise, no study could be found dealing with the quantitative aspects of neutralization of soluble antigen. So I developed an elementary thermodynamic theory of neutralization reactions, and showed that my experimental results were explained by low antibody affinity ("low" in comparison with the reciprocal of the molar IFN concentration at the titration endpoint, which is usually very high).

These studies were published in the first issue of JIR (1980) (to my dismay, there were terrible typographical errors in the two basic equations making them unintelligible; my next paper in JIR (1984) was scrutinized in galley proof by the editor-in-chief Phil Marcus himself and was perfect). I improved on the theory afterwards to make it suitable for analysis of monoclonal antibodies. We demonstrated that an antibody is characterized by two independent parameters: the efficacy of neutralization, and the affinity to IFN. Both of these parameters can be determined from experimental data of neutralization.

To me, this work was just a little technical piece good for diversion (I did it only with the four rules of arithmetic in this age of computers). However, it turned out to be more important than I had thought, as the problem of formation of neutralizing antibody in patients' serum became widely recognized. I was called by Sidney E. Grossberg through WHO to participate in the standardization of IFN and antibody in 1982. Ultimately, a recommendation was made by WHO on how to determine neutralization potency of an antibody and how to express the titer, based solely on my work. The recommendation was repeated thereafter by WHO and also by the ad hoc committee of the ISIR (1988).

I retired in 1988 and freed myself from any research obligations, but my peace was broken as I was invited again by Sidney Grossberg to participate in the WHO informal standardization meeting in Geneva in 1994. I then found that the problem of patient's antibody to IFN had become even more important, and no basic theoretical or experimental studies to revise or refute my previous work had been done. In the meantime, the international standard human antisera against α and β IFNs were prepared. An extensive collaborative titration was conducted by the time of the Geneva meeting under the leadership of Sidney Grossberg at the Medical College of Wisconsin. This great mass of experimental data provided an excellent opportunity to reexamine the methodology of the neutralization assay since the recommendation made by WHO was not the last word but an expedient to be followed until a better method was devised. So, after the 1994 Geneva meeting, I resumed working on the problem in close collaboration with Sidney, and it has turned out to be highly fruitful. The results, soon to be published, should be useful not only for IFN but for any kind of cytokines and other soluble antigens with biological activity.

Reflections on the past and present of IFN research:

I once briefly summarized the history of IFN research in terms of the four periods: the romantic, the dogmatic, the academic, and the business periods [1]. The 1950's and '60s were the romantic period, when the 'soluble factor' that mediates viral interference was discovered, defined solely by its biological activity. Imaginations and hopes of the few founding fathers were limitless, but the whole field looked dubious from the outside, lacking firm grounds. Rescue came, not from biological-medical research, but from work of a chemical nature. Purification and characterization of IFN proteins and molecular cloning of IFN genes in the '70s and early '80s provided a reliable framework for the whole field, even though the knowledge obtained was actually only a portion of the skeleton of the IFN system. So that was the dogmatic period. The ISIR, as our society was initially called, was founded in 1983, an event befitting the time. Then, the field expanded rapidly under the framework thus established, welcoming many newcomers from molecular biology and other fields, and various aspects of the IFN system were investigated using sophisticated experimental systems and techniques through the '80s. So this can be called the academic period.

Biology in general underwent a radical change in the '70s and '80s due to the remarkable developments in molecular and cell biology, spurred especially by the introduction of recombinant DNA technology. The dream of getting massive quantities of pure IFN was ultimately realized, which allowed clinical applications of IFN to be pursued. Basic biology that once was an idyllic activity in academia, now suddenly became potentially, as well as actually, a profit-making enterprise. Research in biology is now mostly directed toward problems that are expected to yield useful results for medical or industrial applications. Molecules and cells, as well as data and information, widely circulate in society as commodities. So, this is to be called the business period, or the baroque age, if you like. Biology has become highly technical. To the extent that it is much closer to technology than to science, an appropriate name for it is 'technobiology'.

These four periods were depicted as a sequence in time, but actually, they overlap each other considerably. Their features are usually recognizable at any time in history, in different proportions.

I wrote this overview more than ten years ago, but the situation does not seem to have changed much. We are still in the business period, with some elements of the academic period. Being in the business period is welcome in that basic research can serve in many ways for the benefit of mankind (through the benefit of some companies and individuals). However, it inevitably has a negative side. Biology, and for that matter natural science in general, has become a powerful social institution, and its workings are intricately woven into the politico-economic system of society. For science to advance, it must depend heavily on the socioeconomic establishment of developed countries. Thus, research is strongly controlled by economic and political powers. Scientists may claim their 'pure' intentions of seeking scientific

knowledge for its own sake or for the benefit of mankind, but, like it or not, their activity can no longer be free from ideological or sociopolitical implications. Then, in what direction should we direct science and technology, and with how much money and manpower? This is the kind of problem very often beyond the power of most practicing scientists. We need wide-ranging investigations in such fields as sociology of science, economics of science, as well as philosophy of science, which are not much in fashion now.

Now, let me change the angle somewhat and complement the above-mentioned history with reflections about the focus of researchers' interest. I think a shift of the focus can be traced through these periods from biological phenomenon to molecule, then to cell, and to whole body [9]. (This seems a fairly general trend in biology, as I had sketched for the history of virology too [10]).

Research on any topic must necessarily start with defining a biological phenomenon, i.e., cutting out a piece of nature from its continuum, usually observable at the macroscopic level. So the initial phase, the romantic period, was the age of phenomenon, in which the topic of viral interference was narrowed down to a soluble factor. By thus focusing on the factor, it soon became clear that the scope of research surpassed viral interference and covered the more general field of resistance to viral infection. Further, as the 'factor' apparently exhibited activities other than viral inhibition, the scope widened beyond virology to include various areas of cell biology.

The ensuing dogmatic period was the age of the molecule, in which molecules of IFN proteins and their genes were the center of concern. By the identification of these molecules, a firm frame of reference was established, which was based, not precariously on biological phenomena, but objectively on physical entity. The long-standing inquiries of IFN researchers into the mechanisms of IFN production and of action could now be investigated using standard methods of molecular biology. In fact, this basic research involving molecules was not particular to IFN. Instead, the field appeared to be smoothly united with, or absorbed into, the molecular biology of animal cells.

As is well known, molecular biology at first concentrated its efforts on bacteria and their phages. However, as the basic molecular mechanisms of replication and phenotype expression became established by the mid-60s, increasing attention was directed to eukaryotic cells. Spurred by a number of unexpected findings, and also by the wealth of interesting biological-medical problems awaiting elucidation, molecular biology of animal cells made tremendous progress in the '70s. This might be looked upon merely as applications of the methods and concepts established for the microbial world to the more complex world of animal cells. However, I think we must recognize here an important change in the eyes of the investigators. That was the change from molecular biology to cell biology. The term 'cell biology' came to be frequently used in the '70s in place of molecular biology, although the research itself remained essentially the same as before in its target and style. This reflects, I believe, the shift of the focus of research interest from molecule to cell. A symbolic event was the initiation of the journal "Cell" in 1974. The papers that appeared there were no different from those in molecular biology journals, and yet the title of the journal appealed well to researchers' mind. In the '50s, the focus was on molecules, and people wanted to clarify the "molecular control of cellular activities", but now what was to be clarified was the "cellular control of molecular activities". So, this period, roughly corresponding to the academic period, is to be described as the age of cell.

Research in cell biology nowadays is largely concerned with problems in higher animals and plants, such as embryogenesis and cytodifferentiation, immunity, cancer, and homeostasis. Thus, much current research apparently aims at understanding the events that occur in whole body of higher living forms, although the actual analyses so far seem to be mostly limited to the cell and molecular levels. The same is true with research on IFN and cytokines in general. They are the agents that work meaningfully in the context of whole body of animals. Although we now have a huge accumulation of experimental data at the cell and molecular levels about cytokines, it is not clear what sort of data among those available are relevant for our understanding of the cytokine network and its workings in vivo. Clinical uses of IFN are certainly bearing fruit, but much more should be gained if we knew better about how IFN works in vivo, as it is integrated into the psychoneuroimmune-endocrine-cytokine system. So, I think, as regards the focus of research interest, we have by now moved from the age of cell to the age of the whole organism. Yet our current situation seems to be that, in spite of the fact that our eyes are directed toward the intact organism, our methodologies of research are not much beyond those of traditional cell and molecular biology. The same applies to many fields of biology. Our biological and medical research is certainly flourishing and yielding valuable results. Nevertheless, I think radically new concepts, theories, or methodologies are needed to meet the demand of the time, the age of the whole organism.

