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# In Tribute to Edward De Maeyer

Paula Pitha-Rowe

Edward de Maeyer died on June 25 as a consequence of unsuccessful heart surgery. It was both unexpected and an unnecessary death. He has been one of the founders of the field of interferon and a scientist who brought interferon to the forefront of immunology and genetics.

De Maeyer obtained his MD at the University of Leuven in Belgium. He started to work on the antiviral activity produced in poliovirus-infected cells called virus inhibitory fluid – VIF, while a postdoctoral fellow in the Enders laboratory in Boston. The VIF was shown later to be identical with a substance called interferon studied in the Isaacs laboratory in London. Edward's first interferon paper was on interferon induction by attenuated measles virus and this started his a lifelong association with interferon. From the Enders laboratory Edward moved to Rockefeller University and then back to Leuven to the Rega Institute, where he, together with new wife Jacqueline de Maeyer- Giugnar, initiated a series of studies on the suppression of chemical carcinogenesis by interferon. The De Maeyers left Leuven in 1965, to join CNRS in the Radium Institute in Orsay, France. By then they had already established a very efficient and productive husband and wife collaboration and this interaction lasted throughout their life.

Edward realized early in his career the power of the mouse model system for the analysis of the fundamental questions of interferon biology. Edward's studies on the genetics of interferon induction by viral infection had an unexpected and a very significant outcome. Utilizing genetics, he was able to identify the locus determining the New Castle Disease Virus (NDV) mediated interferon induction (designated *If*). He also showed

that this locus is on mouse chromosome 3 and has both high and low alleles. Surprisingly the *If* locus was distinct for different virus groups and interferon inducers. A few years later in a collaborative study with our laboratory, he used molecular biology to show that the difference between *If* high and low was not at the level of interferon gene structure. Thus Edward's work predicted, long before we understood the molecular mechanisms of interferon induction and knew about the



EDWARD AND JACQUELINE DE MAEYER

existence of Toll-like receptors, that the virus mediated signaling that leads to the activation of interferon genes is determined by cellular factors that are distinct for different groups of viruses and inducers. Equally imaginative and pioneering were Edward's studies that revealed the interaction of interferons with the innate and acquired immune systems. Here he initiated studies that show that

interferon can either stimulate or inhibit immune responses. Once again his keen insight was far ahead of the general understanding of the immune system at that time, when the interferon mediated inhibition of viral replication was assumed to be a result of a direct antiviral effect of interferon. However as we know these days, the role of interferon both in the innate and acquired immune response has been rediscovered and were Edward still with us, he would be happy to say: "I told you so."

In collaboration with Luc Montagnier, Edward explored other aspects of interferon biology. Thus in the pre-cloning years of early 1970 they were able to isolate the interferon mRNA and identified it by translation into biologically active interferon in primary chick fibroblasts. This collaboration with Montagnier was reinitiated in recent years as they have explored the possibility of using interferon gene therapy for treatment of HIV-1 infection. Thus from experiments in mouse models, Edward leaped to translational research with important implications for the clinical use of interferons.

Edward's science was always a little ahead of its time

and he was a master of presenting complex systems in a clear manner. His sense of humor and gentle nature were very much appreciated by his students and colleagues. For all of us who knew him, he will be remembered as a kind scientist who was one of the most important contributors to interferon research.

The ISICR mourns his loss and sends our condolences to his wife Jacqueline, his family and his friends. This article, written by him, is a tribute to his contributions to the field of Interferon research.

### **HOW I BECAME INTERESTED IN VIRUSES, AND SUBSEQUENTLY IN INTERFERON, AND HOW WE THEN CONTINUED...**

“Without a vivid link to the past, the present is chaos and the future unreadable.” Jason Epstein.

#### **1954-1958 LOUVAIN (E. De Maeyer)**

In 1954, while still a medical student at the University of Leuven, in the Flemish section of the Medical School, I was quite poor and badly needed money. Among the various things I did to earn some, and in spite of my ignorance, or more probably because of it, I wrote a treatise on virology that was sold to the students, and sold well, since in those days there was no textbook of virology in Flemish. The treatise came to the attention of Pieter De Somer, the recently appointed 37 year old professor of microbiology, who told me that he was building an institute of microbiology (called Rega Institute, Rega being the name of a professor at the Louvain Medical School in the 19th century), and asked me to come and work on viruses. De Somer, himself a bacteriologist by training, had just introduced virology as a subject of teaching in the medical school curriculum, and was convinced that it should become a subject of research. This was the time when Jonas Salk was developing the formalin-inactivated polio vaccine, and Pieter De Somer was eager to learn all about poliovirus, and have polio vaccine made by the company (called RIT, for Recherche et Industrie Therapeutique) he had helped to found some years ago (in this respect he certainly was way ahead of his time). When entering Medical School, it had been my intention to become a practicing clinician, but the work of Jonas Salk convinced me that preventing disease, rather than having to cure it, was at least as good an approach to medicine. Maybe I was also subconsciously influenced

by the fact that as a teenager I had read, and enjoyed, *Microbe Hunters* (in German) by Paul de Kruyf. When not attending lectures or clinical demonstrations, I worked in the newly built Rega Institute, participated in the safety testing in rhesus monkeys of the formalin inactivated poliovaccine that was produced, and developed an assay to compare the antigenic potencies of different batches of polio vaccine (P. De Somer et al. *Archiv Ges. Virusforschung*.VIII 430-436 1958). For a whole year I also tried to cultivate poliovirus in macrophages obtained from rhesus monkeys, of which we had a large colony, but had very irregular, mostly negative results. (The idea was that if we could use macrophages to grow the virus, we would not have to kill so many monkeys to get their kidneys). I graduated from medical school in July 1957. This was the year of the world-wide flu epidemic caused by a new strain called A Singapore 57, antigenically quite different from the viruses isolated during the preceding years. While De Somer was in the Congo (then called the Belgian Congo!) busy vaccinating children, with my collaborator, Piet Denys, -then still, a medical student- (and who later, in 1953, spent some time with Alick Isaacs in London), we isolated the Asian flu virus in Belgium, characterized it, and, based on our experience with polio, made a formalin-inactivated vaccine. About one thousand people were inoculated - I still do not understand how I got the nerve to do this- and, in a controlled trial, the vaccine really did offer protection! (E. De Maeyer, P.Denys and P.De Somer, *Acta Clinica Belgica*, XIII 109-124 1958).

Jonas Salk's work was directly based on the demonstration in 1949 by John Enders and his collaborators Tom Weller and Fred Robbins that poliovirus could be isolated and propagated in vitro in cell cultures, for which they obtained the Nobel Prize in 1954. I was therefore quite elated when John Enders, after a phone call from De Somer, agreed to have me as a postdoctoral fellow (and without an interview, since I was still in Belgium) and, financially supported by the De Somers company and a Fulbright fellowship, I took the boat to New York in September '58; I was 26 years old.

#### **1958-1960 BOSTON (E. De Maeyer).**

A few years earlier, in 1954, Tom Peebles and John Enders had isolated and propagated measles virus in cell culture, and at the time of my arrival, the Enders lab

was fully engaged in studying measles virus and in attenuating it through a series of passages in chick embryo cells, with the aim of obtaining a strain suitable for vaccination. I therefore naturally started working with measles virus, and my assigned task was to develop a plaque assay to allow for precise determination of infectious titres (E. De Maeyer, *Virology* 11: 635-638 1960). At the time of my arrival, there were four other postdocs in the Enders lab; I was the only non-American. One of the post-docs, Monto Ho, who had arrived a year before me, was investigating a substance -it really was more of an activity than a substance- made by poliovirus-infected cells, that protected human amnion and renal cells against the cytopathic effect of the virus (Ho and Enders. *PNAS* 45:385-389, 1959, and Ho and Enders, *Virology* 9: 446-477, 1959). This antiviral activity was referred to as VIF, for virus inhibitory fluid, or, depending on the mood of the day, viral inhibitory factor, but of course we all said that VIF stood for “very important fluid”. I was then unaware of Isaacs and Lindemann’s paper on interferon, that had been published a year earlier (the problem of keeping up with the literature has always been with me!), but later I found out that Monto knew about the work, had tested in his polio system some chick interferon received from Alick, found it to be inactive (the concept of species specificity was still a few years away) and concluded that VIF was different from interferon, which of course in strictu sensu it was! (Ho and Enders, *PNAS* 45:385-389 1959 and *Virology* 9: 446-447 1959). The poliovirus strain that was used by Monto to elicit the production of VIF was the chick embryo adapted type II MEF strain, used for oral vaccination, and Monto had observed that VIF was present when the virus had been cultivated in human cells, but not when it had been cultivated in chick embryo cells. Since VIF activity was always determined on human cells, the species specific effect was right there! As Peyton Rous once put it, “the facts are staring us in the face, but we don’t recognize them”!. But more about Peyton Rous later. Sometime during the spring of ’59, and thinking that chick-embryo adaptation had something to do with it, I discussed with Monto and the Chief the possibility of examining whether VIF was also made in cultures infected with the chick-embryo adapted Edmonston strain of measles virus. I found indeed that VIF activity appeared in HeLa and human amnion cell cultures infected with

