Signals

THE **ISICR** NEWSLETTER

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IN THIS ISSUE:

A Farewell Note from Outgoing ISICR President, ELEANOR FISH

Dear friends and colleagues,

It has been a distinct privilege representing the ISICR as President these past two years. I am indebted to many of you who participate in the various committees: Awards, Finance, Meetings, Membership, Nomenclature, Publications, Standards, ensuring that our Society is well organized and contributes to scientific excellence at an international level. I would also like to take this opportunity to thank the Board of Directors for their support, guidance and excellent governance. And a very special thank you to Howard Young, whose tireless efforts on behalf of the ISICR are exemplified, though by no means limited to, production of the ISICR Newsletter.

During my tenure as President, we have welcomed new members into the Society and encouraged their participation in Society business as committee members. Indeed, when committee members' terms have been completed, the intent has been to reach out to newer – dare I say, younger - ISICR members to join committees. Additionally, the ISICR has had a profile at various international conferences, whether by organizing a satellite symposium, or by shameless promotion of our Society. The ISICR extends an invitation to scientists across every continent and offers membership that is not determined by affordability.

These past two years have also seen a strengthening of our partnership with the ICS, through the formation of a Joint Meetings Committee and our annual Joint Boards of Directors Meeting. I am confident that the recent successes of our joint annual meetings is a direct consequence of our 2 Societies collaborating on formulating scientific programs that represent our individual Society's interests and also offer up innovative high caliber topics of mutual interest.

In closing, let me also acknowledge the administrative support of FASEB. And finally, welcome my friend and scientific colleague, Leon Platanias, as incoming President. It is with deep humility and great pride that I depart the office as President of the ISICR.

Eleanor Fish

Future ISICR Meetings

2009 Meeting
Oct. 17 - 21, 2009
Joint ISICR/ICS/SLB
Lisbon, Portugal

2010 Meeting
Oct. 3 - 7, 2010
Joint ISICR/ICS
Chicago, Illinois

ISICR
International Society for Interferon & Cytokine Research

ISICR Election Results

For President 2012-2013

Charles Samuel

Board of Directors 2010-2012

Ganes Sen
Robert Silverman
Friedemann Weber

Special Thanks to the Milstein Family for their continued support of the ISICR

Milstein TRAVEL AWARD Winners

Betsy Barnes	UMDNJ, USA
Brigitte Blanchard Sury	CNRS, France
Viviana Blank	University of Buenos Aires, Argentina
Daniel Burke	University of Toronto, Canada
Lally Chan	The University of Hong Kong, China
Mounira Chelbi-Alix	CNRS, France
Jieliang Chen	Shanghai Med College of Fudan University, China
Wanjun Chen	NIDCR, NIH, USA
Ahmet Civas	Paris Descartes University, France
Ann Cornish	Walter and Eliza Hall Institute, Australia
Alexandre Corthay	University of Oslo Norway
Marco De Andrea	Medical School of Turin, Italy
Heather Ezelle	University of Maryland, Baltimore, USA
Brenda Fredericksen	University of Maryland, USA
Ka Yee Fung	Monash Institute of Medical Research, Australia
Carole Galligan	Toronto General Research Institute Canada
Yiwei Gao	Stony Brook University, USA
Sanjukta Ghosh	Harvard Univ. Sch Public Health, USA
Alan Goodman	Universty of Washington, USA
Nathalie Grandvaux	Université de Montréal, Canada
Claire Greenhill	Monash Institute of Medical Research, Australia
Francesca Gugliesi	University of Turin, Italy
Deborah Hodge	National Cancer Institute-Frederick, USA
Markus Hofer	University Hospital Marburg, Germany
Teresa Hsi	University of Maryland Sch. of Medicine, USA
Hiu (Jessie) Kiu	The Walter and Eliza Hall Institute, Australia
Christopher D. Krause	Mol Genetics, Microbiology & Immunology, UMDNJ, USA
Andrew Larner	Virginia Commonwealth University, USA
Chien-Kuo Lee	National Taiwan University, Taiwan
Christophe Lallemand	CNRS-Inst Andre Lwoff, France
Jana Liskova	1st Medical Faculty, Charles University, CzechRepublic
Barbora Lubyova	Institute of Immunology and Microbiology, Czech Republic
Katherine Martin	Monash University, Australia
Reem Mohamed	Institue of Endemic Diseases, Sudan
Markus Mordstein	University of Freiburg, Germany
Bei Morrison	Taussig Cancer Institute, USA
Kazuhide Onoguchi	Institute for Virus Research, Kyoto Univ, Japan
Anna Overby	University of Freiburg, Germany
Leesa Pennell	University of Toronto, Canada
Hongwei Qin	University of Alabama at Birmingham,USA
Nupur Raychaudhuri	Kellogg Eye Center at Univ. of Michigan, USA
Erin Rogers	Department of Immunology, Canada
Giovanna Romeo	Sapienza University of Rome, Italy
Saleela Ruwanpura	Monash University - Faculty of Medicine, Australia
Martina Schroeder	National University of Ireland Maynooth, Ireland
Marc Servant	University of Montreal, Canada
Martina Severa	Istituto Superiore di Sanità, Italy
Shawna Wall	University of Texas Health Sci Ctr, USA
Jae-Kwang Yoo	University of Toronto, Canada
Raza Zaidi	National Cancer Institute, NIH, USA

