September 1999
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1999 Meeting

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Future ISICR Meetings
2000 Amsterdam
Joint ISICR/ICS
2001 Cleveland, OH
2002 Vienna
Joint ISICR/ICS

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ISICR
INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH

1999 ISICR Awards

The 1999 Milstein Award

MICHAEL KATZE
ADI KIMCHI

Honorary Membership

EDWARD DEMAEYER
DEREK BURKE

Young Investigator Awards

JORGE BLANCO
SANDY DER
SERGEI KOTENKO
SENG-LSAI TAN

The Christina Fleischmann Memorial Award

ISABELLE MARIE

Travel Awards

42 ISICR members were awarded travel awards to attend the 1999 ISICR meeting.

A SPEECH BY PROFESSOR DEREK BURKE AT THE MEETING ON 'INTERFERON: THE DAWN OF RECOMBINANT PROTEIN DRUGS' IN BERLIN, DECEMBER 11TH 1998

We are here to celebrate the contribution that the discovery of interferon has made to the treatment of viral diseases, and of some cancers, and, on a wider stage, to the development and use of recombinant protein drugs. I also want to pay a tribute to Alick Isaacs, interferon's discoverer, as one of the most lively scientific minds that I have known.

It was in early 1957 that Alick Isaacs, with whom I was working on the nucleic acid of influenza virus, dropped into my lab to ask what I was thinking of working on next, for the current project was about complete. I outlined to him an idea I had-to follow 32P labelled flu into cells, a problem that would have been very complex to unravel, as others have since found out, and he in reply, "wondered whether I would be interested in doing something with him on interference, where they had something interesting going on." "They", was of course Alick and Jean Lindenmann, and the "something interesting" was interferon. That conversation determined the course of my scientific life for the next 25 years. So to the first experiment in my lab notebook, called 'Dialysis of Interferon', and dated March 4th, 1957.

The first papers appeared in the Proceedings of the Royal Society that spring. The paper, entitled 'The Interferon' was followed by a stream of publications from Alick's lab, and my first with him, which was modestly entitled 'Studies on the Production, Mode of Action and Properties of Interferon', was published that October. I once asked Alick why he and Jean had called it interferon, and he replied that the physicists had their fundamental particles, proton, neutron etc., so he didn't see why the biologists should not have such a fundamental particle! Maybe Alick had a dream already of how important this discovery was going to be?

Alick was, at that time, just marvellous to work with. I had been trained as a chemist, and thought in terms of precise structures, of homogeneous preparations, and of waiting for purified material before properties could be established. How limited that was! Alick thought as a biologist; in terms of populations, and of the nature of the cellular response. Crucially, we had a bio-assay; an imprecise one to be true, but using this crude bio-assay, it was possible to devise very simple experiments to find out more about this mysterious new substance.

The interferon assay was tedious, as well as being rather inaccurate, and gave much time for conversation. Alick was the leader in such conversation, and ideas for new experiments, political discussion, or identification of snatches of opera that he would sing made the time pass quickly. Alick, too, was adept at determining where the end-point was, with the aid of a hand lens, long before the rest of us could do it, and he had often planned the next experiment before the rest of us had read the assay!

Sometime early on, probably in late 1957, we had a visit from Lord Hailsham, who as Lord President of the Council, carried overall responsibility for the Medical Research Council, and who objected strenuously to the name, pointing out the it was a hybrid of Latin and Greek words - a real mongrel. Oh, what ignorant scientists! It was the same Lord Hailsham, who as Lord Chancellor was required to wear a uniform with a full length wig, an embroidered gown, breeches and shoes with buckles. Proceeding through the House of Lords one day, he spotted a friend whose first name happened to be Neal, a not uncommon British first name - you may have heard of Neal Kinnock - coming out of a room ahead of him, and being a jovial sort of fellow, called out to him. "Neal" he roared. However between the two of them and with their back to Lord Hailsham's friend, were a group of American tourists, who, being good Americans, and overcome by the sight ahead of them, and the call to Neal, did what they thought was commanded: they dropped to their knees in front of the Lord Chancellor! At least we did not have to kneel when he came round the lab!

The early days at Mill Hill were not easy. Alick came back depressed from a seminar tour in the US; for most thought that what he had was only an artefact, and Harry Rubin was calling it "misinterpreton". We were ourselves worried that the interference observed in the assays was due to traces of inactivated virus coming through the tests, but the discovery that June that interferon was stable at pH 2, gave us a method to destroy the virus without destroying the interferon, and we

convinced ourselves and then gradually everyone else, that interferon was real and not an artefact.

Nor was it clear where interferon came from-was it a new sort of antibody, or part of the virus as defective interfering particles turned out to be - and was there one interferon or many? It was not until David Tyrrell discovered the so-called "species specificity" of interferon in 1959 that it became clear that there were a family of interferons. Indeed, it was Norman Finter, in editing that important first book, published in 1966 but conceived much earlier, who took a deliberate decision to use the plural form. We understood so little in those early days, yet those early experiments did establish that interferon was no chimera; no "idle or wild fancy" as the dictionary has it. Interferon did not go the way of other poorly characterised molecules with ill defined biological activity. The chalcones come to mind.

Interest spread, often springing from the visit of a foreign worker to Alick's lab. The Interferon Scientific Memoranda, of which I still have a complete set, was an important early experiment in rapid scientific communication, long overtaken by electronic methods, but it kept this small field in touch with each other. There was one other very important development in the late 50s, and that was the formation of a joint initiative between the MRC, ICI, Wellcome and Glaxo to develop the clinical applications of interferon. The British were determined to try and prevent such a development going to the US, as had happened with penicillin. The joint committee met for the first time I think in late 1958 or early 59, with Alick in the chair. We made lots of mistakes, but it did lead to the first successful clinical trial of interferon against the common cold virus in 1962. By 1967 interferon had become international, the turning point probably being the Ciba symposium in that year; a very important meeting. Tragically, Alick had died earlier that year, and the meeting was dedicated to him. It was the first time that we had met across national boundaries, and I vividly remember Francis Crick telling us all that the first thing we <u>had</u> to do was to make several hundred milligrams of the stuff. How right he was and how hard it was! Some marvellous meetings followed- in Sienna or Louvain, and then there was that New York meeting, called just after the story broke of interferon's action against osteogenic sarcoma, when we were told that since curing cancer cost no more that a B52 bomber, why didn't we just get on with it!

As a consequence, interferon made the front cover of Time in March 1980, with the subtitle "The IF drug for Cancer", but nobody took notice of the "if". The claims of interferon's effect against cancer were oversold, misled initially by the design of the trial in Stockholm, and then exaggerated, sometimes intentionally and sometimes not, by the media and the US cancer lobby. All hell broke loose; a family in Glasgow sold their home in order to buy interferon for their dying son, I was phoned by a senior diplomat who had smuggled Russian interferon into Britain in the diplomatic bag, and who wanted me to inject it into him, and there were many other distressing stories, mainly from people who were themselves terminally ill.

It was my first contact with the media, and I am reminded of the story of a conversation between a politician and a journalist, during a walk in the park during a break in a meeting. Suddenly a frog jumped out in front of them and started to speak: "I am a scientist who has been put under a spell. If you break the spell by lifting me up and kissing me I will serve you forever!" The journalist said to the politician: "Wouldn't that be something for you? Just imagine, you would always have an expert on hand to give you specialist advice!" But the politician said: "No, better not. We all know what scientists are like, they talk too much, know everything better and always want to be the centre of attention. But it would be ideal for you! Editorial offices don't often have science writers or if they do, they are not always very well informed. He would be really valuable for you. So, go on, pick up the frog and kiss him!" The journalist picked up the frog and looked at him briefly before putting him in his pocket. The

politician was amazed and asked: "Why did you put the frog in your pocket instead of kissing him?" To which the journalist replied "Because a talking frog is a hundred times more interesting than the best scientist."

But one of the important things that came out of all the fuss was the funds and the drive to clone the interferon genes. That was very hard; for I think it was the first cloning of a rare messenger RNA, and was a huge scientific achievement, first reached by Charles Weissmann for interferon-α, and almost simultaneously by a former student of Charles', Tada Taniguchi for interferon-β in Japan. A number of other groups, including our own at Warwick, followed in their trail. So much became clear very quickly; the relationship between interferon-α and interferon-β, the multiple interferon-α family, the chromosomal location of the genes, and the start of the unravelling of the control systems that are responsible for the induction of interferon. The cloned interferon could now be purified by immuno-chromatography, using a monoclonal antibody against interferon-α first made by David Secher and myself, and patented by him with a £5 patent when the official UK Agency refused to do so. This new source of material supplemented the material made in Helsinki by Kari Cantell and by Wellcome in a process developed by Norman Finter, and for the first time, clinical trials against cancer and certain virus diseases were possible on a sustained basis.