measles virus, and that more was made in cultures infected with the attenuated, chick cell adapted strain than in cultures infected with the regular Edmonston strain. To see cells become totally resistant to virus infection and present a healthy picture while the controls were destroyed in a matter of days was quite impressive, and I realized that this was potentially very important and made it my major subject of investigation. When I discussed these results with the Chief (by this time Monto had left), he only displayed a mild interest (or at least that’s how it seemed to me), his major preoccupation being the development of a measles vaccine. That this was something that maybe one day could lead to a clinical application was never discussed, and I forgot whether or not it crossed my mind. We were, however, quite convinced that VIF must be part of the natural defense mechanisms against viral infection. Later, the work of Cantell and Tommila on the protection of rabbits’ eyes against vaccinia infection by rabbit interferon came out (K. Cantell and V. Tommila, *The Lancet*, II, 7152:682, 1960), as well as the paper by Hitchcock and Isaacs on the protection of mice against Bunyamwera virus encephalitis (G. Hitchcock and A. Isaacs, *Brit. Med. J.* 5208: 1268-1207, 1960), but the protective effects were so borderline that we considered it more as another demonstration of the antiviral effect of interferon than as a promise of clinical application. In my notebooks, I kept referring to the antiviral activity as VIF.

Then, during the winter 59-60, Alick Isaacs visited the Enders lab and gave a lecture at Harvard Medical School. Talking to Alick, I realized that most probably I was working with interferon; it just seemed the most economical hypothesis. When I go through my notebooks of that period, I find that, whereas on March 3 1960 I still refer to VIF, on April 2 1960, I no longer refer to “measles VIF”, but to “measles interferon”. In the paper published in 1961 describing our results with measles virus, we refer to the antiviral activity as “interferon”, and conclude by saying “it is reasonable to assume that measles interferon, influenza interferon, TIC and VIF may be related though not identical substances” (E. De Maeyer and John F. Enders, *Proceedings of the Society for Experimental Biology and Medicine* 107:573-578 1961). To the best of my knowledge, this is the first paper in which the Chief no longer refers to the antiviral activity as VIF, since by then he was also of the opinion that the induction of VIF

and of interferon were most likely related, if not identical, phenomena. By the time Ion Gresser arrived in the lab, sometime in mid '59, we still referred to the antiviral activity we were working with as "VIF", but manifestly we were not doing too badly, since Ion got hooked, and hasn't left interferon since. (It was also the beginning of a life-long friendship, and, through some quirk of fate, we both ended up with the CNRS in France). Then Jan Vilcek's paper on an interferon-like substance made by Tick-borne encephalitis virus infected chick cells appeared, indicating that this really was a general phenomenon of virus infection (J. Vilcek, *Nature*, 187; 73-74 1960). Early 1960, working on measles virus-induced interferon, I observed that the chick-adapted vaccine strain of Edmonston measles virus induced up to three times as much interferon in human amnion cell cultures than did two strains of wild-type virus (Edmonston and Creel), resulting in smaller viral plaque size when plated on primary human cells and on cells of two different human cell lines. In addition, when comparing the interferon production of attenuated and virulent poliovirus, I also found that more interferon appeared in cell cultures infected with the attenuated type 2 MEF strain than with the virulent strain. This greatly stimulated the Chief's interest, and he mentioned my findings in the James M. Anders lecture he gave at the College of Physicians of Philadelphia on March 2 1960 (*Transactions and Studies of the College of Physicians of Philadelphia*, 4 Ser. Vol 28 No 2. 1960; See also the letter of John F. Enders to E.D.M. of February 2. 1962). I left the Enders lab in the summer of 1960 to go to the Rockefeller Institute in New York and the work on interferon induction by virulent and attenuated virus was continued, and confirmed, by the Chief and his technician Betty Grogan (see letter J.F. Enders to E.D.M. of February 2. 1962). This was probably the only time that the Chief himself did experiments with interferon, and it shows that he really was interested in attenuation and interferon production, as was Alick Isaacs (see letter of Alick Isaacs to E.D.M. of August 1st, 1962). The paper on interferon production and plaque formation by virulent and attenuated measles virus was finally published in 1965 (De Maeyer and Enders, *Archiv Ges. Virusforschung*, XVI, 151-160 1965).

The two years I spent with Enders at the Children's Hospital in Boston were among the happiest of my professional life, and, moreover, were the most fateful,

since I never managed to get completely away from interferon, which was, still is, and will always be a fascinating subject of research. Also, and more importantly, these two years were a source of happiness of a different kind, in that I met at Children's a charming young Swiss lady, by name of Jaqueline Guignard, who was in training as a pediatric endocrinologist with John F. Crigler and who, forty years later, still is with me. Pediatric endocrinology's loss was interferon's gain (not to speak of mine!).

While in Boston I had become interested in tumor viruses and had even done a half-hearted attempt to develop an in vitro assay for measuring virus-induced cell proliferation, using polyoma virus that the Chief had received from B. Eddy and S. Stewart. For reasons I forgot, I used mouse fibroblasts, cultured in roller tubes, and on one occasion did indeed observe foci of cell proliferation, but, to my great disappointment, was never able to repeat it (of course it was all done so much better a few years later by Luc Montagnier and Ian McPherson!). My interest in tumor viruses led me to apply for a grant to go and work with Peyton Rous, of Rous Sarcoma fame, and in September 1960 I became a research associate at the Rockefeller Institute in New York.

### **1960-1961 NEW YORK (E. De Maeyer).**

At the time I started in New York, Peyton Rous was 81 years old, though I probably should say 81 years young, with the energy and intellectual acuteness of someone half his age. Rous received the Nobel Prize when he was 87 years old, mainly for the work on the chicken sarcoma virus he had started in 1910, but also for the fact that, with J. W. Turner and O.H. Robertson, he had developed a way of conserving erythrocytes, and therefore created the first blood bank. Before that, transfusions could only be done directly from donor to recipient! The newly introduced method saved many lives during the first World War, and of course, after the war. Moreover, whenever one is using trypsin to disperse cells for culture, he is using a method first described by Peyton Rous. I found out very quickly that Rous no longer worked with the chicken sarcoma virus that bears his name, but was mainly interested in chemical carcinogenesis. When I told him about my work in Boston, and my interest in the combination of interferon and tumor viruses, he told me very abruptly "don't jump on the interferon

bandwagon"! This was certainly news to me, since I had not been aware that there was such a thing as an interferon bandwagon. However, Rous did agree with my proposal to try and develop an in vitro assay for tumor viruses and, since he was not looking over my shoulder, I was planning to use interferon anyway once I got the assay worked out. The Rous laboratory was on the third floor of Theobald Smith Hall, and so was Richard Shope's laboratory, and I certainly was privileged to have access to both Shope and Rous. Talking to Dick Shope, I became interested in rabbit papilloma virus as a prototype of a virus that induces a benign tumor, which then sometimes degenerates into a metastatic carcinoma, and this seemed like a good enough system to study the effects of interferon on transformation. Encouraged by Shope, and after many trials and errors, I managed to develop an in vitro assay using newborn rabbit skin in organ culture, displaying proliferation of epidermal cells after infection with the papilloma virus (E. De Maeyer, *Science*, 136:985-986 1962). Unfortunately, after I went back to Belgium in September 1961, and wanted to use the assay and study the effects on interferon on transformation, I found out that the Shope papilloma virus only readily infected cells derived from the American cottontail rabbit, and not from the European wild rabbit! Ironically, a comparable assay was described for human papilloma virus in *Science* in 1992 by someone from Pennsylvania State University, called, of all names, Meyers! I sent him a reprint of my '62 *Science* paper, but never received an answer.

In my discussions with Rous and, more frequently, with Shope, I learned about the activation of rabbit papilloma virus by carcinogens, which made me wonder about the possible effects of chemical carcinogens on interferon production.