2009 ISICR Milstein Award Winner: DR. PETER STÄHELI

by Hannah Nguyen

Peter Staeheli, PhD, is Professor in the Virology Department at the University of Freiburg in Germany. He received his diploma and PhD degrees in microbiology and biochemistry from the ETH in Zürich, Switzerland. Postdoctoral training was at the University of Zürich in the Institutes of Medical Virology (Dr. Otto Haller and Dr. Jean Lindenmann) and Molecular Biology (Dr. Charles Weissmann), and at the Scripps Research Foundation, La Jolla, in the Molecular Biology Department (Dr. Greg Sutcliffe). Dr. Staeheli currently directs a molecular virology and immune defence research laboratory, and teaches Basic and Molecular Virology to medical and biology students at the University of Freiburg.

Congratulations on receiving the ISICR Seymour & Vivian Milstein Award! What were your first thoughts when you heard the news?
I was truly surprised when the e-mail with the news came in. Of course, I was very happy.

What does the Award mean to you?
The Seymour & Vivian Milstein Award is the most prestigious award of the ISICR. I feel greatly honored.

Your two main research interests revolve around the study of Bornavirus and the study of interferon and influenza virus. How did you first get involved with these research areas, and what excites you the most about working in these areas?
Interferon and influenza viruses were my first (scientific) love. My interest in Bornaviruses started much later. I got involved in interferon research in 1981 when I became a postdoctoral fellow at the University of Zürich in Switzerland and started to work with Otto Haller, Jean Lindenmann and Charles Weissmann. At that time, the mode of action of interferons was still a mystery, but it was clear that the Mx gene product played an important role in the interferon-mediated resistance of mice toward influenza viruses. Trying to solve these questions was truly exciting.

You have investigated interferon as a candidate emergency drug against pandemic influenza. What are your thoughts on interferon as a candidate emergency drug against the current swine flu H1N1 strain the world is encountering right now?
I believe that the prophylactic use of interferon against pandemic influenza should be considered seriously. Vaccines and viral neuraminidase inhibitors will most likely be in short supply when the virus hits hard. Data from animal experiments show that intranasal application of interferon prior to virus exposure is highly effective. In such settings, interferon was shown to inhibit seasonal influenza virus strains. There is no reason to assume that interferon will be less active against the new swine flu H1N1 strain. Thus, the current challenge is to move this approach towards clinic trials.