In addition, the cloning of the interferon genes has also made possible the cloning of the interleukins and a number of other cellular control factors. A recent copy of Nature showed - as an advertisement - a panoply of such factors, including interferon-γ, and the interferon-γ-inducing factor. It is the discovery of these factors and the unravelling of their role in medicine that is the huge and quite unexpected outcome of interferon research. But that is what science is like; it is important to have primary targets, but it is also very important to be alive to the secondary targets. Who could have planned the Internet? So this evening, we honour those who opened up this field, and we look forward to more good things to come from their successors.

The ISICR Congratulates

Dr. Michel Revel

for receiving the

Israel Award

for his lifetime contributions to science.

New ISICR Members

The ISICR welcomes the following new members. Contact information can be obtained from the Headquarters Office.

KRISHNAN ALLAMPALLAM
Chicago, IL

JON ERIC ANGELL
Baltimore, MD

ANDRE BAFICA
Salvador, Bahia, Brazil

MALGORZATA BIENKOWSKA
Wroclaw, Poland

BERNARD CHARLEY
Jouy-En Josas, France

VANESSA CULL
Murdoch, WA Australia

ANNA CZARNY
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JOSEPH A. DIDONATO
Cleveland, OH

MATTHEW J. FENTON
Boston, MA

GRAHAM R. FOSTER
London, UK

KEE CHUAN GOH
Cleveland, OH

DOLORES GOMEZ
Stony Brook, NY

DAVID P. JACKSON
Leeds, West Yorkshire UK

KAZUKO KITA
Ciba, Japan

JIN-HYUNG LEE
Piscataway, NJ

RENE MICHEL L'HARIDON
Jouy-En Josas, France
BARBORA LUBYOVA
Baltmore, MD
MARZANNA LUSIAK
Wroclaw, Poland
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Stony Brook, NY
KERRI A. MOWEN
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Creteil, France
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Malvern, PA
KRISTI LEANN PETERS
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London, UK
SAVITA PROBHAKAR
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New York, NY
DAVID NOWELL REYNOLDS
Louisville, KY
CHRISTIAN ROSS
Copenhaven, Denmark
OSAMU SHIMOZATO
Frederick, MD
MARIA PURIFICACAO SILVA
Salvador, Bahia Brazil
FULVIA TERENNZI
Cleveland, OH
KIRSTEN C WEINING
Freiburg, Germany
WEI WU
Piscataway, NJ
JIE ZHU
Huddinge, Sweden

PRELIMINNARY PROGRAM

1999 ISICR Meeting with the participation of the EUROPEAN CYTOKINE SOCIETY

Dear Colleagues,

As organizers, we have the great pleasure to welcome you to the 1999 Meeting of the International Society for Interferon and Cytokine Research (ISICR). We would also like to welcome the members of the European Cytokine Society who will join this meeting.
The Meeting will be a large forum which will offer the opportunity to present and discuss the latest advances in basic sciences and clinical applications as regards cytokines, and particularly interferons. The research on interferon and other cytokines is indeed an essential part of biomedical sciences : it ranges from the basic study of gene expression, structure-function relationship, receptors and signal transduction cascades to increasingly important clinical applications in the fields of hematology, viral and infectious diseases, cancer, neurodegenerative diseases and immune disfunctioning.

The plenary sessions have been opened not only to invited speakers but also to the authors of the selected abstracts to ensure both topical and representative contents. Workshop presentations will provide a forum for oral communication. Moreover, ample time will be allowed for poster sessions.

We are certain that the 1999 ISICR Meeting, the last of the millenium, will be a great success thanks to its excellent scientific program. It will undoubtedly bring great benefits to the research and clinical applications on interferon and other cytokines.

We extend a warm welcome in Paris to all of you.

Janine Doly
Chair of the 1999 Organizing Committee

ACKNOWLEDGMENTS

Meeting hosted by :
University René Descartes - Paris V
UFR Biomédicale - Centre Universitaire des Saints-Pères

With the support of :
Centre National de la Recherche Scientifique (CNRS)

This 1999 ISICR Meeting has received the generous financial support of several institutions and companies. The organizers are most grateful to all donators and sponsors contributing to the success of this meeting.

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PRELIMINARY PROGRAM
Subject to change

(Note: due to space limitations, only the presenting author is listed)

SUNDAY, SEPTEMBER 5

1:00 pm - 6:00 pm **Registration**

2:00 pm - 6:00 pm **ISICR and ECS Committee Meetings :**
2:00 - 6:00 Standards Committee (Room Rabelais)
2:00 - 4:00 Meetings Committee (Room Leduc)
2:00 - 4:00 Awards Committee (Room 42)
2:00 - 4:00 Finance Committee (Room 48)
4:00 - 6:00 Membership Committee (Room 42)
4:00 - 6:00 Nomenclature Committee (Room 48)
4:00 - 6:00 Board of Directors Meeting (Room Leduc)

SUNDAY, SEPTEMBER 5

6:00 pm - 6:15 pm **Introduction and Welcome - Amphi Binet**
Dr. Janine Doly, Chair of the 1999 Organizing Committee
Dr. Bryan Williams, ISICR President
Opening remarks
Dr. Didier Fradelizi, ECS Secretary
Opening remarks

6:15 pm - 7:15 pm **Opening Lecture - Amphi Binet**
" Gene expression : mechanism of regulation and transduction "
Yaniv M, *Paris, France*

7:15 pm - 9:00 pm **Get-Together Cocktail Party**

MONDAY, SEPTEMBER 6

8:30 - 10:40 am **PLENARY SESSION 1 (Pl-1) - Amphi Binet**
" Interferon gene expression "
Chairpersons : **Taniguchi T, Hauser H**

8:30 Pl-1.1 **Taniguchi T :** REGULATION OF INTERFERON AND IMMUNE SYSTEM BY THE IRF FAMILY OF TRANSCRIPTION FACTORS
9:00 Pl-1.2 **Hiscott J :** NOVEL POST-TRANSLATIONAL MECHANISMS CONTROLLING THE FUNCTIONAL ACTIVITIES OF THE INTERFERON REGULATORY FACTORS
9:20 Pl-1.3 **Fujita T :** MOLECULAR MECHANISM OF IRF-3 ACTIVATION BY VIRUS INFECTION
9:40 Pl-1.4 **Marié I :** VIRAL INFECTION REGULATES EXPRESSION, NUCLEAR LOCALIZATION, DNA BINDING ABILITY, AND TRANSCRIPTIONAL ACTIVITY OF INTERFERON REGULATORY FACTOR 7 (IRF7)
10:00 Pl-1.5 **Pitha PM :** DOWNREGULATION OF CELLULAR IRFs FUNCTIONS BY VIRAL IRFs
10:20 Pl-1.6 **Ozato K** : THE ROLE FOR ICSBP (IRF-8) IN GAS-MEDIATED TRANSCRIPTION IN MACROPHAGES

10:40 - 11:00 am **COFFEE BREAK**

11:00 am - 1:10 pm **PLENARY SESSION 2* (Pl-2) - Amphi Binet**
" Interferons and other cytokines in infectious diseases : fundamental and clinical aspects "
Chairpersons : **Bréchot C, Pitha PM**

11:00 Pl-2.1 **Bréchot C :** INTERFERONS AND OTHER CYTOKINES IN INFECTIOUS DISEASES : FUNDAMENTAL AND CLINICAL ASPECTS
11:30 Pl-2.2 **Thèze J :** REGULATORY DYSFUNCTION OF THE CYTOKINE NETWORK DURING HIV-INFECTION - THE IL-2/IL-2 RECEPTOR SYSTEM AND ITS THERAPEUTICAL APPLICATIONS
11:50 Pl-2.3 **Belardelli F :** TYPE I INTERFERON IS A POWERFUL INHIBITOR OF *IN VIVO* HIV-1 INFECTION AND PRESERVES HUMAN CD4+ T CELLS FROM VIRUS-INDUCED DEPLETION IN SCID MICE TRANSPLANTED WITH HUMAN CELLS
12:10 Pl-2.4 **Kotenko SV :** IDENTIFICATION OF A CYTOMEGALOVIRUS-ENCODED IL-10 HOMOLOG
12:30 Pl-2.5 **Li X :** GENETIC ANALYSIS OF NFκB FUNCTION
12:50 Pl-2.6 **Taylor DR :** THE HEPATITIS C VIRUS E2 PROTEIN INHIBITS THE DOUBLE-STRANDED RNA-ACTIVATED PROTEIN KINASE PKR AND CONFERS INTERFERON RESISTANCE

