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## **ISICR Business Office**

ISICR@faseb.org TEL: 301-634-7250 FAX: 301-634-7049

#### **ISICR Newsletter Editors**

Howard Young youngh@mail.ncifcrf.gov Fax: 301-846-1673

Seng-Lai (Thomas) Tan tan\_seng-lai@lilly.com

Hannah Nguyen nguyenh@methylgene.com



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# An Interview with Milstein Awardee Dr. John Hiscott

Hannah Nguyen



#### **Biography**

John Hiscott is a Professor in the Departments of Medicine, Microbiology & Immunology and Oncology at McGill University and is the Director of the Molecular Oncology Group at the Lady Davis Institute for Medical Research. Dr. Hiscott received his Ph.D. degree from New York University Medical Center and

completed Post-doctoral training at the Roche Institute in New Jersey and at the Institute for Molecular Biology at the University of Zurich. He is currently a Senior Scholar of the Canadian Institutes of Health Research and is also the Coordinator of the CIHR Program in AIDS Pathogenesis, which is part of the McGill AIDS Center at Lady Davis Institute. Dr. Hiscott is a project leader in an international research consortium involving the Canadian Vaccine Initiative (CANVAC) and Genome Canada, which is directed toward the development of vaccines against cancer and chronic viral diseases. His research interests include: regulation of gene expression in cancer cells, development of immune response modifiers and analysis of the immune response to virus infection. Dr. Hiscott is the 2003 recipient of the Milstein award, the highest honor of the International Society for Interferon and Cytokine Research. He shares this award with Dr. Tom Maniatis of Harvard University. In 2003, he published articles in Science and Cancer Cell on triggering of the immune response to virus infection and the use of oncolytic viruses in cancer therapy.

(Biography courtesy of John Hiscott).

(See Hiscott, page 2)

#### (*Hiscott*, cont. from page 1)

#### Congratulations on receiving the 2003 Milstein Award! What were your thoughts when you first found out that you were a recipient of the Award?

Surprise, disbelief. Certainly I felt very honored. I actually heard about the award in a roundabout way. Keiko Ozato sent an e-mail asking if I would give a presentation at the American Association of Immunologists Conference in April, and at the end of the e-mail she wrote: "By the way, congratulations again on winning the Milstein Award!" There must have been some mix-up with letters, and I ended up finding out as a postscript to an e-mail. It is a great honor to join the list of scientists who have received the Milstein Award, and I am particularly honored to share the award with Tom Maniatis. The Award was long overdue - for Tom Maniatis of course, not me!

#### Congratulations also on your recent Science paper describing the discovery of the kinase for Interferon Regulatory Factor-3 (IRF-3). How did you end up finding the kinase?

It is a long story. We had been looking for that kinase in one form or another for about 4-5 years, as part of our studies on regulation of IRF3 and IRF7. There were many people along the way who had asked: "what's going on with 'the kinase' " - not always politely, I might add! We took a number of different approaches, and in retrospect, accumulated many clues from pharmacological inhibitors, dominant-negative kinase constructs, biochemical purification and yeast two-hybrid screening - all of which kept leading us back to an IKK-related pathway. The immediate set of results that put us on track came from unrelated experiments. Sonia Sharma, a PhD student in the lab, was conducting research on the Ikappa-B kinase family member IKKe and its role in T-cells as a potential regulator of c-Rel. Sonia and I were attending a Conference in Santorini, Greece and after an afternoon of discussing lymphocyte signaling (and other more interesting things), we realized that IKKe was a good candidate kinase for IRF activation. Sonia had the good sense to call back to the lab to get cells set up, so that she could start the

experiment upon her return. A few days after the Conference, Sonia came into my office holding the first of several IKKe kinase assays showing IRF-3 phosphorylation and she looked very excited. Two days later, Dr. Rongtuan Lin appeared at the office door with an IFNA reporter gene - IRF7 - IKKe coexpression result that had us both hitting the roof -2000 fold stimulation of IFN expression. I remember calling someone soon after these first clues and saying: "I think we got this kinase, and it is just about as interesting as anyone could have hoped for!"

Once we had the initial clues, the experiments fell together unlike any other set of experiments I have ever seen, probably because we had been building the necessary reagents for this study for the previous five years. It was really a unique combination of people and talent - Sonia Sharma, Benjamin Tenoever, Nathalie Grandvaux and Dr. Rongtuan Lin - working together non-stop - that made the experiments move so quickly. We got the paper out to Science in December 2002 and thought that Science would: a) like it and let us know very quickly; or b) not like it and let us know very quickly. However, Science took its time, and it wasn't until the end of February 2003 that we got the manuscript back. However what came back was a manuscript completely edited by the editorial staff (along with the usual reviewers' requests for a couple of other experiments). From the beginning, we felt it was necessary to work quickly because both the Maniatis and Akira groups were obviously working in the same area. We had no idea however, that Kate Fitzgerald was also ready to submit. Also in January, Mike Gale called to say that he had a paper out to Science on the HCV NS3/4A protease blocking IRF activation and complained that the reviewers wanted him to identify the kinase involved. I told him that we didn't know much about NS3/4A but did know about the kinase. The fact that both papers (Foy et al.: Sharma et al.) came out together, along with the Bryan Williams and Ganes Sen Perpsectives, helped the impact of the study. It was also gratifying (but a little tense at the end) that Kate's paper (Fitzgerald et al.) was so complementary to ours; they followed TBK/IKK through TLR-TRIF signaling, whereas we worked back from C-terminal IRF-3 phosphorylation.