### **1961-1965 Louvain (E. De Maeyer and J. De Maeyer-Guignard).**

During my three years in the US, I had kept in touch with Piet De Somer, who had come to see me on several occasions, and became greatly interested in interferon. He, of course, immediately thought of interferon as a possible weapon against viral infections, some sort of antiviral penicillin, and when I returned to the Rega Institute, in October '61, work on interferon had already started, with Edgar Schonke and Carlo

Cocito. De Somer hoped that interferon would soon become a very useful broadspectrum antiviral agent. He arranged for Alick Isaacs to receive an honorary doctorate from the University of Louvain, in February 1962 and in spite of the fact that the antiviral penicillin did not materialize as soon as he had hoped, De Somer kept an active interest in the basic aspects of interferon, and for a long time the Rega Institute was an excellent center of interferon research. That was characteristic of De Somer: he was very much involved and occupied by his industrial interests, he was an astute academic politician, elected three times rector of the university, each time for a five year term, but at heart he remained a scientist, interested in the basic aspects of infectious disease. Several virologists who made outstanding contributions to the interferon field started as students with De Somer, and were encouraged, and financially supported, to engage upon a scientific career. Fons Billiau, Ian Desmijter and Eric De Clerq are among them.

It was in Louvain that Jaqueline and I started working together. Having a Swiss diploma she was not allowed to practice medicine until she had passed several exams, which she eventually did to receive a very impressive certificate, signed by King Baudouin! However, by then she had become so interested in interferon that, to my delight, she decided to continue in the lab. But De Somer, in spite of all his qualities, was of the opinion that the place of a woman was at home, and most certainly not in the laboratory (unless as technicians and secretaries, and then usually only until they were pregnant, when they were asked to leave as soon as it started showing, and were told not to come back after the child was born). De Somer was in perfect agreement with the German dictum that defines the place of a woman as "Kinder, Kuche, Kirche"! In this of course he was not alone, in that it was the then common point of view of the medical faculty of Louvain. This became eventually one of the major reasons why we left Louvain four years later, in June 1965. But I should not anticipate; suffice it to say that, for over two and a half years Jaqueline worked with me at the Rega Institute without being paid, but for the last year in Louvain, and with a letter of recommendation from Alick Isaacs (see letter of February 27 1963 to E.D.M. and of April 10 1963 to J.D.M.G.) she obtained a fellowship from the Lady Tata Memorial Foundation (which was indirectly the

cause for our move to France in 1965).

When I arrived at the Rega in '61, Edgar Schonne, a biochemist who had spent some time at the Wistar Institute in Philadelphia, and Carlo Cocito, a molecular biologist who came from A.D. Hershey's lab at the Carnegie Institute in Washington, had started working with rat interferon, principally because Michel Vandeputte was studying tumors in rats, so that a rat colony was available, together with several lines of rat tumor cells. Working on the mode of action of interferon, we showed specific inhibition by interferon of viral but not cellular mRNA in Sindbis virus-infected rat embryo fibroblasts, which I believe was a first, although our speculation as to how this happened was far off the mark (C. Cocito, E. De Maeyer and P. De Somer, *Life Sciences*, 12:759-764. 1962). The paper did not receive much attention principally, I believe, because it came out too early, before anyone was really interested in the molecular biology of interferon action, but Alick was interested when he heard about it (see letter of August 1st 1962. Alick Isaacs to E.D.M). In view of De Somer's interest in the clinical applications of interferon, I did not think that working with rat interferon was the most direct approach to this goal and he agreed, and switched to human diploid fibroblast interferon, but by then I had left, and the work was continued very nicely by Fons Billiau and Erik De Clercq.

I had not forgotten my conversations with Dick Shope at the Rockefeller Institute, and while at the Rega Institute, Jaqueline and I had started our work on the effect of chemical and physical carcinogens of all sorts on the production and action of interferon, and, among other things, we showed stimulation of polyoma virus through the inhibition of polyoma virus induced interferon production by a chemical carcinogen (as reviewed in E. De Maeyer and J. De Maeyer-Guignard, *Ciba Foundation Symposium on Interferon*, 218-235, 1967). When the first results came out (E. De Maeyer and J. De Maeyer-Guignard. *Virology* 20:536-539, 1963, and E. De Maeyer and J. De Maeyer-Guignard in *Cellular Control Mechanisms and Cancer* edited by P. Emmelot and O. Mulbock, Elsevier 1964), Alick Isaacs was quite excited about the suppression of interferon by chemical carcinogens and wrote us a letter of congratulations telling us that it was first class piece of work (letters of Alick Isaacs to

E.D.M of 13 and 20th September 1963, and also of Alick Isaacs to E.D.M of 25 February 1965 and of 3 March 1965). In fact, throughout our stay in Louvain, we were in touch with Alick and kept him informed about our work, which he followed with interest, as attested by some of the attached letters. Early in 1964 I had finally obtained some money to go to London and visit Alick, but then I received a letter from Helio Pereira, informing me about Alick's illness (letter of H. Pereira to EDM of 9th January 1964). After that, there were a few more attempts to bring me over to London (see for example letter of Alick Isaacs to E.D.M. of 14 April 1965), but I never made it, something that I regretted bitterly after Alick's untimely death.

In view of my "poliovaccine past", I was invited in September 1962 to the then annual meeting on polio, which that year took place in Prague. But instead of presenting some old and what I believed to be rather boring results on polio vaccination in Belgium and in the Congo, I took the liberty of talking about my work on interferon in the Enders lab. At the end of the session, I was addressed by a young man (he was about my age, so he was young!) who said that he was also working on interferon and had wanted to ask me some questions after my talk, but could not do so because he was occupied in a booth, interpreting my talk into Russian. This is how I met Jan Vilcek! We continued our conversation in a Beer Hall over some good lager, and immediately got along very well. And so began another life-long friendship. In the fall of 1964, Jan organized what I believe to be the first large international meeting on interferon. at the castle of Smolenice, which belonged to the Academy of Sciences (and was amply equipped with hidden microphones!). Jaqueline and I, as well as Piet De Somer, attended the meeting, where we met a number of people working on interferon that we only knew by name, among which were Kurt Paucker, Kari Cantell and Joseph Sonnabend. Sam Baron and Bob Friedmann were also there, but we had made their acquaintance the year before when they visited us in Louvain and Ed Kilbourne, who also attended. I had met in New York in 1963 when he invited me to give a seminar about our work on interferon and steroids (E.D.M and J.D.M-G *Nature*, 197:724-725 1963). Bob Friedman and Joseph Sonnabend presented the results of some experiments they had done at Mill Hill, showing that the antiviral action of interferon could be inhibited by puromycin, an

inhibitor of protein synthesis. As far as I remember, this was the first indication that interferon acted via the induction of other proteins. Also present was Andre Lwoff; I had told him about my and Monto's work when he was visiting the Enders lab, I believe in 1960, and he had kept an interest in interferon. Alick Isaacs unfortunately was unable to attend because of illness. And when, a few months after that meeting, Jan and Marica decided to flee the Communist regime and cross the iron curtain, sometime late '64, I was extremely happy that I could be of some help, and still think this is one of the better things I have done.

For a number of reasons, among which the fact that Jaqueline and I enjoyed working together but that Jaqueline would never obtain a permanent position at the Rega Institute for reasons I explained earlier, we decided to leave Louvain. Naturally, our first thought was of returning to Boston, where we had such fond memories. Robert B. Berg, one of the postdocs I had met in Enders lab, who in the meantime had become Assistant Professor in Pediatrics at Harvard Medical School and Pediatrician in Chief at the Beth Israel Hospital, offered us some lab space. Together with Bob, we applied and obtained a 3 year NIH grant for studying the effects of carcinogens and steroids on viral replication (grant reference number 1RQ1 CA08151-01), and we were all set to return to Boston. But a few months before we were due to leave, Jaqueline was invited to give a seminar at the Radium Institute in Paris by Raymond Latarjet, whom we had met at a tumor meeting in Amsterdam at which we presented our results on interferon and carcinogens and who, unbeknownst to us, was a member of the Lady Tata Foundation committee that had awarded her a fellowship. When in Paris we told Latarjet that we would soon be moving to Boston, upon which he offered us a laboratory in a new institute he was building on the Orsay campus of the University of Paris, and, with the help of Andre Lwoff who wrote a nice letter of

recommendation, he arranged for us to join the CNRS. This was thirty five years ago, and this is how interferon was introduced as a subject of research at the Radium Institute, which has since become the Curie Institute.

After Ion Gresser left the Enders lab in 1964, some work on interferon and SV40 virus was carried out for a few years by Michael Oxmann, showing a continued interest of John Enders in interferon, but after Mike Oxmann left, the work on interferon came to a halt. In 1972, in collaboration with Luc Montagnier, we isolated interferon mRNA. We dedicated our paper to John F. Enders on the occasion of his 75th birthday anniversary, and in reply he wrote us a very nice letter (letter of John F. Enders to E.D.M. of April 7, 1972), as he also did two years later when we were able to translate the mRNA in a cell-free system (letter of John F. Enders to E.D.M of March 15, 1976). John Enders kept his laboratory at Childrens Hospital until 1977, when he was 80 years old. He died suddenly in 1985, at the age of 88, while sitting in his garden reading poetry to his wife Carol.