1:10 - 2:30 pm **LUNCH**

2:00 - 4:00 pm **Poster Session I Viewing**

4:00 - 7:15 pm **WORKSHOP 1 (W1) - Amphi Weiss**
" Transcription factors of the IFN system "
Chairpersons : **Reich N, Civas A**

4:00 W1.1 **Masumi A:** IRF-DEPENDENT TRANSCRIPTIONAL REGULATION IS MEDIATED BY HISTONE ACETYLASE PCAF
4:15 W1.2 **Bonnefoy E :** HISTONE ACETYLATION/DEACETYLATION POTENTIATES THE TRANSCRIPTIONAL ON/OFF REGULATION OF THE INTERFERON-β PROMOTER
4:30 W1.3 **Lin R :** REGULATION OF INTERFERON AND CHEMOKINE GENE EXPRESSION THROUGH DIMERIZATION OF IRF-3 AND IRF-7
4:45 W1.4 **Yeow WS :** TRANSCRIPTION ACTIVATION OF HUMAN IFN-A GENES BY IRF-3 AND IRF-7

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W1.5 **Karpova AY :** IRF-3A, AN ALTERNATIVE SPLICE ISOFORM OF INTERFERON REGULATORY FACTOR-3, FUNCTIONS AS A DOMINANT NEGATIVE *IN VIVO*
5:45 W1.6 **Civas A :** IRF-3 AND IRF-7 DEPENDENT PATHWAYS IN VIRUS-INDUCED GENE TRANSCRIPTION
6:00 W1.7 **Reich NC :** REGULATION OF THE IRF-3 / DRAF1 TRANSCRIPTION FACTOR IN RESPONSE TO VIRAL INFECTION
6:15 W1.8 **Levi BZ :** PROTEIN-PROTEIN AND DNA-PROTEIN INTERACTIONS AFFECT THE ACTIVITY OF LYMPHOID SPECIFIC IRFs
6:30 W1.9 **Fenton MJ :** DIFFERENTIAL EXPRESSION AND DISTINCT FUNCTIONS OF INTERFERON CONSENSUS BINDING PROTEIN AND INTERFERON REGULATORY FACTOR 4 IN MACROPHAGES.
6:45 W1.10 **Navarro S :** TRANSCRIPTIONAL REPRESSION OF IFN-A PROMOTERS BY THE HOMEO DOMAIN PROTEIN PTX1

7:00 W1.11 **Mamane Y :** NOVEL POST-TRANSLATIONAL REGULATION OF INTERFERON REGULATORY FACTOR-4 ACTIVITY BY THE IMMUNOPHILIN FK506 BINDING PROTEIN 52 (FKBP52)

4:00 - 7:15 pm **WORKSHOP 2 (W2) - Amphi Delmas**
" Interferons and other cytokines in viral diseases "
Chairpersons : **Haller O, Meurs E**

4:00 W2.1 **Haller O :** HIGH VIRULENCE OF ATTENUATED RIFT VALLEY FEVER VIRUS STRAINS IN MICE LACKING A FUNCTIONAL TYPE I INTERFERON SYSTEM
4:15 W2.2 **Masters J :** MYXOMA VIRUS INDUCED ACTIVATION OF CHEMOKINE RECEPTORS
4:30 W2.3 **Pawlotsky JM :** ANTI-VIRAL EFFECT OF INTERFERON ALPHA IN PRIMARY CULTURES OF HUMAN HEPATOCYTES INFECTED BY HEPATITIS C VIRUS
4:45 W2.4 **Katze MG :** REGULATION OF THE INTERFERON-INDUCED PROTEIN KINASE PKR BY INFLUENZA AND HEPATITIS C VIRUSES : TWO DISTINCT STRATEGIES BY PATHOGENIC RNA VIRUSES

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W2.5 **Meurs EF :** IN VIVO EXPRESSION OF HEPATITIS C VIRUS STRUCTURAL AND NONSTRUCTURAL PROTEINS CAN REVERSE THE ANTIVIRAL ACTION OF IFN THROUGH A PKR-INDEPENDENT MECHANISM
5:45 W2.6 **Fernandez JL :** HEPATITIS G VIRUS INFECTION IN PATIENTS WITH CHRONIC HEPATITIS C TREATED WITH INTERFERON ALFA 2b
6:00 W2.7 **Hovanessian AG :** MIDKINE IS A CYTOKINE THAT INHIBITS THE ATTACHEMENT OF HIV PARTICLES TO PERMISSIVE CELLS BY BINDING TO CELL-SURFACE EXPRESSED NUCLEOLIN
6:15 W2.8 **Staeheli P :** RESTRICTION OF BORNA DISEASE VIRUS IN CULTURED MOUSE CELLS IS DUE TO VIRUS-INDUCED INTERFERON
6:30 W2.9 **Martin M :** ANTIRETROVIRAL ACTIVITY OF IFN-τ AND ITS MODE OF ACTION
6:45 W2.10 **Sekellick MJ :** INTERFERON ACTION SELECTS FOR INTERFERON RESISTANT INFLUENZA VIRUS
7:00 W2.11 **Carr DJJ :** THE EFFICACY OF INTERFERON-ALPHA 1 GENE THERAPY AGAINST HERPES SIMPLEX VIRUS TYPE 1 & 2 INFECTIONS

POSTER SESSION I (PI) - Grand Hall
The poster session I will be held on Monday, September 6 and Tuesday, September 7 :
2:00 pm - 4:00 pm
Poster Session I Viewing
Interferon gene expression and transcription factors of the IFN system
Interferon and other cytokines in infectious diseases : fundamental and clinical aspects
Interferons and other cytokines in viral diseases
Interferons and other cytokines in the immune system
Interferons and other cytokines in neurodegenerative diseases and immune disfunctioning
Interferons and other cytokines in differentiation, cell cycle and apoptosis

7:30 pm - 8:30 pm **Women's Forum Session - Room Leduc**
Mrs. Cossart P : " The role of women in the French scientific community "

TUESDAY, SEPTEMBER 7

8:30 - 10:40 am **PLENARY SESSION 3* (Pl-3) - Amphi Binet**
" Interferons and other cytokines in the immune system "
Chairpersons : **Romagnani S, Dy M**

8:30 Pl-3.1 **Romagnani S :** THE TH1/TH2 PARADIGM IN DISEASE
9:00 Pl-3.2 **Rubinstein M :** INTERLEUKIN-18 BINDING PROTEIN: A NOVEL MODULATOR OF THE Th1 CYTOKINE RESPONSE
9:20 Pl-3.3 **Wong M :** RANTES-CCR5 MEDIATED SIGNAL TRANSDUCTION
9:40 Pl-3.4 **Asano M :** ROLES OF IL-1 AND TNF-α IN VARIOUS INFLAMMATIONS
10:00 Pl-3.5 **Gessani S :** IFNs AND HIV-1 gp120 UP-MODULATE β-CHEMOKINES PRODUCTION IN HUMAN PERIPHERAL BLOOD MONOCYTES. ROLE OF MACROPHAGE DIFFERENTIATION
10:20 Pl-3.6 **Coccia EM :** INTERLEUKIN-12 INDUCES EXPRESSION OF INTERFERON REGULATORY FACTOR-1 VIA SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION-4 IN HUMAN T HELPER TYPE 1 CELLS

10:40 - 11:00 am **COFFEE BREAK**

11:00 am - 12:50 am **PLENARY SESSION 4* (Pl-4) - Amphi Binet**
"Interferons and other cytokines in neurodegenerative diseases and immune disfunctioning "
Chairpersons : **Weissmann C, Tovey GM**