# What are your plans now with respect to the IRF-3 kinase?

There are three directions we are following. First, we would like to find the viral determinants that lead to TBK and IKK activation, both in epithelial cells and in dendritic cells, and that of course involves the intensely investigated area of Toll-like receptor (TLR)-dependent and -independent signaling to innate immunity. Second, Dr. Lin and Sun are working on the reconstitution of the IKK pathway in vitro using purified components. We are also interested in the role of TBK and IKK signaling in viral-induced apoptosis. Also, with Dr. John Bell at the University of Ottawa, we recently received a National Cancer Institute Program Grant to study viral oncolysis - targeting tumor cells for destruction with replication competent viruses such as Reo and VSV. The project is multi-centered and spans basic mechanistic research, vector development, pre-clinical models, as well as phase I clinical trials. For this lab, it is an exciting new applied research direction.

# What, in your opinion, are the components of a successful lab?

The people in the lab - postdocs and students with talent, interest and commitment to science - are the key components of a successful lab. Good competitive projects are also essential; there is no sense in pursuing a project with an obscure niche; a broad based project with a strong molecular basis is essential. Collaborations are absolutely critical, in this day and age, that's true more than ever. I said recently at a conference that 'over the years, my collaborators have become colleagues and then have become friends'. They have helped me scientifically and personally in innumerable ways and I am very grateful. There is one thing I would never want to do and that is attempt to do research on a shoestring budget. This happens sometimes and it is so difficult - it's so important to do research with (minimal) budgetary restrictions.

# What are your favorite and least favorite aspects of running a lab?

One aspect of running a lab that is both the best and at the same time the worst is seeing people succeed and moving on. Sometimes it's hard to get people to finish up, and at the same time you don't want to see them go. A wonderful aspect is seeing new results come in that give rise to a multitude of potential new avenues. It makes research so exciting and renewing. Grant and report deadlines are not really my favorite things; sometimes grants write themselves and then other times it is a difficult process. Paper writing is fun for the most part, particularly if there is a clear idea of where the science is going. Another tough aspect of running a lab is motivating people. Ideally you want a group that is always self-motivating, so that when new people join the lab, they know that they are working in a tough competitive area and success is based not on grades but on good scientific results. Interpersonal management can also be a challenge. There are no clear cut rules; everyone has their individual personalities and you try to treat them as such. I try to maintain 3-4 subgroups working on different themes in the lab, and even then there are internal conflicts that sometimes prevent the free exchange of ideas.

## Who are the mentors in your life?

My most important mentors are all the students and postdocs that pass through my life - they continue to teach me good things and sometimes bad things. During research training, I had four mentors, all of whom influenced me greatly. My first mentor was Phil Cheevers, at the University of Western Ontario, who introduced me to scientific life, molecular virology and to motorcycles. My second mentor - my PhD supervisor - was Vittorio Defendi, who at the time had just taken the Chair of Pathology at New York University Medical Center. He was a very dynamic and supportive mentor, and continues to be so to the present. I am always grateful that he tolerated some of my wild antics as a grad student. I then spent one year at the Roche Institute of Molecular Biology in New Jersey, with Sidney Pestka as my mentor. This was an interesting time in interferon research; the different IFN genes had just been just cloned - among the first successes of the fledgling

#### (*Hiscott*, cont. from page 3)

biotech industry - and companies like Genentech, Roche and Biogen were competing to produce IFN for clinical research. I had what turned out to be a unique perspective of the confluence between academic and biotech research. Following that, I spent three years at the University of Zurich, under the supervision of Charles Weissmann, studying the expression of the IFN multigene family. In Zurich, I met some of the most intelligent scientists, including Weissmann himself - a brilliant, driven and dedicated mentor. Life in Europe was also wonderful.

# What do you think is the current and future status of interferon and cytokine research?

This is another exciting period in the long colorful history of interferon and cytokine research. Again there is a new intensity in the field in relation to the role of IFN in innate and adaptive immunity, the relationship between IFNs, pathogen recognition and TLR signaling, viral evasion, not to mention the new discoveries in relation to STATs and cancer. This period is reminiscent of 10 years ago when it became clear that the Jak-STAT signaling paradigm was not exclusive to the IFN system.

#### After your postdoctoral work were you sure that you wanted to pursue your career as an academic scientist? Did you ever regret that decision?

I enjoy what I am doing, it is always changing, and for the most part the lab has maintained momentum over the years, so I don't look back too often. Canadian and provincial agencies have been very supportive of our work over the years, and now that the lab is well-established, I have the freedom and support to pursue projects of interest. The only thing I regret every grueling Canadian winter is not having established my lab elsewhere - in places such as New York or Florida or Paris!