One might find help for conceptual innovations in such newly developing fields as dynamics of complex systems, artificial life and brain science, but I want to point out here that, to approach problems at the level of whole body, one cannot avoid asking about how mind or psyche is involved in the workings of the IFN system. The importance of psychic factors in the immune and other bodily functions is increasingly recognized, and I hope the interaction between the IFN-cytokine system and the mind (not just the neural system or the brain as physical systems) will become a hot agenda in the near future.

To conclude, I would like to outline my current interest in biology. I retired in 1988 and quit all lab work and other worldly businesses (except chairing the ISIR annual meeting held in Kyoto in November 1988), to enjoy myself fooling around with abstract,

philosophical aspects of IFN and biology in general. I became intrigued, in my final years of laboratory life, by analogies that could be drawn between the cytokine network and human language, and I read books on linguistics and semiotics. As I had presented in my honorary member lecture at Florence in 1989, I recognized that IFN, and protein molecules in general, worked as signs representing certain meanings, like words in language [11]. I hoped that such a viewpoint might help to find novel directions for IFN research. However, as I became better acquainted with semiotics (the science of signs), my interest developed toward more general aspects of biology. I realized that not only protein molecules but any molecule in living systems engages in semiosis (sign process) [12]. Semiosis of various forms plays a vital role at every level of living systems, from that of the cell, to individual, to ecosystem. Thus, semiosis is indeed the activity that distinguishes living from non-living beings.

Semiotics is usually concerned with human culture (literature, art, etc.), but is by no means confined to it. Its major concerns are communication and signification (creation of meaning). That communication is essential in the living world is easy to see, from the macroscopic level of animal behavior down to the microscopic level of cells and molecules (e.g., cell-cell interaction by cytokines). It should be noted that communication is not just transmission of physical signal from one element to another. Instead, communication is transmission of message, that is, meaning. The essence of what a living being does, from a single cell to a multicellular organism, is, I believe, to interpret the physical world and create meaning out of it (i.e., signification), and then communicate the meaning to other living beings (what molecular biologists call information transfer, self-replication, etc.), in order to sustain life. In this view, every living organism must be considered to have its own autonomous subjectivity. This view then transcends the bounds of natural science, because natural science deals in principle only with objective things, and biology as a natural science must eventually reduce living beings into matter in order to carry through its aim of objectively explaining life. This, I believe, represents current mainstream biology, and I call it physicobiology. But for a better understanding of living beings, I think we need a different conceptual dimension other than matter, and that is represented, not by soul or spirit, but by the concept of semiosis. A biology with this stance, with sign as its focus instead of matter, is possible, and that is biosemiotics or semiobiology. I don't know if it is of any help for practicing scientists, but I believe this kind of thinking is needed to counter the strong mechanistic trend of present-day biology and medicine [13,14].

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1998 ISICR Meeting: A Big Success

From Eleanor Fish

The 2nd Joint Meeting of the ICS & ISICR was a resounding success! The program organization and calibre of scientific presentations were excellent. Plenary Sessions and Symposia were well attended and oral presentations invariably stimulated discussion and further insights from the audience. The poster sessions were also well attended and highly informative. There were opportunities to attend presentations that were 'overviews' of a particular discipline, and opportunities for focused and in-depth presentations on specific cytokines. This was also an opportunity to get up to date on

outcomes of clinical trials and future prospects for cytokine therapies in the clinic. The extra-curricular activities were outstanding! The venue, Jerusalem, speaks for itself; the Organizing Committee outdid themselves with the social events: a Jerusalem night tour, folklore evening, a visit to the Israel Musesum and a Bedhouin-style banquet. A very special thank you to Ray, Michel, David and Issac.

Ray Kaempfer provides the following facts:

Participants: 728
Accompanying persons: 41
Preregistered: 556
Abstracts: 631
Posters: about 279
Talks: about 352
Banquet: 550 (maximum capacity)
At Crowne Plaza: 238 rooms

All ISICR members wish to express our gratitude and appreciation for the continued support of our society and interferon research by

Seymour and Vivian Milstein.

May 1999 be a happy and healthy year for the Milstein family and the entire ISICR.

ISICR Grad Students and Postdocs: The Next Generation

Are you are postdoc who is trying to figure out the next step to your career?

Are you a grad student who hasn't a clue where you want to do your postdoc?

Would you like to know what ISICR grad students and/or postdocs from other parts of the globe are working on?

Or are you just bored out of your mind waiting for that experiment to finish and have no choice but to read this part of the ISICR newsletter?

If you said yes to any of these questions, this section is for you!

Let me introduce myself: I'm Hannah, and I'm brand new at being a postdoc, in Dr. George Stark's lab, working on aspects of the IL-1/TNF signal transduction pathway. I recently obtained my PhD from Dr. John Hiscott's lab; thanks to John I have met many wonderful members of the ISICR - including my present mentor - through meetings and collaborations. Having said that, if you know of people in the interferon and cytokine fields who are not yet members of the ISICR, get them to join; it's only $10/year, and, well you know the perks - tell them about it!

I'm interested in establishing a special newsletter section just for Grad students and postdocs since we do represent the next generation of scientists who will eventually "run" the interferon and cytokine fields. It would be great if we came to know each other, collaborate, discuss issues that concern us and keep the field as strong as it is and even stronger. There are several ways that this task could be accomplished. **First**, a big thank-you to the ISICR newletter editors, especially Dr. Howard Young, for their support. **Second**, your written contribution would be of enormous help - the more the merrier. If you are interested in having others (such as potential collaborators!) know of what you are working on, let me know by e-mail, phone, fax or mail (all the information is at the end of this section), and it will be presented in upcoming newsletters. **Third**, particular issues could be addressed by inviting an ISICR member who is an expert to write his or her thoughts on the subject in question. Examples of issues would be what are the advantages and disadvantages to working in industry versus an academic setting in the interferon/cytokine field? What opportunities are there in the interferon/cytokine field in France, Canada, Japan or another country? What are issues facing women researchers in the interferon/cytokine field? What is it like to work at the NIH, the Cleveland Clinic Foundation, or other institutions in terms of resources, subject matter or working environment?

If there are any issues you would like to have addressed, by all means let me know. Any feedback would be greatly appreciated.

Of course, there are also everyday lab concerns affecting us that could be discussed as well. Here's one question we can tackle. What do you do if a co-postdoc or student tries to take credit for your idea? Let me know of your advice, and we'll summarize the results in the next newsletter. Looking forward to getting to know you,

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Some Thoughts To Get You Through Any Crisis

1. Indecision is the key to flexibility.
2. Happiness is merely the remission of pain.
3. The facts, although interesting, are irrelevant.
4. Sometimes too much to drink is not enough.
5. Nostalgia isn't what it used to be.
6. There is absolutely no substitute for a genuine lack of preparation.
7. You can't tell which way the train went by looking at the track.
8. The careful application of terror is also a form of communication.
9. Someone who thinks logically is a nice contrast to the real world.
10. Things are more like they are today than they ever have been before.
11. Everything should be made as simple as possible, but no simpler.
12. Friends may come and go, but enemies accumulate.
13. I have seen the truth and it makes no sense.
14. If you think that there is good in everybody, you haven't met everybody.
15. All things being equal, fat people use more soap.
16. If you can smile when things go wrong, you have someone in mind to blame.
17. One seventh of your life is spent on Monday.
18. By the time you can make ends meet, they move the ends.
19. Not one shred of evidence supports the notion that life is serious.
20. The more you run over a dead cat, the flatter it gets.
21. There is always one more imbecile than you counted on.
22. This is as bad as it can get, but don't bet on it.
23. Never wrestle with a pig. You both get all dirty, and the pig likes it.
24. You can observe a lot by just watching.
25. Three correct guesses in a row and you qualify to be an expert.
26. If you don't know where you are going, any road will get you there.