11:00 Pl-4.1 **Weissmann C :** PRION DISEASE AND THE IMMUNE SYSTEM
11:30 Pl-4.2 **Campbell IL :** STRUCTURAL AND FUNCTIONAL CONSEQUENCES OF THE CENTRAL NERVOUS SYSTEM TARGETED EXPRESSION OF IFN-α IN TRANSGENIC MICE
11:50 Pl-4.3 **Gruol DL :** INTERLEUKIN-6 ALTERS THE PHYSIOLOGICAL PROPERTIES OF CENTRAL NERVOUS SYSTEM NEURONS
12:10 Pl-4.4 **Beretta L :** INTERFERONS INDUCE EXPRESSION OF SMN AND SMNc GENES AND RESTORE SMNc PROTEIN LEVEL IN SMA
12:30 Pl-4.5 **Samuel CE :** INTERFERON-INDUCIBLE DOUBLE-STRANDED RNA-SPECIFIC ADENOSINE DEAMINASE (ADAR1): NOVEL REGULATION AND EDITING OF GLUTAMATE AND SEROTONIN RECEPTOR mRNAs

12:50 - 2:00 pm **LUNCH**

2:00 - 4:00 pm **Poster Session I Viewing**

4:00 - 7:00 pm **WORKSHOP 3* (W3) - Amphi Delmas**
" Interferons and other cytokines in differentiation, cell cycle and apoptosis "
Chairpersons : **Hochkeppel HK, Dayer JM**

4:00 W3.1 **Lindner DJ :** A NOVEL APOPTOSIS REGULATOR INDUCED BY IFN-BETA
4:15 W3.2 **Erickson S :** INTERFERON-α INHIBITS T-LYMPHOCYTE PROLIFERATION AND SELECTIVITELY INTERFERES WITH THE IL-2 SIGNALLING PATHWAY
4:30 W3.3 **Haque SJ :** STRUCTURAL BASIS OF SUPPRESSOR OF CYTOKINE SIGNALING (SOCS)-1 AND SOCS-3-MEDIATED INHIBITION OF INTERLEUKIN (IL)-4-DEPENDENT SIGNAL TRANSDUCTION
4:45 W3.4 **Leite-de-Moares MC :** A DISTINCT IL-18-INDUCED

PATHWAY TO FULLY ACTIVATE NK T LYMPHOCYTES INDEPENDENTLY FROM TCR ENGAGEMENT

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W3.5 **Pioli C :** CTLA-4 (CD152) INHIBITS CYTOKINE PRODUCTION BY DOWN-MODULATING THE ACTIVATION OF BOTH NF-κB AND NF-AT TRANSCRIPTION FACTORS

5:45 W3.6 **Novelli F :** INTRACELLULAR RECYCLING REGULATES SURFACE EXPRESSION OF THE IFN-γR2 CHAIN IN HUMAN T LYMPHOCYTES

6:00 W3.7 **Bani L :** INTERLEUKIN-2 γ CHAIN: INTRACELLULAR EXPRESSION ON RESTING CD4T CELLS AND DYSREGULATION BY HIV-1 GP120 IN ACTIVATED CD4 T LYMPHOCYTES

6:15 W3.8 **Brod SA :** CD4+ T CELLS FROM IFN-α FED DONORS PROTECT AGAINST ADOPTIVE TRANSFER OF TYPE I DIABETES (DM) INTO NOD.*SCID* RECIPIENTS

6:30 W3.9 **Bartholomé EJ :** INTERFERON-β INDUCES THE MATURATION OF IL-12-DEFICIENT MYELOID DENTRITIC CELLS ABLE TO INDUCE TH2 TYPE CYTOKINE SECRETION

6:45 W3.10 **Kalvakolanu DV :** CELL DEATH REGULATION BY THE COMBINATION OF IFN-β AND RETINOIC ACID: NOVEL PLAYERS AND NEW PATHWAYS

4:00 - 6:30 pm **WORKSHOP 4 (W4) - Amphi Weiss**
" Multiple sclerosis and autoimmune diseases "
Chairpersons : **Billiau A, Wietzerbin J**

4:00 W4.1 **Capobianchi MR :** LYMPHOMONOCYTE ACTIVATION INDUCED BY MEMBRANE INTERACTION OF PBMC WITH HIV-1-INFECTED CELLS

4:15 W4.2 **Van Weyenbergh J :** TREATMENT OF MUTIPLE SCLEROSIS PATIENTS WITH IFN-BETA DIMINISHES IFN-GAMMA RESPONSIVENESS - DIFFERENTIAL EFFECT OF IFN-BETA *IN VIVO* AND *IN VITRO*

4:30 W4.3 **Lopez-Saura P :** ANTI-INTERFERON ALPHA-2 AUTOANTIBODIES IN MYASTHENIA GRAVIS PATIENTS

4:45 W4.4 **Emilie D :** TREATMENT OF HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS WITH AN ANTI-INTERLEUKIN-10 MONOCLONAL ANTIBODY

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W4.5 **Meager A :** SPONTANEOUSLY OCCURRING AUTOANTIBODIES TO IFN, IL-12 AND GM-CSF IN AUTOIMMUNE DISEASES: CONSEQUENCES FOR PATIENT'S HEALTH

5:45 W4.6 **Vermeire K :** FAILURE OF NOS INHIBITORS TO ENHANCE CIA IN MICE INDICATES THAT REDUCED PRODUCTION OF NO IN IFN-γR KO MICE CANNOT ACCOUNT FOR THEIR INCREASED SUSCEPTIBILITY TO CIA

6:00 W4.7 **Soos JM :** IFN-τ: IMMUNOMODULATORY PROPERTIES AND CLINICAL APPLICATIONS FOR THE TREATMENT OF MULTIPLE SCLEROSIS

6 :15 W4.8 **Loukina G :** ANTI-INTERFERON-γ ABS SLOWS DISEASE PROGRESSION IN SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS (MS)

POSTER SESSION I (PI) - Grand Hall
The poster session I will be held on Monday, September 6 and Tuesday, September 7 :
2:00 pm - 4:00 pm
Poster Session I Viewing
Interferon gene expression and transcription factors of the IFN system
Interferon and other cytokines in infectious diseases : fundamental and clinical aspects
Interferons and other cytokines in viral diseases
Interferons and other cytokines in the immune system
Interferons and other cytokines in neurodegenerative diseases and immune disfunctioning
Interferons and other cytokines in differentiation, cell cycle and apoptosis

7:30 pm **Reception and cocktail offered by the Mayor of Paris at the Town Hall Milstein Awards, ISICR and ECS Honors and Awards Ceremony**

WEDNESDAY, SEPTEMBER 8

8:30 - 10:40 am **PLENARY SESSION 5 (Pl-5) - Amphi Binet**
" Signal transduction : from IFN receptors to interferon stimulated gene expression "
Chairpersons : **Schreiber R, Pellegrini S**

8:30 Pl-5.1 **Schreiber RD :** IFNγ RECEPTOR SIGNALING, SIGNALING DYSFUNCTION AND CANCER

9:00 Pl-5.2 **Stark GR :** WHY STAT1 IS A TUMOR SUPPRESSOR

9:20 Pl-5.3 **Paulson M :** TRANSCRIPTIONAL ACTIVATION BY STAT2 INVOLVES MULTIPLE DISCRETE MECHANISMS, INCLUDING INDIRECT RECRUITMENT OF PCAF HISTONE ACETYLTRANSFERASE BY p300

9:40 Pl-5.4 **Croze E :** DIFFERENTIAL REGULATION OF GENE EXPRESSION IN U5A CELLS EXPRESSING IFNAR2C MUTANTS

10:00 Pl-5.5 **Tavernier J :** FUNCTIONAL ANALYSIS OF TYPE 1 INTERFERON RECEPTORS USING RECEPTOR CHIMERAS

10:20 Pl-5.6 **Goh KC :** REQUIREMENT FOR P38 MAPK IN INTERFERON SIGNALING

10:40 - 11:00 am **COFFEE BREAK**

11 :00 am - 12:50 am **PLENARY SESSION 6* (Pl-6) - Amphi Binet**
" Interferons and other cytokines in cancer : fundamental and clinical aspects "
Chairpersons : **Parmiani G, Fradelizi D**

11:00 Pl-6.1 **Parmiani G :** CYTOKINES IN THE IMMUNE RESPONSE TO HUMAN MELANOMA

11:30 Pl-6.2 **Hashimoto S :** PRODUCTION OF IL-6 ISOMERS BY KB CELLS, PURIFICATION AND INDUCTION OF APOPTOSIS IN HUMAN TUMOR CELLS

11:50 Pl-6.3 **Proietti E :** CYCLOPHOSPHAMIDE INDUCES TYPE I INTERFERON EXPRESSION AND AUGMENTS THE NUMBER OF $CD44^{hi}$ T LYMPHOCYTES IN MICE: POSSIBLE IMPLICATIONS FOR STRATEGIES OF CHEMOIMMUNOTHERAPY OF CANCER