#### What are your favorite activities outside of the lab?

I love scuba diving, which I have done on-and-off for the last 20 years. During the last three years, I have renewed an interest in diving that now includes caves, wrecks and night dives. I'm a warm weather warm water diver, i.e. Carribean-style! Diving is also a good substitute to running, which I love to do but had to stop since I blew out my Achilles tendon. Diving takes you into a complete "other world" peaceful and beautiful. Some days I am more comfortable in the water than out - a truly relaxing sport (when you know how to breathe!). I also love to travel, especially to Europe - I love the history, culture, art. An interest in photography - strictly amateurish - has also been renewed in the digital age.

# You have four wonderful children. Would you encourage or discourage them from becoming a scientist?

I encourage my kids to be the best, at whatever they choose to do. My eldest daughter Rebecca who is now 14 is very literary - a writer, a debater and a voracious reader. She is the best - intelligent, hip, beautiful, and remorseless in her individuality. My other kids active and young - all have their own personalities. Benjamin is 10 and is a great guy to hang out with; he is easy going and sensitive, probably will end up as a major league baseball player or a computer wizard that builds electronic games. Leah is 7 and a happy go lucky tomboy with a tough independent streak. Katerina is 5 and a fun-loving princess. They all keep me very busy and actually very young; when I am not working or traveling, I am invariably shuttling them to one event or another. I can't wait to find out what happens next with them; whatever it is will be interesting!



# ISICR Member Milton Taylor is Honored

The Department of Biology of Indiana University held a symposium from May 28 - 30, 2004, to honor Milton W.

Taylor, PhD, professor of biology, and celebrate the creation of the Taylor Fellowship in Virology. Professor Taylor has researched and taught molecular biology for forty years. During this time, he has worked in the areas of somatic cell genetics, viral replication, and the effects of interferon on viral replication and the immune system. He has also characterized at the molecular level the Amgen consensus interferon. Professor Taylor currently runs one of four ancillary labs selected to participate in a clinical trial funded by the National Institutes of Health (NIH) to investigate the effects of interferon on hepatitis C patients. Professor Taylor teaches the most current scientific topics and cutting-edge tissue culture techniques in virology. Many of Professor Taylor's former students are now prominent scientists at top academic institutions or hold key positions in the biotechnology and pharmaceutical industries. Some of his Ph.D. students have earned their M.D.s and are practicing physicians. Several undergraduates who have worked in Professor Taylor's laboratory have become IU Science, Technology, and Research Scholars (STARS) and Wells Scholars. Two students of his students, Raju Raval and Kathleen Tran, received Rhodes Scholarships. Since joining IU, Professor Taylor has received uninterrupted funding from the NIH and grants from the American Cancer Society, the Damon Runyon Foundation, and industrial groups such as Amgen, Schering Plough, and Eli Lilly. Professor Taylor's lab is also one of four ancillary labs selected to participate in a large clinical project funded by the NIH, to investigate the differences in how African and Caucasian Americans respond to interferon treatment.

Professor Taylor is a fellow of the American Society for Microbiology, an honor reserved for particularly accomplished microbiologists, a fellow of the Indiana Molecular Biology Institute, and a former office holder in the International Society for Interferon and Cytokine Research.

The program for the symposium included two days of talks, three receptions, and the presentation of the fellowship. Former PhD students, post-doctoral fellows, undergraduates, and collaborators of Professor Taylor spoke at the Symposium. Dr. Lawrence Blatt, vice president of biopharmacology at InterMune, Inc. and founder of the Taylor Fellowship, opened the symposium and introduced the first Taylor Fellow.

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# Famous Quote



"If we knew what we were doing, it would not be called research, would it?" ~ *Albert Einstein* 

# Cuba's Center for Genetic Engineering and Biotechnology (CIGB): Cohibas, Mojitos and Interferons

Thomas Tan

Interferons (IFNs) have had its impact in various research areas and medicines and shared many spotlights in the news over the years. But did you know that IFNs



helped jump-start the entire biotechnology program in Cuba? It happened in 1980 when Castro heard about experimental work with IFNs for the treatment of cancer from a meeting with Lee Clark, then president of M.D. Anderson Hospital in Houston, Texas. Impressed with the therapeutic potential of IFNs, Castro immediately made the decision to invest heavily in IFN research, and would use it as a stepping stone for the "new" biotechnology in Cuba.

A group of Cuban scientists led by Manuel Limonta were sent to Lee's cancer hospital and the Helsinki laboratory of Kari Cantell to learn the production of IFNs and soon Cuba was producing its own IFNs for research in molecular biology and biotechnology. Although IFNs did not live up to its expectation as the "magic bullets" predicted at the time, they served as a model for the development of molecular biology and biotechnology in Cuba and spawned several important research-production facilities in the "Western Havana Scientific Pole", including the Center for Genetic Engineering and Biotechnology (CIGB).