WWW

BioCatalog

http://www.ebi.ac.uk/biocat
ftp://ftp.ebi.ac.uk/pub/databases/bio_catal

The BioCatalog is a database of information on software in Molecular biology, genetics and a few other biology domains. Information on any software relevant for biologists is welcome. To add information into the biocat please use the form at: http://www.ebi.ac.uk/biocat/biocat_form.html

Dr. Patricia Rodriguez-Tome
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Biocrawler

http://www.biocrawler.com
http://www.biologie.de

Biologie.de (Biocrawler.com) has now opened their new database. Although still under construction, we have already collected over 7000 biological relevant links in many sections of biology. We are still collecting and we will add more and more categories. Unlike other search engines, which simply collect links, we rate them by counting the numbers of links to this site to get an estimate of importance of this site. Sites with more links to them are rated more important. Additionally we have a search / filter option that allows search and filtered browsing. Only pages containing the search query will be displayed, also in lower categories.

Biologie.de and its associate Chemie.de should be with this step the biggest subject specific information providers in Germany and we are probably one of the biggest link collection provided by professional biologists and chemists the world. In the future we will also feature a specified book and journal section in which the, in our opinion, most relevant scientific books and journals will be presented.

Dipl. Biol. Nils Koesters
webmaster@biologie.de

BLAST Server at NCGR

http://seqsim.ncgr.org

The National Center for Genome Resources is pleased to announce the availabilityof BLAST (Basic Local Alignment Search Tool. Coming soon, the Center will also

offer other powerful similarity search methods, including Smith-Waterman. NCGR's recent acquisition of two specialized DeCypher ES-1920 servers, produced by TimeLogic Corp., allows us to offer these computationally intensive search algorithms. The Center is the first to offer a free, publicly accessible DeCypher server linked to a public sequence database, our Genome Sequence DataBase (GSDB). GSDB contains additional data, unique data sets and annotation not found in other public databases. This breadth of genomic data, combined with the power to analyze data and free access, represents a formidable resource. Nowhere else can users benefit from the combination of comprehensive data access and cutting-edge analysis tools. The DeCypher servers perform a variety of algorithms; in addition to BLAST, NCGR will provide Smith-Waterman, Frame Search, Symmetric Frame Independent, Profile Search in early 1999; and ClustalW by the end of 1998. To support flexibility in similarity searching, NCGR provides searchable subsets of its databases. You may customize your target set by selecting a single or multiple subsets. NCGR is unique among public sequence databases in offering this extremely useful feature. Individual search sets are based mainly on the taxonomic hierarchy but also include sequence tagged sites (STSs), expressed sequence tags (ESTs) and individual human chromosomes. NCGR is grateful to TimeLogic for its support in this effort, particularly TimeLogics contribution of one server for use by researchers. Please contact ncgr@ncgr.org if you have questions.

Michael M. Harpold, Ph.D.
Chief Scientific Officer

PPCMatrix

http://copan.bioz.unibas.ch/software/

PPCMatrix V1.01 is a versatile dotmatrix program for the Apple Macintosh, optimized for the PowerPC. It includes many additional features:

Built in sequence editor, with speech (currently limited to 32k).
Reverse, complement, reverse-complement of sequences.
Reads text, GCG, PIR formats.
Translations (every frame, best ORF, 3-frame nested translation).
Displays alignments of dotmatrix regions that have been selected with the mouse.

The special feature of the program is that it can read large (only limited by available memory) sequences, which can be translated in a special format, the 3-frame nested translation. The 3-frame nested translation can be compared to protein sequences. Thus identifications of sequence similarities are possible even in case of frameshifts (due to sequence errors), or when exons are in different reading frames. The program is released on shareware basis. A 68k version is also available.

Thomas Burglin

Protein Structure Prediction

http://www.cse.ucsc.edu/research/compbio/HMM-apps

We are pleased to announce the availability of a hidden Markov (model HMM) protein structure prediction server. The server has used UCSC's SAM-T98 method to create a library of HMMs, one per PDB structure (about 2500 HMMs total). You can search this database of HMMs with a protein sequence. The iterative method of creating these models is detailed in two upcoming papers available from our WWW site (to appear in JMB (in collaboration with Jong Park and Cyrus Chothia) and to appear in Bioinformatics), and is more sensitive for remote homology detection than PSI-BLAST or ISS. These methods, refinements of our CASP2 methods, formed the core of our CASP3 structure prediction contest entries, the results of which will be announced in December. (http://predictioncenter.llnl.gov/ You will receive by e-mail a list of the PDB identifiers of each hit, as well as a series of pairwise alignments based on the library's HMM for those structures. When the system is unloaded, the search will take a few minutes. Also available on the page are SAM-T98 database searching, alignment comparison, and alignment refinement. The iterative construction of an HMM for SAM-T98 database searching can take a particularly long time when the server is processing many queries. Please wait at least a day before giving up on a search.

Science Literacy

http://www.sandskript.org/sciencebyte/

The majordomo list ScienceByte has been created on August 15, 1998. The objective of ScienceByte is to promote science literacy and foster a scientific culture worldwide through the Internet. Everyone is welcome. You have to subscribe to post articles and receive the digest. Share your enthusiasm for science, help others learn the fundamental principles of physics, chemistry, biology and mathematics. Write informative and entertaining articles on science. Be a leader and mentor to students from all over the world.

Anyone with minimum internet access (like an email account) should be able to participate. If you have java enabled browser, you can access the science-cafe' chatroom for interactive learning and instruction.

Subscription is free. To subscribe, send an email to majordomo@sandskript.org and write in the body of your email message: subscribe sciencebyte
To remove yourself from the list send an email to majordomo@sandskript.org and write in the body of your email message:
unsubscribe sciencebyte

If you ever need to contact the owner of the list, (if you have trouble unsubscribing, or have questions about the list itself) send email to owner-sciencebyte@sandskript.org . To post your message, email to sciencebyte@sandskript.org For more info, archive and chat visit:
http://www.sandskript.org/sciencebyte/
http://www.sandskript.org/chatroom/sciencebyte-cafe.htm
Spread the word. Thank you.

Sequence Alignments and Modeling Software

http://www.cse.ucsc.edu/research/compbio/sam.html

An upgrade of the UCSC HMM software is also available (it does not currently include the SAM-T98 method). The software includes tools for building HMMs from aligned and unaligned sequences using a variety of Dirichlet mixture priors and transition regularizers, and scoring and multiply aligning sequences using the trained HMM. The object code is free for academic use, but our copyright office would like a signed license, the details of which are on the WWW page. For commercial use, send email to sam-info@cse.ucsc.edu. Important additions to recent versions include:
o An option for posterior-decoded alignments
o Local and semi-local training and alignment
o User-defined alphabets
o Reduced space dynamic programming
o Optional internal sequence weighting during training
o Corrected MSF and HSSP file reading

These projects have been lead by David Haussler, Richard Hughey, and Kevin Karplus. The servers include the work of Anders Krogh, graduate students Christian Barrett, Melissa Cline, and David Kulp, undergraduates Rachel Karchin, Nguyet Manh, and Jeffrey Sukharev, and many other members of our computational biology group. The servers are supported in part with a donation from Digital Equipment Corporation. Our research has been supported by NSF, DOE, and other grants as detailed on the WWW page.

STACK 2.0

http://www.ncgr.org/gsdb/data_retrieval.html

STACK version 2.0, is an error compensated database of alignments and clustered EST consensus sequences generated by very exhaustive sequence comparison of all possible sequence fragments against each other. Extremely CPU intensive processing has been used in order to maximize the accuracy of the assignments. The database has been generated using GenBank 103. Alignments of the subsequent clusters are manufactured and are made available in .gde format (GCG compatible). An add database and add toolset is in preparation.