12:10 Pl-6.4 **Chany C :** INTERFERON AND SARCOLECTIN IN THE COORDINATION OF T CELL CLONAL EXPANSION

12:30 Pl-6.5 **Gamero A :** SERINE PHOSPHORYLATION OF STAT1 AND STAT3 IS INDUCED BY TREATMENT OF CELLS WITH UV RADIATION: POTENTIAL ROLE OF p38 MAPK

12:50 - 2:00 pm **LUNCH**

2:00 - 4:00 pm **Poster Session II Viewing**

4:00 -6:45 pm **WORKSHOP 5 (W5) - Amphi Delmas**
" IFN receptors and signalling "
Chairpersons : **Uzé G, Stark G**

4:00 W5.1 **Platanias LC :** THE p38 MAP KINASE IS ACTIVATED BY TYPE I INTERFERONS AND IS REQUIRED FOR TYPE I IFN-DEPENDENT GENE TRANSCRIPTION
4:15 W5.2 **Hertzog P :** CHARACTERIZATION OF THE FUNCTIONS OF TYPE I INTERFERONS AND RECEPTOR SIGNALING FROM KNOCK-OUT MICE
4:30 W5.3 **Müller M :** TYK2 DEFICIENT MICE
4:45 W5.4 **Moroni C :** DIFFERENTIAL REGULATION OF AUUUA-MEDIATED mRNA TURNOVER BY THE p38 MITOGEN-ACTIVATED PROTEIN KINASE AND PHOSPHATIDYLINOSITOL 3-KINASE

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W5.5 **Yeh TC :** A FUNCTIONAL ANALYSIS OF THE TYK2 KINASE-LIKE DOMAIN BY RANDOM MUTAGENESIS
5:45 W5.6 **Der SD :** CHARACTERIZATION OF IFN-REGULATED PATHWAYS USING OLIGONUCLEOTIDE MICROARRAYS
6:00 W5.7 **Bernabei P :** UNBALANCED EXPRESSION OF THE IFN-γR2 CHAIN ENTANGLES IFN-γ-MEDIATED INDUCTION OF STAT-1, IRF-1, AND FAS-L ON HUMAN T, B AND MYELOID CELLS
6:15 W5.8 **Colamonici OR :** ROLE OF THE DIFFERENT DOMAINS OF THE α AND βL CHAINS OF THE IFNαβR IN SIGNALING
6:30 W5.9 **Pollack BP :** THE HUMAN HOMOLOGUE OF THE YEAST PROTEINS, SKB1 AND HSL7 INTERACTS WITH JAK2 AND CONTAINS PROTEIN METHYLASE ACTIVITY

4:00 - 6:30 pm **WORKSHOP 6* (W6) - Amphi Weiss**
" Interferons and other cytokines in hematology and cancerology "
Chairpersons : **Pestka S, Content J**

4:00 W6.1 **Ambrus Sr JL :** NEW POTENT INTERFERON INDUCING AGENTS : THIOLATED POLY rI-MPC
4:15 W6.2 **Lauta VM :** RECOMBINANT INTERFERON ALPHA-2b AS FIRST LINE TREATMENT OF II TYPE MIXED ESSENTIAL CRYOGLOBULINEMIA
4:30 W6.3 **Wilkin JM :** OVEREXPRESSION, PURIFICATION AND LABELLING OF HUMAN INTERLEUKIN-11
4:45 W6.4 **Perea SE :** HUMAN PAPILLOMAVIRUS TYPE 16 (HPV-16) E7 IMPAIRS THE ACTIVATION OF THE INTERFERON REGULATORY FACTOR-1 (IRF-1)

5:00 - 5:30 pm **COFFEE BREAK**

5:30 W6.5 **Waschütza G :** REDUCTION OF SURFACE HYDROPHOBICITY OF HUMAN IFN-β LEADS TO IMPROVED PHARMACOKINETICS
5:45 W6.6 **Weining KC :** PROTECTIVE EFFECTS OF TYPE 1 AND TYPE II INTERFERONS TOWARDS ROUS SARCOMA VIRUS-INDUCED TUMORS IN CHICKENS
6:00 W6.7 **Jablonska E :** TNF-α AND IL-6 AND THEIR SOLUBLE RECEPTORS IN CANCER PATIENTS
6:15 W6.8 **Borden E :** ENHANCING THERAPEUTIC RESPONSE TO INTERFERONS IN MELANOMA

POSTER SESSION II (PII) - Grand Hall
The poster session II will be held on Wednesday, September 8 and Thursday, September 9 :
Wednesday, September 8, 2:00 pm - 4:00 pm **Poster Session II Viewing**
Signal transduction : from IFN receptors to IFN stimulated gene expression
IFN and other cytokines in cancerology and hematology : fundamental and clinical aspects
Interferon induced proteins and their function
Gene therapy in the interferon system and other cytokines
Interferons and other cytokines in non viral infections

7:30 pm **Dinner on the bateau mouche " La Gabarre "**

THURSDAY, SEPTEMBER 9

8:30 - 10:40 am **PLENARY SESSION 7 (Pl-7) - Amphi Binet**
" Function of interferon induced proteins "
Chairpersons : **Williams BRG, Esteban M**

8:30 Pl-7.1 **Williams BRG :** FUNCTION OF INTERFERON-REGULATED PROTEINS
9:00 Pl-7.2 **Lengyel P :** THE INTERFERON-INDUCIBLE NUCLEOLAR P204 PROTEIN BINDS THE RIBOSOMAL RNA-SPECIFIC UBF1 TRANSCRIPTION FACTOR AND INHIBITS RIBOSOMAL RNA TRANSCRIPTION
9:20 Pl-7.3 **Landolfo S :** MOUSE CYTOMEGALOVIRUS (MCMV) REPLICATION STRICTLY DEPENDS ON THE INTERFERON-INDUCIBLE IFI 200 GENES
9:40 Pl-7.4 **Khabar KSA :** CONSTITUTIVE AND IFN-INDUCED ANTIVIRAL ENZYME ACTIVITIES: EXPECTED AND SURPRISING CONSEQUENCES IN GENE-DEVOID FIBROBLASTS
10:00 Pl-7.5 **Silverman RH :** INVOLVEMENT OF A NOVEL IFN STIMULATED GENE FOR PHOSPHOLIPID SCRAMBLASE IN IFN ACTION
10:20 Pl-7.6 **Ghosh A :** A NEW ISOZYME-SPECIFIC CELLULAR EFFECT OF 2-5(A) SYNTHETASE

10:40 - 11:00 am **COFFEE BREAK**

11:00 - 1:10 pm **PLENARY SESSION 8 (Pl-8) - Amphi Binet**
" Gene therapy in the interferon system and other cytokines "
Chairpersons : **Mannoni P, Lebleu B**

11:00 Pl-8.1 **Mannoni P :** GENE THERAPY IN THE INTERFERON SYSTEM AND OTHER CYTOKINES
11:30 Pl-8.2 **Escudier B :** GENE THERAPY WITH INTRATUMORAL INJECTION OF RECOMBINANT-ADENOVIRUS IN LUNG CANCER
11:50 Pl-8.3 **Hiroishi K :** INTERFERON-α GENE THERAPY IN COMBINATION WITH CD80-TRANSDUCTION REDUCES TUMORIGENICITY AND GROWTH OF ESTABLISHED TUMOR IN POORLY IMMUNOGENIC TUMOR
12:10 Pl-8.4 **Muto NF :** INHIBITION OF REPLICATION OF REACTIVATED HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 IN LATENTLY-INFECTED U1 CELLS TRANSDUCED WITH AN HIV-1 LTR-DRIVEN PKR cDNA CONSTRUCT
12:30 Pl-8.5 **Anegon I :** ADENOVIRUS-MEDIATED GENE TRANSFER OF TGFβ1 OR CTLA4 RESULTS IN INDEFINITE HEART ALLOGRAFT SURVIVAL AND MODULATION OF CYTOKINE EXPRESSION DURING REJECTION

12:50 Pl-8.6 **Munafo A :** SAFETY PROFILE, PHARMACOKINETICS AND PHARMACODYNAMICS OF RECOMBINANT HUMAN SOLUBLE TNF RECEPTOR TYPE I (r-hTBP-1) IN HEALTHY VOLUNTEERS

1:10 - 2:00 pm **LUNCH**

2:00 - 4:15 pm **WORKSHOP 7 (W7) - Amphi Delmas**
" Interferon induced proteins "
Chairpersons : **Ozato K, Staeheli P**