The launch of the CIGB marked the beginning of the maturation of biotechnology in Cuba, with an investment of approximately US \$100 million to fully equip modern research in areas covering pharmaceuticals and immunodiagnostics, vaccines, animal, plant, and industrial biotechnology. Endowed with the state of the art equipment (mass spectrometers, electron and scanning microscopes, gamma counters, DNA synthesizers, etc.), production capacities and excellent personnel (60 Ph.D. and 70 M.Sc.), the Center is devoted to the development of new biomedical and agricultural products in all stages, from the cloning and protein expression using recombinant DNA technology to industrial production. Amongst the CIGB's leader products are recombinant Hepatitis B Vaccine (HEBERBIOVAC-HB ®), recombinant alpha 2b IFN (HEBERON ALFA R ® ), recombinant Streptokinase (HEBERKINASE ®), IFN gamma (HEBERON GAMMA ® ), Epidermal Growth Factor (HEBERMIN ® ), Erythropoietin (HEBERITRO ® ), recombinant GSCF (HEBERVI-TAL <sup>®</sup>), a synthetic vaccine against Haemophylus influenzae (QUIMI-HIB ®) and Vaccine for the con-employs over 1000 scientists and engineers.

The CIGB has developed a network of academic relations with the leading group in the field of Biotechnology from Austria, Belgium, Brazil, Canada, Denmark, Finland, France, Germany, Italy, Japan, Mexico, Norway, Spain, Sweden, Switzerland, The Netherlands, and United Kingdom, among other countries. WHO, PNUD, PAHO, UNESCO, UNIDO and FAO are some of the main International Organizations that keep academic relations with the CIGB.

In addition, the international congress Biotechnologia Habana takes place at the CIGB to discuss the main topics related to IFNs and cytokines, prophylactic and therapeutics vaccines, cancer, autoimmune diseases, inflammatory processes, genomic-proteomics and bioinformatics in the new millennium, agriculture, animal health, biosafety, and bioethics. Past programs included sessions on the mechanism of action of IFNs and Cytokines, the central nervous system, where emphasis was on multiple sclerosis trials (with IFN beta and alpha), clinical applications on infectious diseases (mainly hepatitis and AIDS), cancer and angiogenesis control, and modern delivery systems for cytokines. Foreign speakers included Huub Schellekens, Otto Haller, Jan Tavernier, Sandra Pellegrini, Reyes Tamez Guerra, Victor Rivera, Anthony Meager, Najib-ul-Haq, Noe Alvarado, Vladas Bumelis, and Glen Barber.

(See CIGB, page 7)

# An Interview with Pedro Lopez Saura

# 1. How long have you been at the CIGB and what are your current responsibilities at the Center?

I have been at the CIGB since the beginning of the project. At present I am Director for Regulatory Affairs and Clinical Trials.

# 2. What attracted you to the CIGB in the first place?

I was one of the initial group that went to Kari Cantell's lab in 1981. We were enrolled in what was a new and promising "task force". We could not imagine that it would take us for the rest of our lives. The main attraction was, and still is, the possibility of contributing to the healthcare, and development of our country.

# 3. What is the place of the CIGB in relation to the government and academia?

The CIGB is part, and the largest component, of the so called "West Havana Scientific Pole", made by more than 50 scientific, production, teaching, and health services facilities. The main centers of this complex belong to the Council of State, which is the main executive power in the country. Other facilities belong to different ministries such as Health, High Education, Agriculture, and Science and Technology. The CIGB is engaged in academic work as well, including basic research and a very intense relationship with several universities.

# 4. Have the expectations of the CIGB been fulfilled in general in your opinion?

Yes. Our products have been introduced in our society, and are fully available for several important health programs (hepatitis, cancer, cardiovascular diseases), where impact has been achieved, and recognized by the government and the population. At the same time, exports have been increasing and since several years, the center is self-sustaining.

#### 5. What are the current priorities of the CIGB?

To develop new products, mainly with world-wide intellectual property. Particular interest is given to vaccines. A good example is the recently registered anti-Haemophylus influenzae vaccine, which is the first vaccine in the world based on a chemically synthesized antigen.

#### 6. How does the CIGB handle the competition, if any, between other groups in the Western Havana Bio-Cluster for resources and paternity rights over promising projects?

Coordination among groups is the rule, rather than competition. In fact there is no example of a project developed by one center alone. Resources are distributed centrally among the projects in the "Pole".

#### 7. Critics said that Cuba's once vigorous biotechnology now is on the verge of expiration, strangled by increasing social and political tensions. Is this true?

Absolutely not. The last 5 years have seen an "explosion" of new publications, patents, products registrations, and sales, as compared to previous years. I would say it is the contrary, Cuban biotechnology is flourishing.

# 8. Fidel Castro once proclaimed that "Cuba's future must, by necessity, be a future of scientists." Is this the official slogan in Cuba?

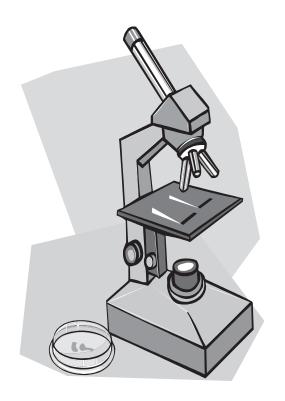
It has been not only a slogan but an official policy during more than 40 years. That sentence was said in a speech in January 1960, when the country had more than 20% illiteracy. We are now harvesting its fruits. (Saura, cont. from page 7)

#### 9. What do you think is the biggest challenge for Cuba to succeed in biotechnology? Do you think Cuba will become a biotechnology powerhouse?