Server Provision
Currently, only EMBnet nodes are eligible to provide this service. STACK uses http://ziggy.sanbi.ac.za/stack/stacksearch.htm
Searches against STACK can yield extended consensus sequences made from constituent ESTs, which in turn yield longer queries for subsequent work. Links and consensus sequences make the process of working with ESTs more simplified, and in some cases, purified entries in the form of SANIGENE can be extracted and used. Searches using the SANBI search engine against STACK 2.0 are linked directly to an ENTREZ linked entry retrieval engine, thus improving the access to other databases such as UniGene and dbEST. A Virtual Transcribed Sequences set of gene-fragments that have matched STACK entries from available human genome sequences will shortly be linked to the STACK-SEARCH engine at SANBI. Drosphila ESTs that have found matches with STACK entries can be found at:
http://gcg.tigem.it/DRES/dres.html

STACK alignments are extremely useful for cSNP discovery, and for provision of scaffolds for further assembly via use of STACK consensi. Occasionally, errors have occurred in manufacture, and a collection of non-included ESTs is distributed with the database. A 2.1 release will contain the adjusted entries.

STACK 2.0 is now available on our FTP site (academic registration for download0: http://ziggy.sanbi.ac.za/stack/stackrequest.htm) and can be searched on our BLAST engine at http://ziggy.sanbi.ac.za/STACK.

STACK 2.0 has been generated from Genbank103 release. It comprises 16 tissue sets. This differs from the previous release as our previous synovial membrane set has been incorporated into the connective tissue set. Genbank103 release was clustered on an SGI origin2000 as well as a Maspar. No claims are made as to the accuracy of the following statistics. We welcome comments and corrections.

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Wise 2.1.12 Beta

http://www.sanger.ac.uk/Software/Wise2/

Wise2.1.12 beta is a beta release of the Wise2 package. This package specialises in the comparions of a DNA sequence at the level of its conceptual translation. In the case of genomic DNA a complete gene prediction algorithm is merged with a protein alignment algorithm in genewise. In the case of EST/cDNA DNA, the ability to find frameshifts errors in the DNA sequence is merged with a protein alignment algorithm. The package can compare either protein sequences or profile-HMMs (made by the HMMER package) to DNA sequences. The algorithms can be run in one-on-one modes or database searching modes. In the database search, a profile-HMM database can be used, such as those produced by Pfam. The source code can be downloaded by anonymous ftp from ftp://ftp.sanger.ac.uk/pub/birney/wise2 in wise2.1.12.tar.gz or in binary format as ftp://ftp.sanger.ac.uk/pub/birney/wise2/binaries

The functionality of the programs can be accessed via a Perl port to the package, or a C API. Contact birney@sanger.ac.uk for more information or read the web site: http://www.sanger.ac.uk/Software/Wise2/Programming/

Ewan Birney
birney@sanger.ac.uk
http://www.sanger.ac.uk/Users/birney/

Reviews of Interest

Choi, P and Reiser, H. IL-4: role in disease and regulation of production. *Clin. Exp. Immunol.* 113:317-319, 1998

Garzinodemo A; Devico AL; Gallo RC. Chemokine receptors and chemokines in HIV infection *Journal of Clinical Immunology.* 18(4), pp 243-255, Jul 1998

Gesbert F; Delespinecarmagnat M; Bertoglio J. Recent advances in the understanding of Interleukin-2 signal transduction. *Journal of Clinical Immunology.* 18(5), pp 307-320, Sep 1998

Kullberg BJ; Anaissie EJ. Cytokines as therapy for opportunistic fungal infections *Research in Immunology.* 149(4-5), pp 478-488, May-Jun 1998

Leonard, WJ; O'Shea JJ. JAKS and STATS: Biological implications. *Ann. Rev. Immunol.* 16:293-322, 1998.

Maghazachi AA; Al-Aoukaty A. Chemokines activate Natural Killer cells through heterotrimeric G-proteins – Implications for the treatment of AIDS and Cancer. *FASEB Journal.* 12(11), pp. 913-924 Aug 1998.

Trusolino L; Pugliese L; Comoglio PM. .Iinteractions between Scatter factors and their receptors – Hints for therapeutic applications. *FASEB Journal.* 12(13), pp 1267-1280, Oct 1998.

Whitman M. SMADS and early development signaling by the TGF-Beta superfamily. *Genes & Development.* 12(16), pp 2445-2462, Aug 15 1998

CLINICAL TRIALS

IDs: MDA-DM-96296, NCI-G97-1206 Phase II Study to Evaluate the Efficacy of Recombinant **Interferon Alpha** in the Treatment of Recurrent Unresectable Meningiomas and Malignant Meningiomas. Contact: Wai-Kwan Alfred Yung, Chair, Ph: 713-794-1285. University of Texas - MD Anderson Cancer Center, Houston, TX

IDs: NCI-95-C-0144C, NCI-T95-0013N, NCI-95-C-0144B Phase II Pilot Study of ATRA plus **IFN-A** for Lymphoproliferative Disorders in Children with Immunodeficiency Syndromes. Contact: Robert P. Nelson, Jr., Principal Investigator, Ph: 813-892-4184. All Children's Hospital – 6900, St. Petersburg, FL

IDs: UNM-1698C, NCI-V98-1479 Phase II Study of Fluorouracil, **Interferon Alfa**, and **Interleukin-2** (FUNIL) for Malignant Carcinoid and Malignant Islet Cell Neuroendocrine Tumors. Contact:: Laurence Elias, Principal Investigator, Ph: 505-272-5837. University of New Mexico Cancer Research & Treatment Center, Albuquerque, NM

IDs: RTOG-9710 Phase II Study of Radiation Therapy Followed by Recombinant **Interferon Beta** in Patients with Supratentorial Glioblastoma Multiforme. Contact: Wai-Kwan Alfred Yung, Chair, Ph: 713-794-1285. Radiation Therapy Oncology Group

IDs: UW-24218-A/E, NCI-V95-0758 Phase IB Study of Outpatient Subcutaneous **Interleukin-2** for Stage IIb/III/IV Mycosis Fungoides. Contact: John A. Thompson, Chair, Ph: 206-548-6346. University of Washington Medical Center , Seattle, WA

ID: E1497 Phase II study of DAB 389 IL-2, an **interleukin-2 fusion toxin**, for previously treated stage II, III, and IV follicular low-grade non-Hodgkins lymphoma. Contact: Jean MacDonald Ph: 617-632-3610. Brookline, MA

ID: AMC-008 A randomized pre-phase II trial of **IL-2**, **IL-12**, or no additional therapy following response to ifosfamide (Ifex)/etoposide chemotherapy for refractory HIV associated non-Hodgkin's lymphoma. Contact: Lawrence Kaplan Ph: 415-476-4082 ext. 409. Birmingham, AL

IDs: IUMC-9708-05, NCI-T97-0027 Phase I Study of Recombinant Human **Interleukin-12** (IL-12) after High-Dose Chemotherapy and Autologous Hematopoietic Stem Cell Support in Patients with Hematologic Malignancies and Solid Tumors. Contact: Michael J. Robertson, Principal Investigator, Ph: 317-274-0843. Indiana University Cancer Center, Indianapolis, IN

NEW ISICR MEMBERS

Mervat Michael Attalla - Cairo, Heliopolis, EGYPT
Sai Krishna Avula - Chicago, IL
George Sabel Bassily - Cairo, Heliopolis, EGYPT
Steven L. Berk – Johnson City, TN
Melissa Brierley - Toronto, CANADA
Haider Abbas Chaleb - Cairo, EGYPT
David R. Fitzpatrick - Herston Qld, AUSTRALIA
Ashraf Haider Ghaleb - Cariro, EGYPT
Khalil Abdel Hamed El Halfawy - Cairo, Giza , EGYPT
Shinji Ichii - Osaka, JAPAN
Takahiko Ito - Galveston, TX
Jyothi Kumaran - Toronto, CANADA
Jo-Ann C. Leong - Corvallis, OR
Diwakar Venkata Lingam - Chicago, IL
Bhanu Prasad Paladugu - Chicago, IL
Reda Nicola Wassef - Cario, Heliopolis EGYPT
Mark Wong - Toronto, CANADA

Book Review: THE STORY OF INTERFERON: THE UPS AND DOWNS IN THE LIFE OF A RESEARCH SCIENTIST

by Kari Cantell

World Scientific, Singapore, 1998, 239 pages (first published in Finnish by Werner Söderstöm Osakeyhtiö in 1993).
Reviewed by : **Pat Fitzgerald-Bocarsly**

This delightful little book is the memoir of Kari Cantell, chronicling

his long and remarkable scientific career. Writing in uncomplicated prose, Cantell describes his impressions of the development of the interferon field and his own crucial role in bringing leukocyte interferon to the clinic. Prior to the advent of recombinant interferon, Cantell's laboratory in Finland was the world's major source of interferon, supplying the natural product used in the initial human trials. Cantell describes streams of international visitors through his laboratory as he freely shared his technology. He never patented his processes or had personal financial gain from his studies, even though his stimulated leukocytes became the basis for the cloning of interferon alpha in Europe.