2:00 W7.1 **Sen GC :** NEW PATHWAYS OF CELLULAR REGULATION BY INTERFERONS AND DSRNA
2:15 W7.2 **Xu Z :** A B SUBUNIT OF PROTEIN PHOSPHATASE 2A IS A TARGET FOR REGULATION BY THE DOUBLE-STRANDED RNA-DEPENDENT PROTEIN KINASE PKR
2:30 W7.3 **Esteban M :** MECHANISM OF NF-κB ACTIVATION BY THE INTERFERON-INDUCED ENZYME PKR: ROLE IN APOPTOSIS
2:45 W7.4 **Julkunen I :** PROTEOME ANALYSIS REVEALS UBIQUITIN CONJUGATING ENZYMES TO BE A NEW FAMILY OF IFN-α-REGULATED GENES
3:00 W7.5 **Bonnet MC :** PKR STIMULATES HIV-1 LTR-DRIVEN GENE EXPRESSION BY ACTIVATION OF NF-κB IRRESPECTIVE OF ITS KINASE FUNCTION
3:15 W7.6 **Tovey MG :** IDENTIFICATION OF GENES INDUCED BY ORAL INTERFERON THERAPY
3:30 W7.7 **de Veer MJ :** SCREENING FOR NOVEL INTERFERON INDUCED ANTIVIRAL PROTEINS USING OLIGONUCLEOTIDE MICROARRAYS
3:45 W7.8 **Kochs G :** HUMAN MxA PROTEIN BLOCKS *IN VIVO* RECONSTITUTED THOGOTO VIRUS POLYMERASE BY RECOGNIZING ASSEMBLED NUCLEOCAPSIDS
4 :00 W7.9 **Blanco JCG :** INTERFERON-γ ACTIVATION OF COX-2 GENE THROUGH MEMBERS OF THE INTERFERON REGULATORY FACTORS (IRF)

4:30 - 5:00 **COFFEE BREAK**

2:00 - 3:45 pm **WORKSHOP 8* (W8) - Amphi Weiss**
" Interferons and other cytokines in non viral infections "
Chairpersons : **La Bonnardière C, Pine R**

2:00 W8.1 **Godot V :** *IN VIVO* TREATMENT WITH RECOMBINANT IFNα 2a PROTECTS C57BL/6J MICE AGAINST SECONDARY ALVEOLAR ECHINOCOCCOSIS
2:15 W8.2 **Lebleu B :** A 37 kDa 2-5A BINDING PROTEIN AS A POTENTIAL BIOCHEMICAL MARKER FOR CHRONIC FATIGUE SYNDROME
2:30 W8.3 **Miettinen M :** ACTIVATION OF NF-κB AND STATs BY GRAM-POSITIVE BACTERIA IN HUMAN MACROPHAGES
2:45 W8.4 **Condos R :** INDUCTION OF STAT-1 AND IRF-1 BY IFN-γ IN TUBERCULOSIS PATIENTS
3:00 W8.5 **Bafica A :** IFN-BETA AND TGF-BETA DIFFERENTIALLY REGULATE IL-12 ACTION IN HUMAN PBMC
3:15 W8.6 **Chevillard C :** STUDY OF GENETICAL FACTORS THAT CONTROL SEVERE FIBROSIS IN HUMAN INFECTED BY SCHISTOSOMA MANSONI
3 :30 W8.7 **Lammas DA :** ATYPICAL MYCOBACTERIAL PATIENTS WITH DOMINANT IFNγR1 DEFICIENCY DISPLAY HETEROGENEITY IN THE DOSAGE OF INTERFERON-GAMMA (IFNγ) REQUIRED TO ACHIEVE A CURATIVE RESPONSE

POSTER SESSION II (PII) - Grand Hall
The poster session II will be held on Wednesday, September 8 and Thursday, September 9 :
Signal transduction : from IFN receptors to IFN stimulated gene expression
IFN and other cytokines in cancerology and hematology : fundamental and clinical aspects
Interferon induced proteins and their function
Gene therapy in the interferon system and other cytokines
Interferon receptors and signalling
Interferons and other cytokines in non viral infections

4:30 - 5:00 **COFFEE BREAK**

ISICR/ICS JOINT MEETING AMSTERDAM

Nov. 5-10, 2000

Famous Quote

"The future belongs to those who believe in the beauty of their dreams."

Eleanor Roosevelt (1884-1962)

The Fellows & Students Corner

Hannah Nguyen

Bioinformatics and NetGenics, Inc.

Guest Writer: Manuel J. Glynias, President and CEO, NetGenics, Inc.

The field of bioinformatics is a rapidly growing and fashionable intrinsic component of scientific research. It is almost impossible to now analyze the infinite amount of data available to scientists without bioinformatics. One now hears of the possibility of doing a PhD or specializing in bioinformatics as a scientific career option.

To give us an insight on bioinformatics, I have the pleasure to introduce you to **Manuel J. Glynias**, President and CEO of NetGenics, Inc. Mr. Glynias has been involved in both commercial and research applications of bioinformatics software for the past 17 years. In 1986, while a graduate student at Case Western Reserve University in Cleveland, Ohio, Mr. Glynias developed MacGene, one of the first sequence analysis programs for the Apple Macintosh computer. Subsequently, he developed GeneWorks, a program marketed and later acquired by Intelligenetics, and Primer Express, a program for designing oligonucleotide primers for the polymerase chain reaction. In 1996, Manuel J. Glynias

collaborated with Nobel laureate Dr. Walter Gilbert to found NetGenics. Mr. Glynias' interests include music, antiquities, history, science and linguistics. I will now leave you to Mr. Glynias who will offer his perspective on bioinformatics and a description of his company NetGenics, Inc., which I am sure will provide inspiration to those who may be interested in pursuing bioinformatics as a career or simply integrating it into their everyday research activities.

Ever since Aristotle, the life sciences have been about observation, experiments, the gathering of data. Because there has never been enough data, biologists has spent very little time analyzing and theorizing, at least compared to their colleagues in the physical sciences. However, the automation of the techniques of molecular biology have led to an astounding increase in the amount of raw data available to the biologist, and the impact that this data will have on biology is hard to conceive. By 2002, we will know the DNA sequence of the entire human genome. The full genomes of two dozen of microbes, including many pathogens, have been determined, with several dozen more in progress. And, of course, the genomes of many plants and animals of economic interest are also being determined with the hope that this information will radically transform agribusiness. Bioinformatics, the application of information technology to the life sciences, has become essential over the last half-decade because, for the first time in the history of the life sciences, researchers have too much data.

Once the gene sequences are known, the real biology starts: What does the gene product do? How is it regulated? What tissues express it, and when? What other proteins does it interact with, and how? In which metabolic pathways does it play a role? How has the gene, or its role, changed through evolution? Does it play a role in disease? Can a small molecule inhibit the gene product, and does that inhibition ameliorate a disease? Answering these questions is impossible without bioinformatics tools to aid scientists in managing, analyzing, sharing and relating data derived from DNA sequencing, micro-arrays, proteomics, SNPs, high throughput screening, etc.

My interest in bioinformatics began when, as a grad student at CWRU in the early 1980's, I determined the cDNA sequence of malic enzyme from ducks, chickens and geese. Soon, I had too much data to handle with paper and pen. The software that existed at the time was cumbersome and only ran on computers that were unavailable to me. With youthful hubris, I decided to teach myself to program and create my own software. This led to the creation of my first business, and put me on the road that eventually led to founding NetGenics. Many other biologists have similar stories about how they came to be interested in bioinformatics. For most of us, bioinformatics is a set of tools that allows us to ask (and hopefully answer) interesting questions about biology.

At this point, you may think that I'm suggesting that every biologist should put down their pipettes and pick up Teach Yourself Java in 21 Days. That's not only unnecessary but possibly harmful. You don't need to know how an internal-combustion engine works to drive a car, so I would argue that you don't need to know how to program to use bioinformatics. I would recommend that biologists familiarize themselves with the kinds of tools used by bioinformatics so that you can apply critical thinking skills (and appropriate levels of skepticism) to the data and analyses produced by these tools. Not every BLAST result says what it may at first appear to say, and you need to know enough to be able to apply you biological intuition and distinguish the exciting new homology from the artifacts of sequence composition and buggy algorithms. There are a number of good tutorials on the web (for example, see Amos Bairoch's list of these at http://www.expasy.ch/alinks.html#Dict). In my case, wanting to understand my data led me to bioinformatics, and I recommend the you follow a similar course. Let the science be your guide, follow your project wherever it may go, and if that means sitting at a computer (and maybe learning a little Java), so be it. Good luck.