The biggest challenge is to become that powerhouse; to enter the so called "first world" market; to have more influence in the country's food production; to contribute in a larger extent to the solution of a great world health problems, such as AIDS, malaria, cancer, etc.

#### 10. When is the next international congress Biotechnologia Habana? What will be the theme this year?

The congresses take place every year. This year there will be two small ones, on vaccine production and fructan chemistry, metabolism, and applications. Next year it will be dedicated to agriculture, and in 2006 to biomedical research and development again, when we'll celebrate the 25th anniversary of IFN production in Cuba.



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## **Cytokines in Cancer and Immunity 5TH Joint Meeting of the The International Society for Interferon and** Cytokine Research (ISICR) and the International Cytokine Society (ICS)

October 21-25, 2004 San Juan, Puerto Rico

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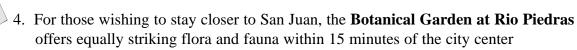
# Ten Cool Things to Do in Puerto Rico

# Puerto Rico has an abundance of places to go and things to do, within or beyond San Juan, if you have the time. Here are some popular ones:

 Bring your bathing suit and hit the beach - Isla Verde Beach is the real San Juan scene. You can rent chairs and umbrellas, and when it's time for a bite, check out Ciao Mediterranean Café, which has live music on the weekends in summer.



- 2. The **Museo de Arte de Puerto Rico**, in Santurce, is a must-see. The permanent collection, housed in a recently renovated neoclassical building, features locally created works from the 17th century to the present.
- 3. **"El Yunque**" United State's National Rain Forest a mountainous, semi tropical rainforest in eastern Puerto Rico. At the higher elevations the waters are actually clean enough to drink and delightful to swim in.



- 5. The **Phosphorescent Bay, Parguera** a small and friendly fishing town with several tourists services, restaurants and superb recreational opportunities. A special variety of luminescent plankton, dinoflagellates, glow like blue fire in the dark as you stir your hand through the water.
- 6. Visit **Mayaguez** the third-largest city of Puerto Rico. The city itself is centered around the impressive Spanish-style Plaza Colon, a tribute to Christopher Columbus, whose stature stands in the middle of the square.
- 7. If you are a golfer, we heard **Dorado Beach and El Conquistador Golf Clubs** are world-class courses and quite famous.



8. Want to see something really cool? Check out the **Arecibo Observatory** - nested in the mountains of Northern Puerto Rico about 30 minutes from downtown Arecibo, off route 625, it is the world largest radar/radio telescope.



9. La Vida Loca! Puerto Ricans take dancing seriously, so dress sharp (as the locals do) and head out into the night. Mango's Café in Punta las Marías, and Rumba in Old San Juan both have live music until very late.

10. The largest rum distillery in the world is the one operated by **Bacardi**, on the outskirts of San Juan. Take the 45-minute tour, which will lead you past the distillery, the bottling plant, and the museum, known as the "Cathedral of Rum." Drink, err we mean "sample" responsibly.

# **TELL US WHAT YOU THINK**

We welcome and appreciate letters that are suitable for publication from ISICR members regarding issues of importance or commenting on articles/information appearing in ISICR newsletters. Letters should be sent to the editor, Howard Young, at the indicated address or email. Letters must be signed and must contain the writer's address and phone number. The editor reserves the right to publish and edit all letters.

# GENGENGENGENGENGENGENGEN

# **OUT TO DINNER MATHEMATICS**

This is pretty neat how it works out.

It takes less than a minute......

Work this out as you read.

- 1. First of all, pick the number of times a week that you would like to have dinner out. (try for more than once but less than 10)
- 2. Multiply this number by 2 (Just to be bold)
- 3. Add 5. (Just because)
- 4. Multiply it by 50 I'll wait while you get the calculator.....
- 5. If you have already had your birthday this year add 1753.... If you haven't, add 1752.....

#### Keep Going

6. Now subtract the four digit year that you were born.

#### Keep Going

You should have a three digit number.

Keep Going

The first digit of this was your original number (How many times you want to eat out each week.)

The next two numbers are ...

Keep going



YOUR AGE in 2003! (Oh YES, it IS!!!!! Scary to think that you are that old)

2003 was the only year it will ever work. IMPRESSIVE, ISN'T IT? (Yes, I know some of you are thinking, why didr

(Yes, I know some of you are thinking, why didn't he run this in last year's newsletter???? It was all the great French wine I had last summer while on sabbatical. It may have blurred my decision. Ed.)