#### Conclusion.

In retrospect, if Alick Isaacs and Jean Lindenmann had not discovered interferon, Ho and Enders would have done so. However, the genius of Alick and Jean consisted not only of discovering the substance, but also of naming it well. After all, the *International Society for Interferon Research*, created by William E. Stewart in 1983, was an immediate success but I am less than convinced that an *International Society for Viral Inhibitory Fluid Research* would have taken off as well.

Augerville-la Riviere. May 1st, 2000

Edward De Maeyer

Jaqueline De Maeyer-Guignard



## Grace Wong's Student Vision

By Thomas Tan

**D**r. Grace Wong is no stranger to the biotech and pharmaceutical worlds. She received a PhD from the University of Melbourne at the Walter and Eliza Hall Institute (WEHI) of Medical Research, Australia, followed by a Postdoc at Genentech. In 1996, Dr. Wong became Head of Apoptosis Research at Millennium Pharmaceuticals, identifying drug resistance genes. In 1998, she joined AstraZeneca as Head of Molecular Genetics, focusing on Alzheimer's disease. From 1999-2002, she was Head of Reproductive Genomics at Serono, seeking new cytokines for treatment of obesity and women's diseases. Unable to suppress her entrepreneurial gene, Dr. Wong recently founded ActoKine Therapeutics (<http://www.actokine.com>).

This article, however, is not about Dr. Wong's accomplishments or her new company. It is about her intense desire to help science students and give something back to the scientific community. Dr. Wong has recently founded Student Vision, a non-profit organization, to nurture the next generation of biotech scientists and entrepreneurs. She has created a bi-monthly forum, the Nobel Pauling Biotech Symposia, held at the MIT faculty club, where biotech students, academicians, and professionals from companies gather to meet and share the newest ideas on cutting-edge biotechnology. We interviewed Dr. Wong to find out about Student Vision and its founder. We, in turn, were reminded of our responsibilities to society, and the joy of working in science.

### **Tell us about Student Vision.**

The Mission of Student Vision is to inspire and provide opportunities for biotech students of all ages. Student Vision has three goals: First, to provide opportunities for academia, biotech and biopharma to meet and to collaborate. The second is to encourage the exchange of ideas and new drug discoveries. The third is to train

science students to be innovative. All are welcome, from novice to expert. We organize and sponsor many activities. For example, we have educational seminars by scientists and entrepreneurs, known as the Nobel Pauling Biotech Symposia. Programs are being developed to teach students basic laboratory skills and to support job search. Members are coached on how to present their ideas and provided with a forum to do so. Eventually, we hope to be in a position to award scholarships to science students. But our work goes beyond professional development. Most importantly, we are building a community of friends and colleagues. For example, we host holiday gatherings on Christmas and Thanksgiving. Much of the work is done by the wonderful volunteers who help run the Symposia.

### **What prompted you to create Student Vision?**

Throughout my career I have been helped and guided by many people. It is impossible to fully acknowledge the roles of my mentors. My mentors are also my good friends to whom I owe a debt of gratitude for all their support of my endeavors.



DR. GRACE WONG

Like many other people, I lost friends on September 11. I was terribly saddened; but I was also awakened. More strongly than ever, I felt the need to keep a promise made to myself years earlier. There never seems to be an appropriate time, but when you feel your own mortality you know that the time is now. With the support of many friends, I gathered my courage, quit my job, and started my two ventures. My twins, ActoKine Therapeutics and Student Vision were born in 2003. Throughout my working life, I have focused on science, paying little mind to my biotech stocks and missing opportunities to be wealthy. Even so, I still have plenty of ideas to share.

### **How did you come up with the idea of the Nobel Linus Pauling Biotech Symposium?**

I knew Dr. Linus Pauling personally. A very special mentor, he taught me how to express ideas, how to see things differently, and told many funny stories. Dr. Pauling won two Nobel Prizes- for Chemistry in 1954

and for Peace in 1962. Sharing his passion for peace with Albert Einstein, he was admired worldwide. The Student Vision Symposia are in honor of the life and works of Dr. Linus Pauling.

Dr. Linus Pauling Jr. has authorized Student Vision to use his father's name. In fact, many scientists inspired by Dr. Linus Pauling have been our speakers at the Nobel Pauling Symposia.

Each Nobel Pauling Biotech Symposium is by invitation only and is free. We do ask everyone, even speakers, to pay towards their own dinners. These symposia provide unique opportunities for people who otherwise could not afford to attend commercial biotechnology meetings. Refreshments are provided throughout the seminars, and we try to maintain a very friendly and informal atmosphere that is conducive to networking and open discussions.

To make networking opportunities plentiful for all attendees, we invite only 150 people. So, this is really an ideal venue for meeting biotech and pharma company executives and decision-makers face-to-face. One student told me that she spoke with more biotech and pharma people in one evening, than she had in her entire life.

### **How do you get the speakers for the Symposium?**

When I was at Genentech, I seemed to be the only scientist without a business card. Many people at conferences gave me cards without my asking. At the time, I didn't see the value of the cards, but never discarded one. I'm glad now, having collected over 10,000 business cards in the past ten years. They are a source of contact information to invite speakers to the symposium. We don't have money to pay for travel or hotel expenses, so we create special symposia for those speakers who come to Boston for other reasons. As you might expect, those who come to speak at their own expense truly support our vision. In appreciation, speakers are presented with memento gifts: mugs, T-shirts, or posters with a photo of Dr. Linus Pauling. There are over 100 confirmed speakers for our symposium series. Your readers can see speaker biographies and photos on our web site ([www.studentvision.org](http://www.studentvision.org)).

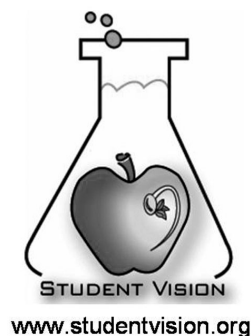
### **Tell us about the Linus Pauling Scholarships.**

My family escaped to Hong Kong from China in a small

boat when I was two. My sister hid me in belongings tied to the front of the boat. We were so poor that there was not even a photo taken of my father before he died. Never dreaming I could become a scientist, I worked hard, and was the fortunate recipient of scholarships supporting me all the way through my PhD. So, I thought it would be a nice idea to create a scholarship fund for under privileged students regardless of their age. Scientific discovery is not only my profession and my dream, it's also my hobby, and it's really fun. I hope through Student Vision we can motivate more students to create the joy of working in science.

### **Where is Student Vision going today?**

We hope to enlist more sponsors to make the Nobel Pauling Symposia even more successful. We hope that in the future speakers and students do not have to pay for their dinner at a Nobel Pauling Symposium. We hope to produce some biology products that will be purchased by biotechnology and pharmaceutical companies. We hope to do fee-for-service (assay, reagents etc) for biotechnology and pharmaceutical companies and we also hope to transform their trash to treasure for new drug discovery. We may call this "trash to cash".



This would allow Student Vision to be financially independent and provide for its continued growth and development of new activities.

### **What's next for Grace Wong?**

I ask myself: What is the real meaning of success? Becoming rich and famous, without giving back to the community, is not full success. I want to create a commercial enterprise where people can learn and be useful; an enterprise, which is a job creating engine, even for people who have not had a chance to be educated. Every individual has potential, and like a dormant seed, should have a chance to grow. I want to plant and nurture as many scientist seeds as possible, creating opportunities for young scientists to meet experts. I want to help establish a foundation granting


Linus Pauling Scholarships to students from around the world who lack financial means for bioscience education. Creating or building an endowment for Student Vision will help support the most creative students. Hopefully, ActoKine Therapeutics can discover new uses for failed drugs in biotech and pharmaceutical company portfolios. Milestone payments and royalties generated by these drugs could allow ActoKine to endow Student Vision.

### **Any advice for our student readers interested in a career in biotech?**

Yes, working hard is sometimes not enough to keep a job. This is especially true for the biotech and pharmaceutical industries. We have to be creative and to be constantly learning about the newest, cutting-edge

techniques just to stay even, much less to get a little ahead.

If your company believes your ideas will one day add value to the bottom line, the company will support you. This is important – to see one’s job as a friendship and a partnership with your employer and coworkers. You can be a productive scientist as long as you are creative, hardworking, healthy, happy, and helpful to others, even when you are 99 years old.