What do you think is your most important research contribution?
I joined Otto Haller and Jean Lindenmann at a time when their biological studies on the Mx system were very well advanced. Clearly, the Mx system was ripe at that time for a detailed molecular analysis. With great support from the laboratory of Charles Weissmann we managed to depart from the point at which we could only describe a fascinating

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biological phenomenon and managed to arrive at a new point from which we could start to characterize the virus restriction factor which really matters. Eventually it became clear that Mx proteins represent interferon-induced molecules that interfere with influenza virus replication. Thus, our research on the Mx system helped to shape the current concept of how interferons inhibit viruses.

What are your current and future scientific goals?
I currently have a strong interest in interferon-lambda which appears to play a substantial role in preventing viral infections via mucosal surfaces. I further would like to better understand which cell types in infected organs can contribute to virus-triggered interferon synthesis and thus constitute the first line of the antiviral defense system. Another topic of interest is the avian interferon system which we currently study in the context of avian influenza. Lastly, it would like to further evaluate the interferons as prophylactic drugs against influenza.

Do you have mentors or scientists that had a significant influence on your career?
Otto Haller, Jean Lindenmann and Charles Weissmann had a great influence. The different characters of these mentors helped to look at scientific problems in many different ways. Under this strong influence, I learned to develop my own sensing system that tells me which scientific questions are of sufficient interest to pursue.

Can you describe the research environment at the Spemann Graduate School of Biology and Medicine, Albert-Ludwigs Universitat Freiburg?
The University of Freiburg did very well in a recent nation-wide competition, designated "Excellence Initiative". As a result of the positive evaluation, the Spemann Graduate School was founded. The graduate school is a formidable platform which helps attracting talented students from all over the world.

What is your idea of relaxation and your idea of ultimate stress?
Sitting in the garden of our house with a glass of Italian wine is highly relaxing. On the stressful side, I may mention the struggle involved when it comes to meeting all deadlines listed in my calendar.

What is your favorite and least favorite thing about Switzerland?
I left Switzerland nearly 20 years ago for a position in Freiburg, Germany. Since Freiburg is located close to the Swiss border, frequent visits are possible and constant access to fresh Swiss chocolate is ensured. I certainly also greatly enjoy hiking in the Swiss Alps. As I live across the boarder, I can easily avoid the less enjoyable sides of Switzerland.

What are some of your extracurricular interests?
Freiburg is a fairly small town in the Black Forest which offers immediate access to excellent off-road biking. Riding home by bike after work or going for longer bike rides in the nearby mountains is great fun.

In your opinion, what are the key elements to doing great research? What advice do you give to scientists in training?
My advice is to start with a truly interesting biological phenomenon, find a working hypothesis and a suitable experimental approach that will ensure funding, recruit motivated students, and work hard to get the research project moving.

2009 ISICR Milstein Award Winner: DR. GLEN BARBER

by Thomas Tan

Glen N. Barber, Ph.D., holds the Eugenia J. Dodson Chair in Cancer Research, is leader of the Viral Oncology Program, and associate director for Basic Research at UM/Sylvester, and professor in the Department of Medicine at the University of Miami Leonard M. Miller School of Medicine.

Barber's laboratory is focused on developing novel virus-based therapies to treat cancer and his research has contributed key insights into mechanisms of innate immunity to viral infection and malignant disease.

Barber did his post-doc work at the University of Washington, Seattle and spent nearly a year at the University of Tokyo, before becoming an assistant professor in the Department of Microbiology and Immunology at Emory University School of Medicine, Atlanta, Georgia. Barber joined UM in 1999.

Congratulations on receiving the Milstein Award this year! How did you first find out and where were you?
I received an e-mail in my office at the University of Miami, from Dr Eleanor Fish.

What does the Award mean to you?
It's obviously very gratifying to be acknowledged by colleagues for your contributions to the field. It's also an acknowledgment of past and present lab member's efforts and contributions. So I am also happy for them.