The book is punctuated by Cantell's remembrances of his initial adventures into science and how he ended up studying interferon, the personalities who made major contributions to the interferon field and of his personal friendship with many of these individuals. Within the pages are detailed many scenarios with which scientist readers will find commonality: the frustrations of laboratory science, the (sometimes) misunderstanding of the scientific community, the joy of "Eureka!", the phenomenon of being ahead of the mainstream thought processes, and the frustrations of dealing with other scientists with difficult personalities. Included in the book is an album of photos, beginning with an 8 year-old schoolboy Cantell, and including various family photos, photos of prominent interferonologists, lab pictures and of meeting with Fidel Castro at the inauguration of the Interferon Institute in Havana, Cuba.

Although this memoir is written for the educated layman with little prior knowledge of interferon, the book also has appeal for the interferon professional who wants to appreciate the history behind the science. This book is especially recommended for the youngest generation of interferon scientists who have grown up exclusively in the molecular age. For them, Cantell provides a poignant history of where the science has come from, and the steps leading to our current path.

1998 ISICR Committees Minutes

Minutes of the Board of Director's and Advisory Board Meeting October 26, 1998

Present: Board of Directors
F. Belardelli, O. Haller, S. Pestka, R. Schreiber, H. Schellekens
Present: Advisory Board
S. Baron, E. Borden, E. de Maeyer, F. Dianzani
Absent: E. Knight, R. Friedman, I. Gresser, A. Hovanessian

The President of the Society, Dr. Bryan Williams, opened the meeting as scheduled at 2:00 pm on Monday, October 26, 1998. A number of items were discussed in accord with the agenda for the meeting.

1. Announcements from the Chair
Dr. Williams noted the election of Otto Haller, Huub Schellekens and Ara Hovanessian to the Board of Directors. Dr. Samuel Baron was elected Treasurer, replacing Dr. Ernest Knight and Dr. Sid Pestka was re-elected Secretary.

2. 1999 Budget Discussion and Approval
The financial report, prepared by Dr. Ernest Knight, was presented by Dr. Williams and approved by the Board of Directors.

ISICR PROPOSED BUDGET FOR 1999 (see page 19)

3. Contract with Mary Ann Liebert for JICR
The contract had been reviewed by the Publications Committee who recommended the Board of Directors approve the signing as soon as possible with a minor modification. (Subsequent discussions with Mary Ann Liebert resulted in the signing of the original contract with approval of the Officers of the Society.

4. Contract with FASEB

The contract with FASEB was discussed and it was recommended that ISICR continue with the present arrangements. However, the Board also recommended that our FASEB consultation, Dr. George Galasso, present two reports next year to the Officers and the Board rather than the monthly report to the President. Dr. William will relay this request to Dr. Galasso.

5. Venues for the 2002 Meeting
Dr. Williams informed the Board of the ongoing discussions of the 2002 ISICR/ICS Meeting venue. A decision was made subsequently by the Meetings Committee to recommend Vienna as the site. This needs to be confirmed by the Board.

6. Relationships with ICS and the Society for Leukocyte Biology
Dr. Williams informed the Board about discussions with the ICS and SLB concerning the possibility of some form of combined organization, perhaps through FASEB. Any proposal will be

discussed with input from the Officers, Board and Membership.

The meeting was adjourned by Dr. Bryan Williams at 3:30 pm.

Minutes of the ISICR International Council Meeting 1:30 p.m., October 27, 1998

Present: C. Czarniecki, USA; E. Fish, Canada; R. Fleischmann, USA; O. Haller, Germany; K. Hosoi, Japan; Y. Iwakura, Japan; E. Lundgren, Norway; P. Marcus, USA; N. Naruse, Japan; S. Pestka, USA; Y-I. Satoh, Japan; G. Sen, USA; R. Silverman, USA; G. Stark, USA; and B. Williams, USA.

The meeting was opened by President Bryan Williams and the following reports were then presented.

1. The Publications Committee Report (see the detailed Publications Committee report) was presented by Dr. Robert Fleischmann. During this time Dr. Philip Marcus provided a summary of the number of papers submitted and accepted as well as other information about the progress of the journal.

2. The Nomenclature Committee Report was presented by Dr. Erik Lundgren (see Nomenclature Committee Report for the full summary of the presentation).

3. The Secretary's Report and the Treasurer's Report were presented by Dr. Sidney Pestka (see respective reports for the full summary of the presentation).

4. The Membership Committee Report was presented by Dr. Sidney Pestka for Heinz-Kurt Hochkeppel (see Membership Committee Minutes for full summary of the presentation).

5. The Meetings Committee Report was given by Dr. Christine Czarniecki. There were 675 registrants at the Jerusalem meeting. The organizers raised $200,000 towards the meeting. The San Diego meeting had 333 attendees. The organizers raised $40,000 towards the meeting and the ISICR provided $12,000. After expenses approximately $15,500 was returned to the ISICR with a profit of $3,500. Future meetings of the ISICR have been approved for Paris in 1999, Amsterdam in 2000 and Cleveland in 2001. The Committee also selected Vienna in 2002. Shanghai was suggested for 2003 and Melbourne in 2004. The 2002 meeting will be submitted to the ISICR Board for official approval. The other sites will be approved in 1999 and 2000 respectively. (See the Meetings Committee Report for more detailed information.)
Respectfully submitted,

Sidney Pestka
Secretary, ISICR

Minutes of the ISICR Archive Committee

A statement outlining the purpose of the Archive and the functions of the Committee was recently prepared by the Chairman, circulated to the members of the Committee and agreed unanimously. Dr. Marcus has agreed to publish this statement in a forthcoming issue of the Journal of Interferon and Cytokine Research.

There being no other matters requiring discussion in the short term, the ISICR Archives Committee decided not to hold a meeting in Jerusalem.

N.B. Finter
Chairman, ISICR Archives Committee

Awards Committee Notes

In the ISICR/ICS joint meeting in Israel, the president has presented the society awards to the following winners: The Milstein Award to Otto Haller, Honorary membership Drs. Samuel Baron and Peter Knight, The Milstein Young Investigator Awards, Yitzhak Ben-Asouli, Rongtuan Lin, Christian Park, and Christina Fleischman Award, Xiaoxia Li, Jinjiao Guo received the newly created Viragen Award, for excellence in Interferon research. In the latter three categories, young, pre-doctoral members did very well (award recipients are all graduate students). In addition, 36 ISICR members have received Travel Awards.

A new award: Viragen Award for Excellence in Interferon Research. Viragen Inc (Florida, USA) has created a new $500 award for basic or clinical research in the interferon field. Details of application will be announced in the next Newsletter. See the check box in the Abstract form.

Broadening Young Investigator Awards Eligibility in the 1999 Annual Meeting in Paris. The ISICR President and the Awards Committee wish to broaden the eligibility of The Milstein/Christina Fleischman Young Investigator Awards. The new format will allow pre-doctoral students, post-doctoral fellows, as well as junior independent investigators in various institutions to apply for the awards. The Award committee will announce more detailed information in the next newsletter.