Readers who are interested in supporting Student Visions’ mission and becoming speakers, sponsors, or volunteers can contact Student Vision ([www.studentvision.org](http://www.studentvision.org)). 

## **Dilbert’s Rules of Order**

1. I can only please one person per day. Today is not your day. Tomorrow is not looking good either.
2. I love deadlines. I especially like the whooshing sound they make as they go flying by.
3. Tell me what you need, and I’ll tell you how to get along without it.
4. Accept that some days you are the pigeon and some days the statue.
5. Needing someone is like needing a parachute. If he isn’t there the first time, chances are you won’t be needing him again.
6. I don’t have an attitude problem, you have a perception problem.
7. Last night I lay in bed looking up at the stars in the sky, and thought to myself, where the heck is the ceiling?
8. My reality check just bounced.
9. On the keyboard of life, always keep one finger on the escape key.
10. I don’t suffer from stress. I am a carrier.
11. You are slower than a herd of turtles stampeding through peanut butter.
12. Do not meddle in the affairs of dragons, because you are crunchy and taste good with ketchup.
13. Everybody is somebody else’s weirdo.
14. After any salary raise, you will have less money at the end of the month than you did before.
15. Eat one live toad first thing in the morning and nothing worse can happen to you that day.
16. If it wasn’t for the last minute, nothing would get done.
17. When you don’t know what to do, walk fast and look worried.

# NEW MEMBERS

The ISICR welcomes the following new members to our society and invites them to participate in the Annual meeting, serve on ISICR committees and/or the newsletter Editorial Board. For information on any of these activities, please contact the ISICR membership office ([www.isicr.org](http://www.isicr.org)), ISICR President Keiko Ozato or Howard Young. Full contact information for the new members can be obtained from the Business Office.

<b>Anna Marie Aguinaldo</b> Monrovia, CA	<b>John Fong</b> Toronto, Canada	<b>Bernd Kaspers</b> Munchen, Germany	<b>Milan Popovic</b> Ulm, Australia
<b>Michal Alter-Koltunoff</b> Haifa, Israel	<b>Serge Y Fuchs</b> Philadelphia, PA	<b>Michael Soo Ho Kim</b> Bundall, Australia	<b>Richard M. Ransohoff</b> Cleveland, OH
<b>Annika Antonsson</b> Bristane, Australia	<b>Martina Fuchsberger</b> Melbourne, Australia	<b>Hsiang-Fu Kung</b> Pofulam Road, Hong Kong	<b>David M. Reynolds</b> Frederick, MD
<b>Sarah-Jane E. Beavitt</b> Melbourne, Australia	<b>Grant Gallagher</b> Newark, NJ	<b>Bing Hua Li</b> Shanghai, China	<b>Giovanna Romeo</b> Rome, Italy
<b>Liang Chu</b> Shanghai, China	<b>Daniel J. Gough</b> Melbourne, Australia	<b>Marie Chia-Mi Lin</b> Pokfulam, China	<b>Matthew J. Ruddy</b> Buffalo, NY
<b>Daniel T. Clarke</b> Brisbane, Australia	<b>Nathalie Grandvaux</b> Montreal, Canada	<b>Jianguo Liu</b> New York, NY	<b>Shamith A. Samarajiva</b> Clayton, Australia
<b>Ann Cornish</b> Parkville, Australia	<b>Rouha M. Granfar</b> Gold Coast, Australia	<b>Nicholas W. Lukacs</b> Ann Arbor, MI	<b>Bernadette Swart</b> North Adelaide, Australia
<b>Peter J. Crack</b> Melbourne, Australia	<b>Amy Marie Hicks</b> Winston-Salem, NC	<b>Joao T. Marques</b> Cleveland, OH	<b>Mesplede Thibault</b> Paris, France
<b>Richard J. D'Andrea</b> North Adelaide, Australia	<b>Douglas J. Hilton</b> Parkville, Australia	<b>Albert S. Mellick</b> Gold Coast, Australia	<b>Jin Hui Wang</b> Shanghai, China
<b>Jeane De Freitas</b> Melbourne, Australia	<b>Hubertus Hochrein</b> Munich, Germany	<b>Liliana B. Munoz</b> Woolloongabba, Australia	<b>Trevor J. Wilson</b> Melbourne, Australia
<b>Genevieve Despars</b> Canberra, Australia	<b>Linn Sara Margareta Hjortsberg</b> Stockholm, Sweden	<b>Andrew D. Nash</b> Richmond, Australia	<b>Grace H.W. Wong</b> Chestnut, MA
<b>Catherine C. Drinkwater</b> Richard, Australia	<b>Hiroaki Ikeda</b> St. Louis, MO	<b>Susie-Jane Noppert</b> Clayton, Australia	<b>Dakang Xu</b> Melbourne, Australia
<b>Natalie Dror</b> Haifa, Israel	<b>Aaron T. Irving</b> Brisbane, Australia	<b>Kirrily Anne O'Hara</b> Nedlands, Australia	<b>Zi Lai Zhang</b> Shanghai, China
<b>Karen Anne Duca</b> Blackburg, VA	<b>Nicole Jackson</b> Sydney, Australia	<b>Chi Ong</b> Parkville, Australia	

## PIs/Senior Investigators!!

**Urge your fellows/students to join and maintain their membership in the ISICR. Remember membership for fellows/students is only \$10/year!!!!**

# Clinical Trials

Phase II study of Oblimersen and **interferon alfa** in patients with metastatic renal cell cancer. Contact: Kim Allyson Margolin, MD, Study Chair, Beckman Research Institute, City of Hope Comprehensive Cancer Center, Duarte, California, 91010-0269, Phone: 626-359-8111. Study ID Numbers CDR0000298756; CHNMC-PHII-42; NCI-5828

Randomized phase III trial to compare the effectiveness of isotretinoin and **interferon alfa** combined with vitamin E to that of observation in treating patients who have undergone surgery and/or radiation therapy for stage III or stage IV head and neck cancer. Contact: Dong Moon Shin, MD, Study Chair, University of Pittsburgh Cancer Institute. Study ID Numbers CDR0000271174; E-1301

Phase II trial to study the effectiveness of combining **interferon alfa** and isotretinoin with paclitaxel in treating patients who have recurrent small cell lung cancer. Contact: Joseph Aisner, MD, Study Chair, Cancer Institute of New Jersey. Study ID Numbers CDR0000304430; E-E6501

Randomized trial of therapy of early phase chronic myelogenous leukemia with high-dose Imatinib Mesylate (Gleevec) alone or in combination with **Peg-Alpha Interferon (PEG-Intron)** and **Sargramostin (GM-CSF)**. Contact: Jorge E Cortes, MD, M.D. Anderson Cancer Center, Houston, Texas, 77030, Phone: 713-794-5783, E-mail: jcortes@mdanderson.org. Study ID Numbers ID02-534

Study of Viral Resistance to Antiviral Therapy of Chronic Hepatitis C (Virahep-C), to test the hypothesis that African-Americans respond less well to combination **pegylated interferon** and ribavirin therapy than Caucasian-Americans who have chronic hepatitis C genotype 1 and who were not previously treated with either **interferon** or ribavirin. Contacts in multiple US states; e.g. Melissa Gast, BA, Phone: 415-502-8612, E-mail: gastm@itsa.rcsf.edu, University of

California, San Francisco, San Francisco, California, 94143; Principal Investigator: Norah Terrault, MD, MPH. Study ID Numbers Virahep-C; U01 DK60329

Randomized phase II trial to compare the effectiveness of voriconazole with or without **interferon gamma** in treating patients who have aspergillosis or other fungal infections. Contact: Thomas John Walsh, MD, Study Chair, Pediatric Oncology Branch, National Cancer Institute. Study ID Numbers CDR0000298887; NCI-03-C-0111.

Treatment of patients with metastatic melanoma using recombinant vaccinia and fowlpox viruses encoding the tyrosinase antigen in combination with **interleukin-2**. Contact: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754, Toll Free: 1-800-411-1222, TTY: 301-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, E-mail: prpl@mail.cc.nih.gov. Protocol Number: 03-C-0080.

Relationship between religiosity and spirituality and immune functioning, as measured by **interleukin-6** blood plasma level among terminally ill cancer patients. Contact: Colleen S McClain, MA, Calvary Hospital, Bronx, New York, Phone: 646-207-3563, E-mail: cmclain@fordham.edu. Principal investigators: Barry Rosenfeld, PhD, Fordham University; William Breitbart, MD, Memorial Sloan-Kettering Cancer Center. Study ID Numbers F31 AT001769-01.