Among your many contributions to the field of cytokine research, can you name one of which you're most proud of?
Our recent work on STING, bringing to light the importance of this molecule in DNA as well as RNA-regulated innate immune pathways, was an enjoyable piece of work. Hiroki Ishikawa did a great job and I was pleased that he obtained a nice publication for all his hard work.

Thinking back, how has the trajectory of your scholastic pursuits influenced your career choices and present position? Did you have a role model?
Well, I've always been intrigued with cancer research and so gravitated towards that and ended up being part of a cancer research center. While in Seattle, with Michael Katze, I became interested in evaluating the potential deregulation of known innate immune pathways, such as those governed by PKR. Of course a lot more is known about innate pathways now and it will be interesting to evaluate their potential role in cancer. I didn't have a role model, though was impressed by much of the work from labs in the early 90's that unraveled the IRF and Jak/STAT pathways. The labs that started to unravel the Toll-dependent and independent pathways were impressive too!

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What do you think are some of the mandatory/key components of a successful lab?
Motivated lab members (and some money for the research…)

Can you give us a brief overview of the Sylvester Comprehensive Cancer Center (SCCC) and what are your current priorities as the Associate Director of SCCC?
The SCCC at the University of Miami Leonard M. Miller School of Medicine is the major institute in Southern Florida for cancer-related research, diagnosis, and treatment. Nearly 4000 new cases of cancer are reported here each year. There are over 100 clinical trials in progress. Physician and scientist members of the SCCC are all associated with a translational research program, such as the Viral Oncology Program, which I presently direct, or one of several other programs such as the Tumor Immunology or the Breast Cancer Program. There are atypically high levels of viral-associated malignant diseases in the Southern Florida region, which is why the Viral Oncology Program started. I mention this, in that many of these types of cancer respond to interferon treatment and other anti-viral drugs. Needless to say many of these viruses probably target innate immune pathways to remain latent, events which may contribute towards the transformation process.

As Associate Director of Basic Research I help oversee a number of the SCCC programs as well as ensure that we have up-to-date technology to facilitate research for our members.

If you weren't a scientist, what would you be?
I don't know. I wanted to be a professional soccer player but there was one small problem; I wasn't good enough….

What keeps you up at night and what's your idea of relaxation?
Aside from the recession, terrorism, world poverty etc? The neighbor's cats fighting, thinking about the next series of experiments and agonizing about how my soccer team will do at the weekend. All at the same time…

Relaxation? I'm lucky enough to have a boat, which helps you make the most of living in Miami. When time allows, I like golfing, reading history, keeping up to date with the soccer games in England and am occasionally known to drink a beer. I like cooking, but I don't want to mention it too much in case my lab members make fun of me. You can multi-task some of these. For example, sticking the soccer on the telly, rustling up Rognons au de Veau flambés au Madère, while drinking beer…

This year's ISICR meeting will take place in Lisbon, Portugal. What are you most looking forward to?
I'm looking forward to the seminars and to meeting colleagues and old friends. Of course the restaurants in Lisbon are an attraction also…

Who will you thank during your acceptance speech at the Milstein award ceremony?
Past mentors and lab members as well as the Milstein family and the ISICR Awards Committee!

Dr. Charles Weissmann

Charles Weissmann obtained his M.D.(1956) and Ph.D.degrees (1961) at the University of Zürich. After 7 years at the NYU School of Medicine as postdoc, Assistant and then Associate Professor he became Director of the Institute of Molecular Biology, University of Zürich in 1967. In 1999 he moved to the MRC Prion Unit, University College, London as Senior Scientist. In 2004 he was appointed Chairman of the Department of Infectology, Scripps Research Institute, Florida. He has contributed significantly to our understanding of RNA virus replication, developed site-directed mutagenesis and reverse genetics, discovered quasispecies in viral populations, cloned the human interferon alpha genes and produced recombinant interferon in E.coli, cloned the prion gene and demonstrated that its knockout in mice abrogated prion replication and conferred protection from prion disease.