## **NEW ISICR MEMBERS**

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

Wei-Chun Chou Taipei, Taiwan

James G. Cripps Louisville, KY

**Filip Culo** Zagreb, Croatia

**Eileen M. Fay** Dallas, TX

Christine L. Fisher Toledo, OH

**Jun Gao** Shanghai, China

**Mireia Guerau-de-Arellano** Boston, MA

**Hisashi Harada** Richmond, VA

**Ying Huang** Indianapolis, IN

**Panagiota Iliopoulou** Boston, MA

**Cynthia L. Johnson** Dallas, TX

Trine N. Jorgensen Denver, CO

**Brian Keller** Dallas, TX

**Endre Kiss-Toth** Sheffield, UK Signe E. Larsen Aarhus, Denmark

Haiying Li Toledo, OH

**Peng Liang** Nashville, TN

Alexander N. Narovlyansky Moscos, Russia

Ramesh B. Potla Cleveland, OH

Kate D. Ryman Shreveport, LA

**Corneliu Sanda** Bloomington, IN

Michael F. Smith Charlottesville, VA

**Kirk A. Staschke** Indianapolis, IN

**Dalit Strauss-Ayali** Rehovot, Israel

**Albert K. Tai** Boston, MA

**Jill A. Trendel** Toledo, OH

**Chunfu Wang** Dallas, TX

**Ping Zhao** Shanghai, China



# **Meeting of Interest**

#### Neuroendocrine-Immune Interactions EuroConference on Cytokines in the Brain: Expression and Action of Cytokines in the Brain and Pathophysiological Implications

Supported by the European Commission, Research DG, Human Potential Programme, High-Level Scientific Conferences (Contract No: HPCF-CT-2001-00038)

Giens (near Toulon), France, 8-13 October 2004

Chair: **Robert Dantzer** (INSERM Bordeaux, F) Vice-Chair: **Rainer H. Straub** (Universität Regensburg, D)

#### **Speakers will include** P. Eikelenboom (VU Amsterdam., NL) P. Patterson (Caltech, Pasadena, US) S. Allan (Manchester U., UK) V. Arolt (Münster U., D) R. Itzhaki (Manchester U., UK) V. Perry (Southampton U., UK) L. Capuron (Emory U., US) K. Kelley (Illinois U., Urbana, US) S. Poole (NIBSC Potters Bar, UK) T. Cartmell (NIBSC Potters Bar, UK) B. Kieseier (Düsseldorf U., D) S. Rivest (Laval U., CA) N. Castanon (INSERM Bordeaux, F) B. Leonard (Galway U., IRL) F. Tilders (VUMC Amsterdam, NL) M.-L. Cuzner (UC London, UK) M. Lynch (Trinity College Dublin, IRL) A.-M. VanDam (VUMC Amsterdam, NL) C. Dijkstra (VUMC Amsterdam, NL) M. Maes (Maastricht U., NL) D. Vivien (Caen U., F) U. Dirnagl (Humboldt U. Berlin, D) M. Mehler (NY Coll. of Medicine, US) H. Wekerle (MPI Martinsried, D) M. Dubois-Dalcq (Inst. Pasteur Paris, F) P. Parnet (INSERM Bordeaux, F) H. Widner (Lund U. Hospital, S)

#### Scope of the conference

Cytokines have been characterised in the early eighties as paracrine and autocrine communication molecules between immune cells and between immunocytes and other peripheral cells, such as fibroblasts and endothelial cells. They play a key role in the regulation of the immune response and the coordination of the host response to infection. Cytokines have also been found to be expressed in the brain, in endothelial cells, glial cells and neurons. Their local expression and actions mediate not only the brain response to immune and non-immune injury, but also the central component of the acute phase reaction. However, their role is not restricted to pathology, since they appear to be involved in brain development and plasticity. The objectives of this conference are to review the most recent developments in this new field at the interface between neurosciences and immunology, and to discuss the pathophysiological implications of the expression and action of cytokines in the central nervous system. The key elements of the brain cytokine system will be presented first, with an emphasis on their spatial and temporal distribution in the brain. This will be followed by a review of the mechanisms of action of cytokines in the brain, from the perspective of the clinical manifestation they mediate. The role of cytokines in neurogenesis and brain development will then be discussed before a comprehensive review of their role in immune and non-immune mediated neuropathologies. The conference will end with a review of why and how cytokines can be implicated in various forms of psychopathology.

This conference should be of interest not only to those who are already involved in the field, but also to neurobiologists as well as immunologists who are willing to understand how the knowledge gained in one scientific discipline can help and fecund the concepts and methods of a different field.

It is open to researchers world-wide, whether from industry or academia. Participation will be limited to 100. The emphasis will be on discussion about new developments. The conference fee covers registration as well as full board and lodging. Grants will be available, in particular for nationals under 35 from EU or Associated States.

#### **Deadline for applications: 11 June 2004**

Scientific Programme and on-line Application at: http://www.esf.org/euresco/04/mc04140 For printed copies, contact the EURESCO Office:

European Science Foundation, EURESCO Office, 1 quai Lezay-Marnésia, BP 90015, 67080 Strasbourg Cedex, France

## **Clinical Trials**

More information on this list can be obtained at <u>http://clinicaltrials.gov</u> [CT], <u>http://www.centerwatch.com/search.asp</u> [CW], or <u>http://clinicalstudies.info.nih.gov</u> [CCNIH]. We welcome submissions from the ISICR membership for listings in this section.