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NetGenics is a privately held company that develops and deploys information technology (IT) solutions to accelerate the drug discovery process. The company's SYNERGY* software framework enables a research organization to link diverse computing requirements within an enterprise-wide information infrastructure.

The SYNERGY framework permits integration of the diverse data that is part of the drug discovery process, including sequence, gene expression and genomic data, and chemical structure information. Using NetGenics products and services, pharmaceutical companies can combine their own proprietary data with information from companies like Incyte, as well as with public and government-sponsored data available over the Internet. At a time when

pharmaceutical companies are undergoing mergers, working across sites distributed throughout the world, and spending an increasing proportion of the research budget on collaborations, NetGenics software framework provides a basis for integrating data between widely separated geographical sites without requiring that the data undergo resource-intensive transformation.

NetGenics services extend a pharmaceutical research department's capabilities by providing outsourced system administration, collaborative software development and end-user support functions. NetGenics provides its comprehensive research IT solutions to several leading global pharmaceutical companies, including Abbott Laboratories and American Home Products (AHP) Corporation. The agreement with AHP calls for NetGenics to progressively establish seven SYNERGY installations at AHP units, including Genetics Institute, Wyeth-Ayerst, and Lederle. Through this collaboration, NetGenics will link all AHP sites to support a fully synchronized and distributed architecture for computational and bioinformatics research services and software.

NetGenics was established in June 1996 and is headquartered in Cleveland, Ohio. Its current investors include International Biotechnology Trust PLC (IBT), a fund managed by the Rothschild Bioscience Unit, John Pappajohn, Edgewater Private Equity, Oxford Bioscience Partners, Incyte Pharmaceuticals, Venrock Associates, Crystal Internet Venture Fund, and Casdin Life Sciences Partners.

Important Facts

The ant always falls over on its right side when intoxicated.

All polar bears are left-handed

REVIEWS OF INTEREST

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Billiau, A, Heremans, H, Vermeire, K & Matthys, P. Immunomodulatory Properties of Interferon-γ: An Update. *Ann. NY Acad. Sci*. 856:22-32, 1998.

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Fantuzzi, G & Dinarello, C. Interleukin-18 and Interleukin-1β: Two Cytokine Substrates for ICE (Caspase-1). *J. of Clin. Immunol*. 19:1-11, 1999.

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Svanborg, C, Godaly, G & Hedlund, M. Cytokine Responses during Mucosal Infections: Role in Disease Pathogenesis and Host Defence. *Curr. Op. In Microbiology* 2:99-105, 1999.

Viola, JPB & Rao, A. Molecular Regulation of Cytokine Gene Expression during the Immune Response. *J. Clin. Immunol.* 19:98-108, 1999.

DR. NOAH BUDDY'S HANDY REFERENCE GUIDE TO SCIENTIFIC TERMINOLOGY

aminoacyl---An -NH/sub2 that's a real jerk
apical membrane---That green bumpy stuff on the outside of a baby dill
asymmetry---Where you bury dead people
beta-sheet---Linen you only bring out for company
CA/sup{2+} channel---The all-milk TV station
chemotaxis---A cab which provides drug therapy
detergents---What women do when telling a guy to take a hike
diglyceride---What you scream out when trying to kill a glyceride

hippocampus---Where hippos go to university.
microtome---An itty bitty book
pachytene---Adolescent elephants
plastid---Drunk
prokaryote---In favour of take-out food
redox---Rusty cattle
taxol---Liberal plan for increasing revenue
From: Aliquotes iv.v (journal)
rogerb@microsoft.com
Science humor collected by Joachim Verhagen (jcdverha@xs4all.nl)

New Lerner Research Institute (LRI) at the Cleveland Clinic Foundation

The Cleveland Clinic Foundation's Lerner Research Institute celebrated the grand opening of its new 280,000 square foot research building in late May. The state of the art facility includes 73 new laboratories and 60 staff offices. Up to a dozen core or centralized facilities are now established at the LRI, including centralized glassware cleaning, cell culture services and media preparation, mass spectroscopy and gene expression analysis based on the Affymetrix Gene Chip system. Recipient of the 1999 Cleveland Engineering Society Design and Construction Award for Excellence, the new LRI building was constructed and equipped at a cost of $87.3 million.

The Lerner Research Institute is comprised of more than 100 primary investigators and 750 scientists and supporting employees. Its nine departments include Biomedical Engineering, Cancer Biology, Cell Biology, Molecular Biology, Molecular Genetics, Immunology, Molecular Cardiology, Neurosciences and Virology. Considerable emphasis is directed toward establishing collaborative investigations with clinical departments through various bridge programs.
Common interests based upon various aspects of interferon biology link many of the interdepartmental research programs thriving at the Lerner Research Institute. As Chairman of the LRI, Dr. George R. Stark has attracted a group of basic researchers who share interests in the signal transduction mechanisms of interferons and interferon target gene expression. Eight laboratories within the Institute conduct research on different facets of interferon biology. **Dr. George R. Stark's** laboratory employs mutant cell lines to investigate pathways of interferons, tumor necrosis factor and interleukin-1. **Dr. Bryan Williams'** group studies molecular mechanisms of interferon action, with particular focus on dsRNA-dependent protein kinase PKR and protein tyrosine phosphatases. **Dr. Robert Silverman's** team uses 2-5A antisense technology to target gene expression for hydrolysis by RNase L. Collaborations with Dr. Williams' group include investigations of interferon-induced gene expression using gene chip technology. **Dr. Thomas Hamilton's** laboratory studies how IL-4 interferes with interferon-stimulated signal transduction pathways. **Dr. Ganes Sen's** group is focused on identification of double-stranded RNA binding proteins and analysis of their function within cells. **Dr. Andrew Larner's** work focuses on the role of Raf/MAPK signaling in interferon induced gene expression. **Dr. Ernest Borden's** research centers on basic investigations on molecules such as antiestrogens, retinoids and cytokines that augment interferon signal transduction and antitumor effects. Finally, **Dr. Richard Ransohoff's** studies examine interferon-regulated chemokine production and multiple sclerosis and interferon-β specific regulation of βR1 expression.

WWW

Biomedpage

http://come.to/biomedpage

Announcement of a new version of the -non commercial- Biomedpage. With protocols in molecular biology, FREE medline access, dalmatian section, yeast two-hybrid systems and lots more. Please have a look at http://come.to/biomedpage and
http://members.tripod.de/biomedpage

Cytokine Gene Polymorphism in Human Disease

http://www.pam.bris.ac.uk/services/GAI/cytokine4.htm

Cytokine Reviews database
A searchable reference database containing 1,000 cytokine review citations, from 1990 to May 1999.

1 - List of Human Cytokine Gene Polymorphisms
2 - In vitro Expression Studies
3 - In vivo Disease Association Studies

Commments, corrections and additions are welcomed: please E-mail to: jeff.bidwell@bris.ac.uk

ModBase

http://guitar.rockefeller.edu/modbase/

ModBase is a queryable database of many annotated comparative protein structure models. The models consist of coordinates for all non-hydrogen atoms in the modeled part of a protein. They are derived by an automated modeling pipeline relying mainly on the program MODELLER. The database currently contains 3D models for su bstantial segments of 15-23% of proteins in the genomes of M. genitalium, M. jannaschii, E. coli, S. cerevisiae, and C. elegans. In total, there are models for 3,732 proteins. The database also includes fold assignments and alignments on which the models were based. In addition, special care is taken to assess the overall quality of the models and their accuracy at the residue level. In the future, ModBase will grow to reflect (i) the growth of the sequence databases, (ii) the growth of the database of known protein structures, (iii) and improvements in the software for calculating the models. It is expected that the Swiss-Prot +TrEMBL protein sequence database will be processed by the end of 1999. ModBase is introduced in R. Sanchez & A. Sali. Proc. Natl. Acad. Sci. USA 95, 13597-13602, 1998.

Mview
Release 1.37

http://mathbio.nimr.mrc.ac.uk/nbrown/mview/

MView is a free tool for converting the results of a sequence database search into the form of a multiple alignment of hits stacked against the query. For completeness, existing multiple alignments can be post-processed in the same way. A typical application is the generation of a colorized Web page from a BLAST or FASTA search allowing quick assessment of the hits in terms of sequence conservation patterns alongside the scoring information.