Minutes of the ISICR Meetings Committee

The meeting was called to order on Monday, October 26, 1998 at 3:00 p.m. Present were members Michael Katze, Yu-Ichiro Sato, Larry Pfeffer, Bob Silverman; ad hoc members Tom Cesario, Janine Doly, Ray Kaempfer, Huub Schellekens, George Stark, Bryan Williams, and guests Paul Hertzog, Xin Yuan Liu, Josef Schwarzmeier (substituting for Gunther Adolf). Also present were Jan Vilcek and Joost Oppenheim representing the International Cytokine Society (ICS).

The meeting was chaired by Christine Czarniecki.

Dr. Czarniecki opened the meeting by welcoming new members joining the ISICR Meetings Committee and asking all attendees to introduce themselves.

Old Business: The Guidelines for ISICR Meetings Organizers were revised and finalized. Copies were distributed to current meetings organizers and submitted to Dr. Pestka for archiving.

2002: At last year's meeting in San Diego three submitted proposals (Dr. Liu/ Shanghai; Dr. Hertzog/Melbourne; Dr. Adolf/Vienna) were discussed. The Committee agreed to make a decision regarding the site with input of the ICS since the plan is to hold this meeting as a joint ICS/ISICR Meeting. At the request of Jan Vilcek, the current President of the ICS, this discussion took place in Jerusalem. After presentations from Dr. Liu, Dr. Hertzog and Dr. Schwarzmeier (replacing Dr. Adolf) a closed session discussion took place (ISICR Meetings Committee members, ad-hoc members and ICS representatives) to priorize the three proposals. The ICS representatives informed us that they have chosen Hawaii as the site for their 2001 Meeting and were therefore opposed to holding a joint ICS/ISICR meeting in Melbourne in 2002. Vienna was therefore selected for the 2002 meeting. The committee suggested Shanghai in 2003 and Melbourne in 2004. These latter sites must be confirmed in 1999 and 2000. It was agreed that this recommendation would be submitted to the ISICR Board for official decision and notification.

1997 - San Diego: Dr. Tom Cesario summarized the financial report from last year's ISICR meeting in San Diego. There were 333 attendees. Registrations and donations brought in $201,829 of which $40,000 was received in contributions and $12,000 was provided by the ISICR. After expenses of $186,257, $15, 572 was returned to the Society.

1998 - Jerusalem: Dr. Ray Kaempfer reviewed the status of the current joint ICS/ISICR Meeting. As of that afternoon, there were 722 registrants and the Organizers estimate that they have passed the "break-even" point. With regards to fund-raising, approximately $200,000 was raised and almost all of that has been collected. Dr. Kaempfer felt that the Organizers worked closely together and made all decisions together and this was an important aspect of planning a joint meeting. There was a discussion of electronic submissions. Well over two-thirds of the abstracts were submitted electronically. Submission of registrations worked well. Due to differences in systems, future guidelines for submission of abstracts should prohibit the use of special characters beyond symbols.

1999 - Paris: The 1999 meeting will take place September 5 - 9, 1999 in Paris, France and it will be a meeting of the ISICR only. Dr. Janine Doly introduced Dr. Laurence Lomme and they summarized the status of plans for that meeting. The UFR Biomedicale, Universite Rene Descartes has been chosen as the meeting site. A first announcement was distributed at the Jerusalem meeting. A website has been set up at **www.univ-paris5.fr/upr37/** with detailed information. There was a discussion of facilities available at the site, availability of hotel rooms for meeting attendees, and fund-raising. Dr. Doly assured the committee that the site could adequately meet our meeting room and audio-visual needs. She also agreed to look into reserving a block of reasonably priced rooms at a nearby hotel and to request assistance in raising funds from local ISICR members who have had past success in this area, such as Dr. Bernard Lebleu, Dr. Ara Hovanessian and Dr. Michael Tovey.

2000 - Amsterdam, Netherlands: This meeting will be a joint ICS/ISICR meeting and the meeting dates are November 5-10. Dr. Huub Schellekens and his committee are currently working on ideas for organization of the program.

2001 - Cleveland, Ohio: Dr. George Stark informed the committee that the dates have been set for October 7 to 12 and Meetings Coordinators, an organization that we have used for past meetings has been chosen to work on the coordinating of this meeting. The Scientific Organizing Committee has been chosen and the Sheraton is the venue.

Other business: It was emphasized that the ISICR Secretariat must work closely with the local Meeting Organizers and ISICR Committee Chairs to ensure that ISICR Committee Meetings are scheduled at optimal times during the meeting.

The meeting was adjourned at 5:00 PM.
Respectfully submitted,
Christine W. Czarniecki
Chair, ISICR Meetings Committee

Minutes of the First ISICR Membership Committee *Internet* Meeting, held September 1998

Participants:
Miklos Degré, Heinz-Kurt Hochkeppel (chair), Antonis Koromilas, Aseem Kumar, Eliane Meurs, and Howard Young

Since none of the Members of the ISICR Membership Committee will be able to attend the 2nd Joint Annual ICS/ISICR Meeting in Jerusalem, October 1998 it was decided to organize an Internet Committee Meeting instead, chaired by H.K. Hochkeppel. According to the suggestions of the Membership Committee Members, H.K. Hochkeppel worked out a meeting agenda, and, according to the agenda, an exchange of recommendations and suggestions was carried out during most of September. The conclusions/ recommendations of the Internet Meeting are summarized in these minutes.

As of September 29, 1998, ISICR had a total of 785 Members. 723 Members (in comparison 699 in 1997) are Paid Members (628 Regular Members, 87 Student Members, 6 Corporate Sponsors, and 2 Emeritus Members), 15 Honorary, and 47 Associate Members. 610 Members have renewed their

Membership, 10 renewed with bad address, and 103 New Members joined ISICR. There are presently 149 Active members who paid in 1997 but have not yet renewed, and further 80 ones who paid in 1996 but have not yet renewed. For suspension are marked 94 Members whose last dues payments were in 1995, and further 112 whose last dues payments were in 1994. The total Paid, Honorary, and Associate Membership is rather consistent. The members we loose through suspension is more or less compensated by the recruitment of New Membership. However, one can also state that the Society is not growing. Therefore, additional efforts are necessary to maintain our Membership and to more aggressively recruit new members.

1.Maintenance of ISICR Membership
The loss of ISICR Membership is partly due to the fact that many Members do not keep record of their own Memberships (due dates) or are simply too lazy to renew. It is recommended to alter the application form, clearly encouraging payment by credit card. Specifically, a new category of payment should be included that automatically renews and bills the credit card on a yearly basis, as an additional option of credit card payment. This could also include the journal subscription. We often loose track of members who move to new locations. They mostly forget to inform ISCIR or FASEB. FASEB should be in charge to investigate whether there are some useful characteristics that could perhaps help us identifying the major group of these potentially lost candidates. For example, are the majority of them postdocs moving to new labs within a country or to other countries? Laboratory heads who are ISICR members should be encouraged to automatically inform FASEB (by e-mail) about such moves. In earlier times the ISICR councilors of the individual national chapters were informed once a year by the ISICR secretariat about Past Members in their national chapter, and were asked to contact and encourage them to renew ISICR Membership. This was also a mean of tracing Members who moved to other places. Since FASEB is in charge, this procedure has been abandoned. It should be revived. In addition, FASEB is encouraged to automatically send out renewal forms to all Members as well as remind them simultaneously by e-mail on a yearly basis. This might be one way to increase the renewal rate. Other Societies (AAI, SASM) do this already with success.

2.Recruitment of New Membership
Many scientists and institutions are still not aware that ISICR exists. Therefore, it is recommended to put an advertisement in a couple of good journals describing our Society. The advertisement rates for Cell and Science seem to be reasonable and could reach our target audience of scientists. It is again proposed to create a onepage flyer describing ISICR and all the advantages of becoming a Member of the Society. The poster which was created by E. Fish and which was distributed to the International Councilors of ISICR for further distribution was an excellent idea but a one time event. A flyer could be produced and distributed more easily, frequently and efficiently to the various labs, institutions, as well as to authors of JICR, Cytokine and other related journals, may be even as e-mail attachment. In these flyers and in the journal advertisement it should be made well-known that Student and Postdoc Memberships are only $10. In addition, also in the ISICR membership application form this particular payment reduction should be emphasized more clearly. Finally, the Membership Committee requests that the Editors of the JICR consider creating a new yearly award based on the best manuscript whose first author is either a graduate student member or postdoctoral fellow member of the ISICR. Membership in the ISICR must have been established prior to submission of the article. The award decision would be based on nominations from the Membership with the final decision made by the editorial board.