 Phase I Study of Anakinra to Treat Advanced Cancers that Produce Interleukin-1. *Contact:* National Cancer Institute (NCI), 9000 Rockville Pike, Bethesda, Maryland, 20892, Patient Recruitment and Public Liaison Office 1-800-411-1222 <u>prpl@mail.cc.nih.gov</u> TTY 1-866-411-1010. Study ID Numbers 030281; 03-C-0281

 Phase I/II Study of HTLV-I-Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP) Using the Humanized MiK-beta-1 (IL-2R/IL-15R) Monoclonal Antibody. *Contact:* Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754. Toll Free: 1-800-411-1222; TTY: 1-800-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, Email: prpl@mail.cc.nih.gov. Study Number: 04-N-0071

3. Investigating the Use of **Interleukin-12** and **Interleukin-2** to Treat Children with Neuroblastoma. *Contact:* National Cancer Institute (NCI), 9000 Rockville Pike, Bethesda, Maryland, 20892, Patient Recruitment and Public Liaison Office 1-800-411-1222 <u>prpl@mail.cc.nih.gov</u> TTY 1-866-411-1010. Study ID Numbers 030252; 03-C-0252

4. The PRECISE Trial: Survival Study of **IL13-PE38QQR** Compared to GLIADEL® Wafer in Patients with Recurrent Glioblastoma Multiforme. Contacts in 12 American States, Canada, Germany, Isreal, The Netherlands and The United Kingdom. Study ID Numbers IL13PEI-301-R01; PRECISE Trial

5. Ingested **Interferon Alpha:** Prolongation or Permanence of the "Honeymoon" Phase (enhance B cell survival) in Newly Diagnosed Type 1 Diabetes Mellitus. *Contact:* Staley Brod, M.D. 713-500-7046 <u>Staley.A.Brod@uth.tmc.edu</u>, Dept. of Neurology, Rm MSB 7.044, Univ. of Texas-Houston Medical School, Houston, Texas, 77030. Study ID Numbers NCRR-M01RR02558-0135; M01RR02558

## **Clinical Trials, continued**

6. Prevention of cognitive decline in Alzheimer's disease by ingested **interferon alpha**. *Contact:* Staley A. Brod, M.D. 713-500-7046 <u>staley.a.brod@uth.tmc.edu</u>, University of Texas - Houston, Gerontology Center of the UTMSI, Houston, Texas, 77030. Study ID Numbers NCRR-M01RR02558-0120

 Phase II Study of Low-Dose PEG-Interferon alfa-2b in Patients with Metastatic Melanoma Over-Expressing Basic Fibroblast Growth Factor. *Contact:* Kelly Filchner, MSN, RN, OCN, CCRC, Network Clinical Studies Coordinator, St. Luke's Hospital & Health Network, 801 Osturm Street, Bethlehem, PA 18015. Tel: 610-954-3582 Fax: 610-954-3583 <u>filchnk@slhn.org</u>. Centerwatch study posting 2835

8. Immunotherapy Using Cyclosporine, **Interferon gamma**, and **Interleukin-2** After High-Dose Myeloablative Chemotherapy With Autologous Stem Cell Transplantation in Treating Patients With Refractory or Relapsed Hodgkin's Lymphoma. Contacts in 48 American States, Australia, Canada, New Zealand, Puerto Rico, and Switzerland. Study chairs: Allen R. Chen, MD, PhD, Sidney Kimmel Cancer Center and Sharon Gardner, MD, Kaplan Cancer Center. Study ID Numbers CDR0000330135; COG-AHOD0121

9. The INSPIRE Trial: A Phase III Study of **Interferon gamma-1b** for Idiopathic Pulmonary Fibrosis (IPF). *Contact:* InterMune, Inc., Brisbane, California, 94005 <u>www.inspiretrial.com</u> Study ID Number GIPF-007

10. **Infliximab** (**Remicade**®; combination of part human and part mouse **tumor necrosis factor**) to Treat Non-Infectious Scleritis. *Contact:* National Eye Institute (NEI), 9000 Rockville Pike, Bethesda, Maryland, 20892; Patient Recruitment and Public Liaison Office 1-800-411-1222 <u>prpl@mail.cc.nih.gov</u> TTY 1-866-411-1010. Study ID Numbers 040065; 04-EI-0065

 Phase I Study of T Cell Large Granular Lymphocytic Leukemia in Humanized MiK-Beta-1 Monoclonal Antibody Directed Toward the IL-2R/IL-15R Subunit (CD122) *Contact*: Patient Recruitment and Public Liaison Office, Building 61, 10 Cloister Court, Bethesda, Maryland 20892-4754. Toll Free: 1-800-411-1222; TTY: 1-800-594-9774 (local), 1-866-411-1010 (toll free), Fax: 301-480-9793, Email: prpl@mail.cc.nih.gov. Study Number: 04-C-0089

12. **Anakinra** to Treat Patients with Neonatal Onset Multisystem Inflammatory Disease. *Contact:* National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 9000 Rockville Pike, Bethesda, Maryland, 20892; Patient Recruitment and Public Liaison Office 1-800-411-1222 <u>prpl@mail.cc.nih.gov</u> TTY 1-866-411-1010 Study ID Numbers 030298; 03-AR-0298

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### **Reviews of Interest, continued**

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# WWW

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

#### **Antibody Source Page**

http://www.antibodyresource.com/onlinecomp.html Has a lot of useful info regarding locating antibodies

#### CancerSource

www.cancersource.com

Resource site for health professionals and cancer patients. Includes the latest on cancer research, a searchable drug database, clinical trial information and online conferences and talks. Requires free registration.