Dr. Sidney Grossberg

Sidney Grossberg received his M.D. degree (1954) at the Emory University School of Medicine. His post-graduate training in internal medicine at Duke University was interrupted by two-years' service in the U.S. Army Medical Corps in Korea and Japan. After Duke and a year's post-doctoral fellowship at the Johns Hopkins Hospital, he joined the Microbiology faculty at the University of Minnesota Medical School (1959-1962), and continued as Assistant Professor of Microbiology at Cornell University Medical College (1962-1966), during which he had a sabbatical year with André Lwoff at the Pasteur Institute. From 1966 to 1997 he served as Chairman of the Department of Microbiology and Walter Schroeder Professor at the Medical College of Wisconsin; during this period he spent sabbatical years with Luc Montagnier at the Pasteur Institute (1974) and Ernest Borden at the University of Wisconsin – Madison (1989). He produced the NIH Reference Standards for mouse and human alpha, beta, and gamma interferons, several of which became WHO International Standards, and directed the international collaborative studies required to establish their potency. He identified potent biological and low-molecular-weight chemical inducers of IFN, described chemical stabilization and reactivation of IFNs, described IFN inhibition of cell differentiation, and demonstrated high-affinity nuclear receptors for IFN-beta and –gamma. He identified linear and conformational epitopes on IFN-beta and contributed to our understanding of the quantification of IFNs and other cytokines and their antibodies. He discovered the phenomenon of virus-induced hyperlipemia and identified a novel murine retrovirus constitutively infecting human cells. From 1987-2008 he was Chairman of the ISICR Standards Committee.

CHRISTINA FLEISCHMANN AWARD WINNER

Special thanks to the Fleischmann Foundation for the continuing support of this award

Caini Liu, Ph.D.
Dept. Immunology
Lerner Research Institute
Cleveland Clinic
Cleveland, OH

SEYMOUR & VIVIAN MILSTEIN YOUNG INVESTIGATOR AWARD WINNERS

Special thanks to the Milstein Family for their continuing support of the ISICR Milstein awards

Hiroki Ishikawa, Ph.D.
Cancer Center
University of Miami
Miami, FL

Xiao-Ling Li, Ph.D.
Dept. Microbiology and Immunology
University of Maryland
Baltimore, MD

Benjamin tenOever, Ph.D.
Dept. Microbiology
Mount Sinai School of Medicine
New York, NY

Niamh Mangan, Ph.D.
Centre for Innate Immunity
Monash University
Clayton, 3006 Victoria, Australia

Ramtin Rahbar, Ph.D.
Dept. Immunology
University of Toronto
Toronto, Ontario, Canada

NEW ISICR MEMBERS

We welcome all the new members to the ISICR and encourage their participation in the annual meeting as well as ISICR committees and initiatives.