3.Associate Membership:
It is recommended to maintain the ISICR Associate Membership application form for new applicants unchanged. In addition, it is recommended that Active Associate Members of ISICR need to reapply for renewal of their Associate Membership Status on an annual basis.

Respectfully submitted
Heinz-Kurt Hochkeppel

Minutes of the ICISR Nomenclature Committee 25 October 1998

Present: Erik Lundgren (Chair), Eleanor Fish, Jerome Langer, Juana Wietzerbin, Bryan Williams

1) Standardized nomenclature for the interferon regulatory factors (IRFs). Currently there are seven factors using this nomenclature (IRF1 through IRF7), and at least two closely related proteins (p48 and ICSBP) that do not. There is high similarity in the DNA-binding domains of all family members, and the DNA binding property is probably the major criterion for inclusion in this family. The fact that several factors operate outside the IFN system is a complicating factor, although this can be mitigated by the definition through the DNA-binding domain.

One proposal would assign the designations IRF-8 to p48 and IRF-9 to ICSBP. Erik will confer with major investigators in the area who are attending the meeting. If a decision is made to standardize nomenclature, it will also be important to inform the database or nomenclature people associated with the genome project, so that the names "IRF-8" and "IRF-9" are not assigned to other proteins.

2. Avian IFN genes. A proposal was received from John Lowenthal, Peter Staeheli, Ursula Schultz, Margaret Sekellick and Philip Marcus for nomenclature of avian Type I IFN genes. The proposal reviewed recent progress in cloning and purifying avian interferons and proposed relationships between them.

Although some elements of the proposal were well documented, such as the

designation of certain avian IFNs as IFN-(, members of the committee raised several questions:

(1) Criteria for classification. Chicken IFN1 and ChIFN2 lack sufficient sequence identity with mammalian IFN-∀ and IFN-∃ to use sequence information for definitions; however, ChIFN1 and IFN2 are serologically distinct. Lowenthal et al. proposed that ChIFN1 and ChIFN2 "...are the true chicken homologues of mammalian IFN-∀ and IFN-∃, respectively.", using as criteria the inducibility of ChIFN1, but not ChIFN2, by the imidazoquinoline, S-28463, and by a statement about the promoter structure. Drs. Lowenthal et al. suggest that inducibility by S-28463 can be used to distinguish avian IFN-∀ from IFN-∃, but the basis for such a generalization as a means of classification was not clear to the committee. Furthermore, the statement regarding the promoter structure was not sufficiently specific to permit evaluation. This issue led to a general discussion, which was not resolved, on how to define and distinguish IFN-∀ and IFN-∃.

(2) The information on the duck and turkey IFNs were insufficient to determine their relationship to the chicken IFN1 and IFN2 genes. The alignments and amino acid comparisons presented are for ChIFN1 to TuIFN and DuIFN; comparable comparisons for ChIFN2 were not presented. Eleanor Fish will discuss these matters with Philip Marcus. Follow-up:

1) On Monday, 26 October, a discussion on the IRFs was held, including Erik Lundgren, Eleanor Fish, Paul Hertzog, Jerry Langer and David Levy. Erik had also spoken with Keiko Ozato, who did not attend. The proposal that arose was to rename the factors:
ISCBP - IRF-8
p48 - IRF-9.
Under this proposal, the acronym "IRF" would be redefined to mean: "IFN consensus sequence regulatory factor", which is related to a functional property of the entire family. This proposal will also be discussed with other investigators. If implemented, appropriate individuals at GenBank will be consulted to ensure that these designations have not already been assigned.

(2) After further discussion, the relationship of ChIFN1 and ChIFN2 to the designations "IFN-∀" or "IFN-∃" remained unclear, as did the phylogenetic relationships of each chicken IFN to duck and turkey.

The committee will continue to consider this issue as new information becomes available.

Erik Lundgren Jerome A. Langer

Minutes of the ISICR Publications Committee October 1998

The ISICR Publications Committee met on October 26, 1998 at the Annual Meeting of the ISICR. Members present and participating in discussion were Drs. Patricia Fitzgerald-Bocarsly, Bob Fleischmann, Dhan Kalvakolanu, and Phil Marcus (ex officio). In addition, Drs. Sid Pestka and Bryan Williams participated in discussion.

The following topics were discussed by the Committee.
1. The Publications Committee discussed the latest version of the proposed contract between the ISICR and Mary Ann Liebert.
a. The following key features present in the proposed contract were noted:
1) Renewable terms for Editors, Section Editors, Editorial Board
2) One price subscription for all members around the world, reflecting the international status of the society
3) Royalties on advertising sales
4) The JICR will now be available on-line on the WEB
b. The following key concern was noted:
1) The identification of who will pay for the Abstracts Issue is ambiguous. It is recommended that the wording of the proposed contract be changed to state "The Publisher will absorb the cost of paste-up, printing, and binding of the Program and Abstract Book, provided that the Abstracts are printed 4 to a page."
c. The Publications Committee agrees in principle with the proposed contract and encourages the Board of Directors to negotiate with all vigor to achieve a signed contract as soon as possible.
2. The Publications Committee discussed the membership of the Editorial Board, particularly with regard to the relative representation of women. Pat Fitzgerald-Bocarsly will compare the membership in the Society and on the Editorial Board to determine if representation is disproportionate. All agreed that principle qualifications for Editorial Board membership should be support of the JICR through publications in the journal, appropriate and timely reviews of submitted manuscripts, and international reputation.
3. The Publications Committee heard the status report of the JICR from Phil Marcus.
a. Phil reported that the journal appears to be in very good shape. The number of manuscripts submitted is ahead of recent years and the number of accepted manuscripts is at the best level that it has ever been.
b. Phil reported that the expedited two week review has become a popular choice. It has worked well, with reviewers meeting the deadline in almost every instant. There does not appear to be a bias towards either acceptance or rejection of papers submitted for expedited two week review.
c. Dr. Marcus reported that there are still members of the Editorial Board do not support the JICR by publishing in the journal. The Publications Committee recognizes that the impact factor of the JICR will not improve until the members of the ISICR and most particularly the members of the Editorial Board of the JICR publish their best articles in the journal. The Publications Committee encourages them to do so.

Respectfully Submitted,
W. Robert Fleischmann, Chair

Minutes of the ISICR Committee on Standards October 26, 1998

The attendees were Francesco Antonetti, Ronald Bordens, Colin Brand, Josef Brzoska, Kazuo Hosoi, Wendy Jones, Yoshimi Kawade, Aida Sterin-Prync, Monica Tsang, Louis Westreich, and Sidney Grossberg (Chairman). Dr. Grossberg opened the meeting at 15:00 and asked the attendees to introduce themselves and state their affiliations. Members of both ISICR and ICS were present.

I. Report on the 4th World Health Organization (WHO) Consultation on Cytokine Standards
Dr. Bordens summarized the salient results of the WHO Cytokine Standards meeting held 9 October 1998 in Washington and distributed a copy of his report to the International Federation of Pharmaceutical Manufacturers Association (IFPMA). The WHO process for certifying international standards was explained, which involves holding consultative meetings of experts to (i) review technical information, (ii) advise the WHO Expert Committee on Biological Standardization (ECBS), and (iii) make recommendations for further action.