#### **CMS Molecular Biology Resource**

#### http://restools.sdsc.edu/

A compendium of electronic and internet accessible tools and resources for Molecular Biology, Biotechnology, Molecular Evolution, Biochemistry and Biomolecular Modeling.

#### **Cytokines Web**

cmbi.bjmu.edu.cn/cmbidata/cgf/CGF\_Database/cytweb/

Provides information related to cytokines and their receptors, including classification, structural information, potential uses in therapy and other cytokine internet links.

#### **Frontiers in Bioscience**

#### http://www.bioscience.org/

Frontiers in Bioscience is a unique journal which offers distinct advantages over the traditional print journals which include a rapid review process, free, world-wide access, elimination of the need for reprints, use of multimedia to enhance presentation of the data, significant reduction in the cost of publication, elimination of the cost of publishing color images, significant improvement in scientific communication and use of searchable terms, texts, and key words, linkage between the references cited in a given article with those listed in the MEDLINE or other databases, and linkage of the methods presented in a given article with product information and a detailed methodology presented by the manufacturer.

Frontiers in Bioscience is more than a journal, it is a virtual library. FBS presents many databases valuable to scientists and physicians which include, among others, a tumor atlas and a gene knockout database. To save the time and energy of scientists and physicians, FBS offers the forms of the Web Sites valuable to researchers in an organized fashion. In addition, FBS presents papers of world best scientists in full text in special issues of "Encyclopedia of Bioscience". These manuscripts which are available through the MEDLINE database will be periodically revised making this platform a unique and a valuable scientific treasure. As of January 2000, the content of the Frontiers in Bioscience will be included in E-Biomed, a valuable virtual library being developed by NIH. The manuscripts included in E-Biomed are presented in full text and free of charge to the public.

(websites continued)

#### MIRAGE

http://www.ifti.org/

MIRAGE (Molecular Informatics Resource for the Analysis of Gene Expression) is a web site dedicated to methodologies, tools, and technologies relating to gene expression information. MIRAGE is a web resource of the Institute for Transcriptional Informatics (IFTI), Pittsburgh PA 15230-2556 USA.

#### **Molecular Biology Sites**

bioinformatics.weizmann.ac.il/ mb/molecular\_biol\_sites.html Links related to molecular biology tools.

#### NWFSC Molecular Biology Techniques Forums

http://micro.nwfsc.noaa.gov/forums/ This is a professional forum for reader-submitted techniques, tips, and questions concerning molecular biology. Ask questions on specific problems or submit a favorite technique or protocol.

#### **RNA Interference Resource Site**

http://www.orbigen.com/RNAi\_links.php Provides extensive literature, internet links, relevant information and a list of research groups specializing in RNA interference technology

#### Search the NIH Website

http://www.nih.gov/google/google.search.nih.html



# **Things To Ponder**



Can you cry under water?

When I was young we used to go "skinny dipping," now I just "chunkydunk."

If money doesn't grow on trees then why do banks have branches?

Why do you have to "put your two cents in"... but it's only a penny for your thoughts"? Where's that extra penny going to?

Once you're in heaven, do you get stuck wearing the clothes you were buried in for eternity?

Why does a round pizza come in a square box?

How is it that we put man on the moon before we figured out it would be a good idea to put wheels on luggage?

Why is it that people say they "slept like a baby" when babies wakeup like every two hours?

Why are you IN a movie, but you are ON TV?

Why do people pay to go up tall buildings and then put money in binoculars to look at things on the ground?

How come we choose from just two people for President and fifty for Miss Universe?

I signed up for an exercise class and was told to wear loose-fitting clothing. If I HAD any loose-fitting clothing, I wouldn't have signed up in the first place!

Wouldn't it be nice if whenever we messed up our life we could simply press 'Ctrl Alt Delete' and start all over?

Stress is when you wake up screaming and then you realize you haven't fallen asleep yet.

If raising children was going to be easy, it never would have started with something called labor!

Brain cells come and brain cells go, but fat cells live forever.

## INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH

9650 Rockville Pike, Bethesda, Maryland 20814-3998 USA Telephone # (301) 634-7250 ◆ Fax # (301) 634-7049 WEBSITE http://www.isicr.org ◆ EMAIL: *isicr@faseb.org* 

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# **CALL for CANDIDATES**

The positions of ISICR Secretary and Treasurer will become open at the end of 2005. The ISICR is very grateful to Drs. Sidney Pestka and Sam Baron for their

loyal and dedicated efforts on behalf of the society. Both of these individuals have indicated their desire to step down from serving at that time. In order to have an orderly transition, we will hold elections this fall for these 2 positions so Drs Pestka and Baron can work with the incoming officers during 2005. If you are interested in serving the society in either of these two essential positions for 2006-2008, please consider placing your name on the ballot. Interested individuals should contact Howard Young (youngh@ncifcrf.gov).

INTERNATIONAL SOCIETY FOR INTERFERON and CYTOKINE RESEARCH

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