Changes in this release include:

- o Extension to the full BLAST suite of programs, notably tblastn by popular demand.
- o Column names added to numeric fields (score, expect, etc) for search programs in BLAST/FASTA suites.
- o Limited control from command line allowing a subrange of alignment columns to be extracted and displayed.
- o Semi-automatic input format detection based on filename or extension and specific program/version of BLAST or FASTA suite determined automatically.

MView allows filtering of the input by score, e-value thresholds, psi-blast search cycle, etc., provides a choice of coloring schemes and palettes for protein or nucleotide sequences, and can generate consensus patterns.

Currently recognised input formats include:
NCBI BLAST (2.0 series)
blastp, blastn, blastx, tblastn, tblastx, psi-blast
NCBI BLAST (1.4 series)
blastp, blastn, blastx, tblastn, tblastx
WashU BLAST2 (2.0)
blastp, blastn, blastx, tblastn, tblastx
FASTA (3.0 series)
fasta3, tfastx3
FASTA (2.0 series)
fasta, tfastx
MaxHom/HSSP
and the following flatfile formats:
Pearson, PIR, MSF, CLUSTAL

Alternative output formats are also supported: plain text, Pearson, PIR, and MSF, for export to other programs. See the Web page for the most recent information. This software requires Perl (version 5) and runs on UNIX systems.
See http://mathbio.nimr.mrc.ac.uk/nbrown/mview/ for details and ftp/installation instructions, and also the article: Brown, N.P., Leroy C., Sander C. (1998). MView: A Web compatible database search or multiple alignment viewer. Bioinformatics. 14(4):380-381.

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Octopus

Octopus, the new release of Visual BLAST and Visual FASTA, is now available. Please, go to: http://www.lmcp.jussieu.fr/~durand/HtmlDoc/software/octopus/octo_main.html for more information.
Patrick Durand

PSIPRED

http://globin.bio.warwick.ac.uk/psipred

PSIPRED is a new Web based protein structure prediction server available from the Jones group at the University of Warwick, U.K. The server is now running on a dedicated machine, and is now ready for public access. Three prediction methods are currently implemented:

PSIPRED - Prediction of protein secondary structure

MEMSAT2 - Prediction of transmembrane protein structure and topology
GenTHREADER - Prediction of protein tertiary structure by fold recognition
Note that at CASP3 (http://predictioncenter.llnl.gov/casp3), PSIPRED was the most accurate secondary structure prediction method tested, achieving an overall 3-state accuracy (Q3) of 77% across 24 prediction targets.

(Please note that commercial users will need to obtain a software license from the University of Warwick to access the server)
FAX: +44 (0)181 913 8545

Sequence Viewer

http://www.ncgr.org/sv

The National Center for Genome Resources is pleased to announce the release of Sequence Viewer, a graphical utility that dynamically retrieves and navigates genetic sequence data. Sequence Viewer, a free, public tool, is available today at http://www.ncgr.org/sv. Visit our newly redesigned, easy-to-navigate Web site to try out Sequence Viewer and all our other software tools. Sequence Viewer joins a suite of tools enabling researchers to access, visualize and analyze gene sequence data. This Java-based, user-friendly tool anyone with a Web browser may access it was developed to satisfy researchers need for graphical representations of nucleotide sequences in the Genome Sequence DataBase (GSDB) and detailed descriptions of sequence annotation. Sequence Viewer enables users to quickly find a region of a sequence that integrates with a gene, rather than searching through a lengthy, complex flatfile report. It also can be used as a QC tool to readily locate mistakes in feature position.

The tool serves dual roles as a quick visual overview of a sequence and as a mechanism to hone in on a specific region to glean in-depth information about features of the segment such as sequence tagged sites (STSs). Sequence Viewer s display can be scaled and customized, and users can easily distinguish between features on the forward strand and the reverse strand. Annotated biological features are displayed as bars in feature panes, which can be scrolled. A base pair ruler indicates base pair position. Sequence Viewer also aids users by integrating with other GSDB tools for database searching. NCGR's Web-based query or search tools developed for use with GSDB, including Ad Hoc, Excerpt, Flatfile and Maestro, can be accessed directly from Sequence Viewer. In particular, Sequence Viewer has been integrated with our Maestro tool -- sequences identified in Maestro can be viewed in Sequence Viewer as well as flatfile format.

To learn more about Sequence Viewer's benefits, visit www.ncgr.org/sv. If you have questions about using Sequence Viewer, please write us at svproject@ncgr.org.

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

The National Center for Genome Resources is dedicated to enhancing the understanding of life through the research, development and application of knowledge systems that support biological discovery. NCGR, a nonprofit organization based in Santa Fe, N.M., helps solve biological problems by facilitating the rapid evaluation and analysis of broad range of data.

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Daily Virology News

Retroscreen Virology and All the Virology on the WWW are launching a new FREE OF CHARGE service for those interested in virology. We have arranged for a virology-related email newsfeed from over 300 international news sources including the New York Times and BBC online. If you would like to receive these email updates please register at the Retroscreen Website: http://www.retroscreen.com/daily_virology_news.htm

or at All the Virology on the WWW: http://www.tulane.edu/~dmsander/dvnreg.html

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CLINICAL TRIALS

PROTOCOL IDS: JHOC-98011606, NCI-V98-1468, JHOC-9806.
Interferon alfa Plus **GM-CSF** in Treating Patients With Newly Diagnosed Chronic Phase Chronic Myelogenous Leukemia. Richard J.

Jones, Chair, Ph: 410-955-2813, Johns Hopkins Oncology Center.

PROTOCOL IDS: FHCRC-1272.00, NCI-H98-0009. Total-Body Irradiation, Busulfan, and **Interferon Alfa** Followed by Peripheral Stem Cell or Bone Marrow Transplantation in Treating Patients With Multiple Myeloma. William I. Bensinger, Chair, Ph: 206-667-4933, Fred Hutchinson Cancer Research Center

PROTOCOL IDS: MDA-DM-93-117, NCI-G96-1088, MDA-DM-93117. Combination Chemotherapy with or Without **Interleukin-2** Plus **Interferon Alfa** in Treating Patients with Advanced Melanoma. Sewa Singh Legha, Chair, Ph: 713-796-1221, University of Texas - MD Anderson Cancer Center.

PROTOCOL IDS: CBRG-9808, NCI-V98-1493. Combination Chemotherapy and Biological Therapy In Treating Patients With Kidney Cancer That Is Metastatic or Cannot Be Removed Surgically. Gamini S. Soori, Chair, Ph: 402-393-3110, Cancer Biotherapy Research Group

PROTOCOL IDS: SVMC-ONC-222P, NCI-V96-0886. Vaccine Therapy, Chemotherapy, and **Gm-CSF** In Treating Patients with Advanced Pancreatic Cancer Charles L. Wiseman, Chair, Ph: 213-484-7575, St. Vincent Medical Center - Los Angeles.

PROTOCOL IDS: HNMC-94087-94-11-1, NCI-V94-0590. Combination Chemotherapy and Peripheral Stem Cell Transplantation Followed by **Interferon Alfa** in Treating Patients with Multiple Myeloma. George Somlo, Chair, Ph: 626-359-8111, Beckman Research Institute, City of Hope.

PROTOCOL IDS: MSGCC-9851, NCI-V98-1513, MSGCC-1198006. Chemotherapy and Peripheral Stem Cell Transplantation Followed by Immunotherapy in Treating Patients With Chronic Myelogenous Leukemia. Aaron P. Rapoport, Chair, Ph: 410-328-1230. Marlene & Stewart Greenebaum Cancer Center, University of Maryland.

PROTOCOL IDS: MRMC-CTCA-9801, NCI-V98-1449. Biological Therapy Following Chemotherapy and Peripheral Stem Cell Transplantation in Treating Patients With Cancer. Oscar Francisco Ballester, Chair, Ph: 847-872-4561, Midwestern Regional Medical Center.

PROTOCOL IDS: JWCI-BB-IND-7004, NCI-V97-1281. **Interleukin-4** and Bacterial Toxin in Patients With Recurrent Malignant Astrocytoma.. Robert Wheeler Rand, Chair, Ph: 310-998-3978, John Wayne Cancer Institute.

PROTOCOL IDS: NCI-96-C-0113F, NCI-T96-0029N, NCI-MB-386. **Interleukin-12** in Treating Patients with AIDS-Related Kaposi's Sarcoma Robert Yarchoan, Chair, Ph: 301-496-0328, Medicine Branch, Bethesda, Maryland.