A Phase I study of subcutaneous "**CYT 99 007**" (**interleukin-7**) in patients with refractory non hematologic malignancy. Contact: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754, Toll Free: 1-800-411-1222, TTY: 301-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, E-mail: prpl@mail.cc.nih.gov. Protocol Number: 03-C-0152.

Phase I investigation of **interleukin-12 (NSC 672423)/pulse interleukin-2 (Aldesleukin)** in children with persistent and/or refractory neuroblastoma. Contact: National Cancer Institute (NCI), 9000 Rockville Pike, Bethesda, Maryland,

20892, Patient Recruitment and Public Liaison Office  
Phone: 1-800-411-1222, e-mail: prpl@mail.cc.nih.gov,  
TTY: 1-866-411-1010. Study ID Numbers 030252; 03-  
C-0252

Pilot imaging study to assess the distribution of **IL13-  
PE38QQR** cytotoxin infusions in patients with  
recurrent, resectable, supratentorial malignant glioma.  
Contacts: David Croteau, MD, FRCP(C), Phone :  
847-295-8678, E-mail : dcroteau@neophrm.com;  
Amy Grahn, Phone: 847-295-8678, E-mail :  
agrahn@neophrm.com. Duke University Medical  
Center, Durham, North Carolina, 27710; Sandra  
Tourt-Uhlig, RN, Phone: 919-681-6757, E-mail:  
tourt001@mc.duke.edu; Denise Lally-Batts, NP,  
Phone: 919-684-3862, E-mail:  
lally001@mc.duke.edu. Principal Investigator: John  
Sampson, MD, PhD. Study ID Numbers IL13PEI-  
105

Evaluation of Single Nucleotide Polymorphism (SNP)  
(e.g. **cytokines, chemokines, adhesion molecules**)  
in patients with and subjects without Age-related  
Macular Degeneration (AMD). Contact: Patient  
Recruitment and Public Liaison Office, Building 61, 10  
Cloister Court, Bethesda, Maryland 20892-4754, Toll  
Free: 1-800-411-1222, TTY: 301-594-9774 (local), 1-  
866-411-1010 (toll free), Fax: 301-480-9793, E-mail:  
prpl@mail.cc.nih.gov. Protocol Number: 03-EI-0155.

Combination chemotherapy with or without **Colony-  
stimulating Factors** in treating women with breast  
cancer. Contacts in multiple US States and in Canada  
e.g. Omar Atiq, MD, Phone: 870-535-2800, E-  
mail: aliq@dnamail.com, Arkansas Cancer Clinic,  
P.A., Pine Bluff, Arkansas, 71603; Paul L. D. Walde,  
MD, Phone: 705-759-1234, E-mail:  
davidwalde@home.com, Algoma District Medical  
Group, Sault Sainte Marie, Ontario, P6B 1Y5. Study  
Chairs: Mark Norman Levine, MD, Cancer Care  
Ontario-Hamilton Regional Cancer Centre; Edith A.  
Perez, MD, Mayo Clinic Cancer Center. Study ID  
Numbers CDR0000068520; CAN-NCIC-  
MA21; AMGEN-CAN-NCIC-MA21; NCCTG-  
CAN-NCIC-MA21; BMS-CAN-NCIC-  
MA21; JANSSEN-CAN-NCIC-MA21; P-  
UPJOHN-CAN-NCIC-MA21.

A Phase I/II pilot study of sequential vaccinations with  
rFowlpox-PSA (L155)-TRICOME (PROSTVAC-F/  
TRICOM) alone, or in combination with rVaccinia-  
PSA (L155)-TRICOME (PROSTVAC-V/TRICOM),  
and the Role of **GM-CSF**, in patients with prostate  
cancer. Contact: National Cancer Institute  
(NCI), 9000 Rockville Pike, Bethesda, Maryland,  
20892, Patient Recruitment and Public Liaison Office  
Phone: 1-800-411-1222, e-mail:  
prpl@mail.cc.nih.gov, TTY 1-866-411-1010. Study  
ID Numbers 030176; 03-C-0176

Cardio Vascul-Grow (**Human Fibroblast Growth  
Factor 1**) for treatment of coronary heart disease.  
Contact: Mary Riggs, Phone: 301-208-9100, E-mail:  
maryr@c2r.net, St. Joseph Medical  
Center, Towson, Maryland, 21204. Principal  
Investigators: John C Laschinger, M.D., John Boehmer,  
M.D. Study ID Numbers CVGE-2002-01.

Study of both established (e.g. mineral ions, bone  
markers, PTH-Vit D system, TMP-GFR) and novel  
(e.g. **Fibroblast Growth Factor-23** and MEPE)  
constituents of the phosphorus metabolism pathway  
(important for cellular metabolism and bone structure) in  
a collection of blood and urine samples. Contact:  
Patient Recruitment and Public Liaison Office, Building  
61, 10 Cloister Court, Bethesda, Maryland 20892-  
4754, Toll Free: 1-800-411-1222 TTY: 301-594-  
9774 (local), 1-866-411-1010 (toll free), Fax: 301-  
480-9793, E-mail: prpl@mail.cc.nih.gov. Protocol  
Number: 03-D-0254.

Phase I study of aerosolized **Sargramostim (GM-  
CSF)** in patients with metastatic melanoma to the lung.  
Contacts in multiple US States and in Canada e.g. John  
C. Michalak, MD, Phone: 712-252-0088, E-mail:  
shoa@pionet.net, Siouxland Hematology-  
Oncology, Sioux City, Iowa, 51101-1733;  
Muhammad Salim, MD, Phone: 306-766-2203 E-  
mail: msalim@scf.sk.ca, Allan Blair Cancer  
Centre, Regina, Saskatchewan, S4T 7T1. Study  
Chair: Svetomir Markovic, MD, PhD, Mayo Clinic  
Cancer Center. Study ID Numbers  
CDR0000068654; NCCTG-N0071

ISIS 2302-CS22, Phase II, double-blinded, active-  
controlled study of Alicaforsen (ISIS 2302) Enema, an

antisense inhibitor of **ICAM-1**, for the treatment of patients with mild to moderate active ulcerative colitis. Contact: ChinYin Lim, Phone: 1-800-679-ISIS, Chicago, Illinois. Study ID Numbers ISIS 2302-CS22

An investigation of the **inflammatory response** (keyword **interferon, cytokine**) in Severe Acute Respiratory Syndrome (SARS). Contact: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754, Toll Free: 1-800-411-1222, TTY: 301-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, E-mail: prpl@mail.cc.nih.gov. Protocol Number: 03-I-0240.

Phase I trial to evaluate the safety of **PDGF-B** and a limb compression bandage in venous leg ulcers.

Contact and Principal Investigator: David J. Margolis, M.D., Phone: 215-898-4938, E-mail: dmargoli@cceb.med.upenn.edu, University of Pennsylvania, Philadelphia, Pennsylvania, 19104. Study ID Numbers NIAMS-044; N01 AR-9-2238

Randomized Phase III trial of hyperthermic isolated limb perfusion and melphalan with or without **Tumor Necrosis Factor** in the patient with localized, advanced, extremity melanoma. Contact: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754, Toll Free: 1-800-411-1222, TTY: 301-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, E-mail: prpl@mail.cc.nih.gov. Protocol Number: 03-C-0137

## Signal Transducers and Activators of Transcription (STATs) Activation and Biology

**Edited by:** Pravin B. Sehgal, M.D., Ph.D. New York Medical College, Valhalla, New York, USA David E. Levy, Ph.D. New York University School of Medicine, New York, New York, USA Toshio Hirano, M.D. Osaka University School of Medicine, Osaka, Japan c. 750pp, including colour plate section, publication due December 2003

The year 2003 marks the tenth anniversary of the first use of the acronym "Stat" (also written "STAT") in the scientific literature for a family of transcription factors which rapidly transduce cytokine- and growth factor-elicited signals from the plasma membrane to the cell nucleus thereby activating gene transcription (thus, Signal Transducers and Activators of Transcription). The only fully comprehensive reference for what is known about STAT proteins and their biology, this book describes the current state of ongoing research in this broad area, and looks toward the future to try to predict the discoveries that lie ahead. With contributions from the very best experts in the field, it will prove useful to both the novice and the expert, providing a didactic overview of the STAT transcription factor field, a summary of past literature, current developments, and new uncharted, perhaps controversial, ideas and questions about STAT activation and biology.