A. Cytokine Standard Preparations. Updated information was presented on current standards for various cytokines, growth factors and cytokine-binding proteins and receptors, including: interleukin-2 soluble receptor, activin A (human recombinant), recombinant hepatocyte growth factor/scatter factor (96/564), and a proposed reference reagent for hepatocyte scatter factor precursor (96/566), insulin-like growth factor (96/538). Supplemental information was presented for bone morphogenetic protein-2 reference reagent (93/574), Flt 3 ligand reference reagent (96/532), IL-10 reference reagent (93/722), and stem cell factor reference reagent (91/682), which were to be recommended as WHO reference reagents.

B. Monoclonal Antibodies. The therapeutic use of monoclonal antibodies was proposed as a future topic for discussion to include a review of their specificity, the differences and similarities in their complementary determining regions, and orphan drug issues.

C. IFN-Alpha Standards International Collaborative Study. The WHO collaborative study on interferon-alpha, recently concluded by the U.K. National Institute for Biological Standards and Control (NIBSC), was discussed. The study affirmed the need for homologous standards, in addition to recognition of considerations of existing clinical and product safety history, product-specific calibrations, and the need to minimize discontinuity between existing WHO International Standard preparations and existing products. The NIBSC proposed to address specific concerns on final potency assignments of any newly proposed standard preparations by collecting additional titration results from manufacturers. An objective would be to determine product-specific potency determinations in relationship to the original 69/19 standard and the proposed replacement 94/784, as well as to existing standards. This NIBSC - sponsored study would include 69/19, 94/784, the appropriate new subtype standard, and the manufacturer's in-house interferon standard. No recommendations on interferon-alpha standardization are to be made to ECBS at its late October 1998 meeting, with a target, however, to present them at the ECBS meeting in fall 1999. Discussions of the standard for consensus interferon (94/786) was deferred until all the other interferon-alpha potency issues are resolved.

D. IFN - beta Standards International Collaborative Study. The current Interferon-beta collaborative study by NIBSC has been stayed because of the report from some laboratories of marked variations in the potencies measured, increasing the probability of the need to repeat the analyses. The problem may be due to the marked affinity of interferon-beta for glass surfaces.

II. Discussion and recommendations of the ISICR Standards Committee

A. The IFN-alpha International Collaborative Assay Study. The question was posed as to the best approach to finalize potency assignments in relation to how manufacturers use their own in-house standards and assays. Dr. Brand expressed concern that potency values provided by some manufacturers in the 1997 NIBSC study were obtained in assays that were different from those employed in routine support of their IFN product. To address concerns on potency assignment, NIBSC has proposed asking manufacturers to analyze the homologous interferon reference preparations with their assay systems in a smaller collaborative study to be undertaken soon. Dr. Bordens outlined plans for such a proposed manufacturers' workshop meeting to discuss the protocol and organization of a study that would allow the most acceptable final potency assignments. Various issues and concerns were raised in discussion, specifically:
(1) The problem of discontinuity in the collaborative study's proposed potencies compared to the values established by the manufacturers;
(2) The resolution of possibly conflicting values obtained by manufacturers of the same alpha subtype or mixture;
(3) The short time-frame allowed for completion and analysis of the study;
(4) The need for an historical link to current WHO International Standards;
(5) The need for having more than one statistical group to analyze the data collected from the participants; and
(6) The issue concerning dual calibration relative to 69/19 versus 97/784.

The ISICR committee unanimously recommended including in the manufacturers' study protocol the current WHO International Standard alpha subtype preparations for testing. Dr. Prync asked about possibly addressing the matter of specific activity; it was noted that the candidate standards prepared at NIBSC have only

nominal protein amounts such that specific activity assessments would not be possible. Dr. Grossberg emphasized the important difference between a Laboratory Unit (LU) (that is, a dilution endpoint, e.g., producing a 50% reduction in response) and an International Unit (IU) (a proportionate value calibrated relative to an established WHO International Standard).

The ISICR Committee also recommended that the manufacturers' study protocol should consider carefully the types of assays allowed for specific subtype calibration in order to enhance the chance to produce consistent results. Dr. Grossberg suggested that comments on study design should be solicited from those who were to attend the NIBSC January 1999 manufacturers' workshop meeting by distributing beforehand a draft protocol for comments to be returned to NIBSC prior to the meeting. Mr. Hosoi stressed the importance of calibrating in-house standards very carefully and connecting them to the appropriate International Standard.

B. The IFN-beta International Collaborative Assay Study. Dr. Grossberg reported on the status of the IFN-beta collaborative study, stating that 15 laboratories had received the test materials. Some laboratories reported titer losses during the course of testing the preparations. Tony Meager of NIBSC has asked the ISICR Committee to consider whether a new study be instituted with new preparations made up in siliconized glass ampules, or continue the current study by distributing additional samples of the same materials that would be resuspended and handled by methods that would compensate for the stickiness of the protein, for example, by using sodium dodecyl sulfate (SDS). Dr. Grossberg pointed out that it probably would take at least 18 months to start the process over. It was noted that SDS might be toxic for some cells and that this approach did not deal with the problem of the intrinsic recoverability and stability of the standards.

Mr. Hosoi presented his data from Toray Industries showing that the method for the preparation of the glass containers was critical to the quality and stability of human fibroblast IFN-beta. His data showed that the original NIBSC ampule content was accurate, but the ability to recovery active IFN-beta was poor and variable. He recommended that the study be repeated with siliconized glass ampules. Mr. Antonetti did not observe such losses in his laboratory (nor had Drs. Jones, Prync, or Grossberg); he pointed out that there were differences in values obtained using various cell line-virus combinations, which he felt was more problematic and could affect final assignment of potency, impacting different manufacturers differently.

Mr. Hosoi recommended that the best conditions for preparing highly purified fibroblast HuIFN-beta are to distribute it in siliconized glass ampules with sorbitol for freeze-drying and reconstitute it in a buffer with 5% serum. Mr. Antonetti and Dr. Jones agreed to test their companies' respective CHO-produced rHuIFN-beta products under the above conditions to determine recovery and stability of biological activity and communicate the data to NIBSC.

After extensive discussion, the ISICR Committee unanimously recommended that new IFN-beta standard materials be prepared in siliconized ampules by NIBSC, using the best conditions to assure maximum recovery and stability.

C. Need for New Cytokine Standards. Some of the problems encountered in cytokine standardization might be avoided by the establishment early in their development of standard preparations. Dr. Grossberg stressed the importance of early involvement of cytokine producers. He urged manufacturers not only to provide an adequate quantity of new cytokines to NIBSC early in the development process for NIBSC to prepare standards but also to provide financial assistance to NIBSC to allow the expeditious preparation of interim reference reagents with an arbitrarily assigned unitage. The process would help address a point raised earlier about assignment of unitage for new preparations and their use in research.

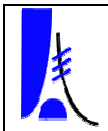
D. Need for Standardization of Cytokine Bioassays. Various comments pointed out the broad differences in bioassay methods and techniques. A question was raised as to whether WHO could act to recommend standardized bioassays. Dr. Grossberg responded by indicating that WHO has recommended standard bioassays, e.g. for antibiotics; thus, it is possible to do so. An attempt to establish a standard bioassay for IFNs was unsuccessful. Should it be deemed desirable to recommend to WHO a bioassay for a given cytokine, a group of scientists or a scientific society would have to champion the idea.

There being no further business, the meeting was adjourned at 17:40.

Respectfully submitted,
Ronald Bordens
Louis Westreich
Sidney Grossberg

ISICR PROPOSED BUDGET FOR 1999

Travel Awards, 1999 Meeting	$	50,000
FASEB Expenses		26,000
Salary Secretary's Office		9,600
Office Expenses - Officers		4,100
Financial Report – 1997		2,500
Travel		4,000
Consulting		1,800
Miscellaneous		300
TOTAL	**$**	**98,300**



ISICR
5 - 9 September 1999
PARIS - FRANCE

Important Dates for the 1999 Meeting

Deadline for the submission of abstracts

March 12, 1999

Deadline for the
submission of awards
application
March 12, 1999

Deadline for
early registration
June 1, 1999

Notification of
acceptance of papers
July 5, 1999

Fees will be refunded with a FF 300 – deduction (for handling fees), if written confirmation of cancellation is received by
July 16, 1999

No refund will be made after
July 16, 1999

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EXCEPTIONAL MEETING