Divided into 3 sections: I) Proteins and their Regulators; II) Mechanisms of Activation of and Transcriptional Regulation by STAT protein; III) Biological Impact of STAT Activation

### Contributors include:

**James E. Darnell, Jr., Bernd Groner, Peter C. Heinrich, Douglas J. Hilton, James N. Ihle, Ian Kerr, Warren Leonard, Kenneth M. Murphy, Lloyd J. Old, John O'Shea, Norbert Perrimon, Robert D. Schreiber, George Stark**

To receive a full contents/author list, and to order a copy at the special pre-publication price of \$89.50 (valid until 1<sup>st</sup> November), please contact Clare Nehammer at Kluwer Academic Publishers: [clare.nehammer@wkap.com](mailto:clare.nehammer@wkap.com)



## **Biotechnology Industry News.**

<http://biz.yahoo.com/news/biotechnology.html>

The title speaks for itself: Get the latest news in the industry world here.

## **The Cancer Genome Anatomy Project.**

<http://cgap.nci.nih.gov/>

The goal of the NCI's Cancer Genome Anatomy Project is to determine the gene expression profiles of normal, precancer, and cancer cells, leading eventually to improved detection, diagnosis, and treatment for the patient. By collaborating with scientists worldwide, such as the Ludwig Institute for Cancer Research and Lund University, CGAP seeks to increase its scientific expertise and expand its databases for the benefit of all cancer researchers. The "Pathways" option gives a wide range of very nice schematic diagrams of biological pathways and proteins.

## **ExPASy Molecular Biology Server.**

<http://www.expasy.org/>

The ExPASy (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB) is dedicated to the analysis of protein sequences and structures as well as 2-D PAGE.

## **The Mouse Knockout and Mutation database**

<http://research.bmn.com/mkmd>

- find phenotypic information on any knockout generated and reported to date
- link to a relevant review on a mouse model of selected human diseases including cancers, metabolic disorders, cardiovascular diseases & many more.
- find out who provides the mouse model and how it has been used in the related fact files.

To search the database you will need to become a member of BioMedNet. Registration is free and only takes a few minutes at <http://www.bmn.com>

Your search will provide opportunities from an unrivalled wealth of information with

- over 8000 entries
- over 3000 unique genes to browse
- single and compound mutations
- classical mutations of cloned genes
- comprehensive coverage of neurological, immunological and physiological knockouts

- live links to MGD, SwissProt and MEDLINE and to abstracts and full text articles in ScienceDirect and BioMedNet Reviews.

No product dealing in this area matches the Mouse Knockout & Mutation Database for advanced searching, concise format, and expert editorial board input. And with new entries added weekly, you can be sure of comprehensive coverage. Ask your librarian about gaining institutional access.

Meanwhile you can search free abstracts at <http://research.bmn.com/mkmd>

With best wishes,

The MKMD Team  
[mkmd@biomednet.com](mailto:mkmd@biomednet.com)

## **Oligo Calculator**

<http://burst.sparklist.com/scripts/nph-tpl?U=764&M=5547589&MS=3262433>

For testing sequences! BioSource Custom Oligo website offers an oligo calculator tool! Try our oligo calculator tool for assessing compatibility of DNA sequences in molecular applications. This tool allows the user to enter a sequence, including any 3' or 5' modifications, and determine the T<sub>m</sub>, molecular weight, TD and extinction coefficient.

## **Online Analysis Tools.**

<http://molbiol-tools.ca/>

Includes bioinformatics tutorials, DNA, RNA, transcription or protein analyses, and other useful molecular biology tools.



**Public blast server and emboss server at the GBF, Braunschweig.**

<http://ngfnblast.gbf.de/ebblast.html>  
<http://ngfnblast.gbf.de/uk/emboss.html>. Introductory page:  
<http://ngfnblast.gbf.de/uk/index.html>

Yours sincerely  
Werner Müller  
Email: [wmueller@gbf.de](mailto:wmueller@gbf.de)

**The Protein Kinase Resource.**

<http://pkr.sdsc.edu/html/index.shtml>

The Protein Kinase Resource (PKR) aims to become a web accessible compendium of information on the protein kinase family of enzymes. This resource will include tools for structural and computational analyses as well as

links to related information maintained by others. The PKR is a collaborative project of protein kinase researchers and computational biologists working to create a database integrating molecular and cellular information.

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**2004 American Association of Immunology Guest Symposium**

**April 20, 2004 Washington D.C**  
(time/date to be finalized).

**Frontiers of Interferon (IFN) and Cytokine Research**

Chair: Keiko Ozato

Speakers (titles are subject to change)

**Marc Ghany** - NIDDK, NIH "IFN therapy for HCV patients"

**Tomohiko Tamura** - NICHD, NIH "IRFs and IFN/cytokine production in dendritic cells"

**John Hiscott** - McGill University, Montreal, Canada "IRF3 activation and IKK"

**Keji Zhao** - NHLBI, NIH "The role of the chromatin remodeling complex BAF in IFN/viral responses"

Note: The ISICR does not support travel to this meeting.

**AAI 2005 Meeting**

*The ISICR has once again been invited to organize a guest symposium at the 2005 AAI meeting in San Diego, California April 2 - 6. Any ISICR member who will be attending the meeting and would like to organize the symposium, please contact Howard Young.*

# ISICR PRELIMINARY MEETING PROGRAM

Sunday, 26 October 2003

Opening and Welcome

Awards Ceremony

Plenary Lecture

Hall A

*Prof James Darnell, Rockefeller University New York*

4:30 PM - 6:30 PM

Welcome Reception

Mezzanine Level--6:30 PM - 8:30 PM

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Monday, 27 October 2003

## SIGNAL TRANSDUCTION

Plenary -- Hall A

8:30 AM - 10:30 AM

*Dr Curt Horvath, Mount Sinai School of Medicine*  
*Dr Thomas Decker, University of Vienna, Austria*  
*Prof David Levy, New York University School of Medicine, USA*

## SYM 1A – Gene Regulatory Networks

Concurrent Symposium -- Hall A

11:00 AM - 1:00 PM

*Prof Bryan Williams, Lerner Research Institute, USA*  
*Dr Steve Gerondakis, The Walter and Eliza Hall Institute of Medical Research, Australia*  
*Prof David Hume, Institute for Molecular Bioscience, Australia*  
*Prof Nancy Reich, Stony Brook University, Australia*

## SYM 1B – Viral Infections

Concurrent Symposium -- Meeting Room 2

11:00 AM - 1:00 PM

*Dr Stephen Kent, The University of Melbourne, Australia*  
*Prof Ian Frazer, University of Queensland, Australia*  
*Dr Eleanor Fish, Toronto General Research Institute, Canada*  
*Dr Wayne Kindsvogel, ZymoGenetics, USA*

## SYM 1C - Drug Development

Concurrent Symposium -- Meeting Room 1

11:00 AM - 1:00 PM

*Dr Stephen Foster, AstraZeneca, UK*  
*Dr Glen Begley, Amgen, USA*  
*Dr Andrew Wilks, Cytosia Pty Ltd, Australia*  
*Dr William Brissette, Pfizer, USA*  
*Dr Andrew Nash, Amrad Corporation Limited, Australia*

## INNATE IMMUNITY

Plenary -- Hall A

2:00 PM - 4:00 PM

*Luke O'Neill, Trinity College Dublin, Ireland*  
*Prof John Hiscott, McGill University, Canada*  
*Prof Christine Biron, Brown University, USA*

## WKS 1A - Infectious Disease

Workshop -- Hall A

4:30 PM - 6:30 PM

## WKS 1B - Gene Regulation

Workshop -- Meeting Room 2

4:30 PM - 6:30 PM

## WKS 1C - Cytokines and Cancer

Workshop -- Meeting Room

14:30 PM - 6:30 PM

Tuesday, 28 October 2003

**POSTGRADUATE STUDENT BREAKFAST  
WITH SPEAKERS 7.00 AM**

**NEGATIVE REGULATION**

**Plenary Hall A  
8:30 AM - 10:30 AM**

*Prof Nicos Nicola, The Walter and Eliza Hall Institute of Medical Research, Australia  
Dr Akihiko Yoshimura, Kyushu University, Japan  
Dr Wallace Langdon, The University of Western Australia, Australia*

**SYM 2A – Inflammation (SCIL Symposium)**

**Concurrent Symposium -- Hall A  
11:00 AM - 1:00 PM**

*Prof Brian Foxwell, Kennedy Institute of Rheumatology Division, UK  
Prof John Hamilton, The University of Melbourne, Australia  
Prof Patrick Matthys, University of Leuven, Belgium  
Dr Graham Guy, Singapore  
Prof J. Schrader, Vancouver Canada*

**SYM 2B - Models of Receptor Signalling**

**Concurrent Symposium -- Meeting Room 2  
11:00 AM - 1:00 PM**

*Dr Mark Gutheridge, Hanson Centre, Australia  
Dr Matthias Ernst, Ludwig Institute for Cancer Research, Australia  
Dr Shaun McColl, Australia  
Dr Leo Koedermans,*

**SYM 2C - Stem Cells**

**Concurrent Symposium -- Meeting Room 1  
11:00 AM - 12:30 PM**

*Dr Paul Simmons, Peter MacCallum Cancer Centre, Australia  
Prof Anthony Whetton, UMIST, UK  
Prof Perry Barlett, University of Queensland, Australia*

**FREE AFTERNOON-TRIP TO GREEN ISLAND**

**Poster Judging/Wine and Cheese**

**Mezzanine Level  
6:00 PM - 8:00 PM**

Wednesday, 29 October 2003

**TUMOUR IMMUNITY**

**Plenary -- Hall A  
8:30 AM - 10:30 AM**

*Dr Robert Schreiber, Washington University, St Louis, USA  
A/Prof Mark Smyth, Peter MacCallum Cancer Centre, Australia  
Prof Christopher Parish, John Curtin School of Medical Research, Australia*

**SYM 3A – Regulation of Gene Expression**

**Concurrent Symposium -- Hall A  
11:00 AM - 1:00 PM**

*Prof Keiko Ozato, National Institutes of Health, USA  
Dr Frances Shannon, ANU, Australia  
Dr Takashi Fujita, The Tokyo Metropolitan Institute of Medical Science, Japan  
Prof Paula Pitha, Johns Hopkins, Baltimore, USA*

**SYM 3B - Dendritic Cells**

**Concurrent Symposium Meeting Room 2  
11:00 AM - 1:00 PM**

*Prof Mark Suter, University of Zurich, Switzerland  
Dr Francine Briere, Schering-Plough, France  
Dr Meredith O'Keeffe, The Walter and Eliza Hall Institute of Medical Research, Australia  
Dr Hubertus Hochrein, Technical University of Germany, Germany*

**SYM 3C – CNS Disease, Pathogenesis and Therapy**

**Concurrent Symposium -- Meeting Room 1  
11:00 AM - 1:00 PM**

*Dr Daniel Carr, The University of Oklahoma Health Sciences Center, USA  
Dr Iain Campbell, The Scripps Research Institute, USA  
Dr Tom Lane, University of California, USA  
Dr Peter Crack, Monash Institute of Reproduction and Development, Australia*

(Wednesday continued)

**GENOMICS**

**Plenary -- Hall A  
2:00 PM - 4:00 PM**

*Dr Thomas Gingeras, Affymetrix Inc, USA  
Prof Michael Katze, University of Washington, USA  
Dr Warren Alexander, The Walter and Eliza Hall Institute of  
Medical Research, Australia*

**WKS 2A - Signal Transduction**

**Workshop -- Hall A  
4:30 PM - 6:00 PM**

**WKS 2B - Inflammation**

**Workshop -- Meeting Room 2  
4:30 PM - 6:00 PM**

**WKS 2C - Clinical Application**

**Workshop -- Meeting Room 1  
4:30 PM - 6:00 PM**

**CONFERENCE DINNER AT  
ABORIGINAL CENTRE  
6.00 PM**



**Thursday, 30 October 2003**

**SYM 4A - Interferon Regulated Genes  
Concurrent Symposium -- Hall A  
8:30 AM - 10:30 AM**

*Prof Ganes Sen, Cleveland Clinic Foundation, USA  
Dr Divaker Choubey, Loyola University Chicago, USA  
Dr Chris Clarke, Peter MacCallum Cancer Centre, Australia  
Dr Steve Ralph, Griffith University, Australia*

**Sym 4B - Apoptosis  
Concurrent Symposium -- Meeting Room 2  
8:30 AM - 10:30 AM**

*Dr Vanessa Marsden, The Walter and Eliza Hall Institute of  
Medical Research, Australia  
Prof Peter Hersey, University of Newcastle, Australia  
Prof Robert Silverman, Cleveland Clinic, USA  
Dr Akinori Takaoka, University of Tokyo, Japan*

**SYM 4C - Immune Responses  
Concurrent Symposium -- Meeting Room 1  
8:30 AM - 10:30 AM**

*Prof Claude Bernard, La Trobe University, Australia  
Prof Thomas Kay, St.Vincent's Institute of Medical Research,  
Australia  
Dr Howard Young, National Cancer Institute, USA  
Dr Chris Clegg, ZymoGenetics Inc. USA  
Dr Fabien Mackay, Garvin Institue , Sydney, Australia*

**NOVEL CYTOKINES AND SIGNALLING  
Plenary -- Hall A  
11:00 AM - 1:00 PM**

*Dr George Stark, Cleveland Clinic Foundation, USA  
Dr S. Kotenko New Jersey, USA  
Dr L Plataniias, Chicago, II USA*



**Closing**

**Hall A  
1:00 PM - 1:30 PM**



## Reviews of Interest

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- Younes A, Aggarwall BB. Clinical implications of the tumor necrosis factor family in benign and malignant hematologic disorders. *Cancer*. 2003 Aug 1;98(3):458-67.

## Peter Scott's Tutees' intelligence test

A quick test of intelligence. Don't cheat! Because if you did, the test would be no fun. There are no tricks to the test.

Read this sentence:

FINISHED FILES ARE THE RESULT OF YEARS OF SCIENTIFIC STUDY COMBINED WITH THE EXPERIENCE OF YEARS.

Now count the F's in that sentence. Count them **ONLY ONCE**: do not go back to count them again. See below...

Don't look yet...

Keep going..

Just a bit more...

nearly there...

ANSWER:

There are **six** F's in the sentence.

A person of average intelligence finds three of them.

If you spotted four, you're above average.

If you got five, you can turn your nose at most anybody.

If you caught six, you are a genius.

There is no catch. Many people forget the "OF"'s. The human brain tends to translate them as V's and not F's. Interesting, huh?

# DOWN UNDER LINGO or How to speak Australian

(modified from www.ausimports.com)

When your in the “**Land of Oz**” or “**Down Under**”, there are a few words and phrases you might expect to hear.

**G’day mate! Ow ya goinn’? Orright?** - A typical Australian greeting.

**No worries mate!** - A typical Australian reply.

**She’ll be right mate!** - A frequently used reply to any problem, big or small.

**”Too right” or “fair dinkum”** could be roughly translated as “you bet”.

If you travel in the country you are “**in the bush**” or “**outback**”. If you go a really long way into the bush you might reach the mythical “**Black Stump**” which is about as far inland as you can go. Any place on “**the other side of the Black Stump**” is a really long way inland.

If you’re “**roughing it**” (camping) with your “**swag**” (sleeping bag) you could run into a “**Joe Blake**” (snake) when your having your “**tucker**” (dinner).

Toilets in the bush are usually pretty basic and called “**dunnies**”, never bathrooms which is where you find the bath.

If you get lost you are “**up the creek**” or “**up a gum tree**”(in trouble).

If you meet someone whose a bit crazy, he or she is “**a galah**”. Some one who is clever has “**no flies on him/her**”. An unsophisticated Australian is called an “**ocker**” or “**yobo**”. A crazy Aussie is “**mad as a meat-axe**”. A dishonest one is “**as crooked as a dogs hind leg**”.

In Oz, if a man refers to “**trouble and strife**”, he is talking about his wife. “**Billy lids**” are the kids. Women are known as “**sheilas**”; men are “**blokes**”. If you go to the beach, which most Australians do often, watch out for the “**noah’s arks**” (sharks).

Practice these Aussie slangs at happy hours/coffee breaks!

**Smoko:** smoke or coffee break

**Your shout:** If you value your well being you should buy the next drink

**Wanna Rage?** Would you like to drink vasts amounts of alcohol with me until we both drop?

**He’s Blotto:** Inebriated beyond the capacity to stand up

**Have a Chunder:** The delicate act of regurgitation

**You pong:** Dear me, we do smell don’t we

**Bloody oath!** I am in total agreeance with you

**You Drongo:** A rather dimwitted person

**Pull ya head in:** You may be correct in your assertion but shut up

**Rack off:** Your presence is not longer required

So “**hoo-roo mate**” or “**ta tar**” (goodbye) and remember, always pronounce Aussie as in “**mozzie**” (mosquito).

*Many thanks to Pat Fitzgerald-Bocarsley for her service on the newsletter editorial board. Pat is stepping down as the Journal of Immunology is overwhelming her with work. Volunteers for the editorial board (we have no money so we can't pay anything) are needed and always welcome. Don't miss this opportunity to be creative and help make the JSICR even better. Anyone wishing to volunteer for the editorial board should contact Howard Young.*

**INTERNATIONAL SOCIETY FOR INTERFERON and  
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