Manel Amri
Univ of Sciences & Tech Houri Boumediene, Algiers, Algeria

Joseph Ashour
Mount Sinai Sch of Med, New York, NY USA

Kin Yi Au
Univ of Hong Kong, Hong Kong, China

Brigitte Blanchard
CNRS/FRE2937, Villejuif, France

Viviana Blank
Univ of Buenos Aires, Buenos Aires, Argentina

Susanna Bosi
Eurand S P A, Trieste, Italy

Joanne Bradbury
Univ of Queensland- Australia, Mullumbimby, Australia

Lally Chan
Univ of Hong Kong, Hong Kong, China

Olivia Chan
Univ of Toronto, Toronto, Canada

Jieliang Chen
Shanghai Med Col of Fudan Univ, Shanghai, China

Jean-Francois Clement
Universite de Montreal, Montreal, Canada

Alexandre Corthay
Univ of Oslo Inst of Immunology, Oslo, Norway

Nir Friedman
Weizmann Inst of Science, Rehovot, Israel

Ka Yee Fung
Monash Inst of Med Rsch, Melbourne, Australia

Yiwei Gao
Stony Brook Univ, Huntington, NY USA

Sanjukta Ghosh
Harvard School of Public Health, Boston, MA USA

Alan Goodman
Univ of Washington, Seattle, WA USA

Simon-Pierre Gravel
Universite de Montreal, Montreal, Canada

Ai Harashima
Univ of Miami Sch of Medicine, Miami, FL USA

Teresa Hsi
Univ of Maryland Sch of Med, Baltimore, MD USA

Lih-Hwa Hwang
Natl Yang-Ming Univ, Taipei, Taiwan

Hiroki Ishikawa
Univ of Miami, Miami FL USA

Bruce Jaffee
Novartis, Cambridge, MA USA

Ronald Jubin
PBL InterferonSource, Piscataway, NJ USA

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NEW ISICR MEMBERS

Hanna-Leena Kauppinen
Finish Red Cross BTS, Helsinki, Finland

Catherine Kennedy
Monash Inst. for Med Rsch, Clayton, Australia

Jung-Ae Kim
Yeungnam Univ, Gyeongsan, Korea

Timinori Kimura
Ritsumeikan Univ, Shiga, Japan

Hiu (Jessie) Kiu
Walter & Eliza Hall Inst of Med Science, Melbourne, Australia

Hiroyasu Konno
Univ of Miami Sch of Medicine, Miami, FL USA

Asha Kulkarni-Almeida
Piramal Life Sciences Limited, Mumbai, India

Jana Liskova
Charles Univ-Prague, Prague, Czech Republic

Caini Liu
Cleveland Clinic Fnd Lerner Rsch Inst, Cleveland, OH USA

Michael MacNamara
Salveson Stetson Group Wayne, PA USA

Niamh Mangan
Monash Univ, Clayton, Australia

Katherine Martin
Monash Univ, Clayton, Australia

Jenny Miu
McGill Univ, Montreal, Canada

Kotaro Miyake
NIAID, Bethesda, MD USA

Shinya Nakajima
Nakajima Clinic, Osaka, Japan

Kazuhide Onoguchi
Inst for Virus Rsch, Kyoto, Japan

Leesa Pennell
Univ of Toronto, Toronto, Canada

Hongwei Qin
Univ of Alabama-Birmingham, Birmingham, AL USA

Nupur Raychaudhuri
Univ of Michigan Kellogg Eye Ctr, Ann Arbor, MI USA

Shlomit Reich-Zeliger
Weizmann Inst of Science, Rehovot, Israel

Michael Robek
Yale Univ Sch of Med, New Haven, CT USA

Leonor Roguin
Univ of Buenos Aires, Buenos Aires, Argentina

Francis Ruscetti
NCI, Frederick, MD USA

Martina Schroeder
UI Maynooth, Maynooth, Ireland

Marc Servant
Universite de Montreal, Montreal, Canada

Ha Youn Shin
Stony Brook Univ, Huntington, NY USA

Hakan Steen
Temple Univ, Philadelphia, PA USA

Shadi Swaidani
Cleveland Clinic Fndn Lerner Rsch, Cleveland, OH USA

Benjamin TenOever
Mount Sinai Sch of Med, New York, NY USA

Hazel Tye
Monash Inst of Med Rsch, Melbourne, Australia

Francois Veronique
Inst Pasteur, Paris, France

Estanislao Nistal Villan
Mount Sinai Sch of Med, New York, NY USA

Shawna Wall
Univ of Texas Hlth Sci Ctr SA, San Antonio, TX USA

Marta Wlodarska
Univ of British Columbia, Vancouver, Canada

Mehdi Yeganeh
Univ of Sherbrooke, Sherbrooke, Canada

M. Raza Zaidi
NCI, Bethesda, MD USA

New Member MINIBIOs

Dr Martina Schroeder, PhD
Lecturer for Immunology and Global Health
Host Pathogen Interaction Laboratory
Institute of Immunology
National University of Ireland Maynooth
Maynooth, Co.Kildare, Ireland
http://biology.nuim.ie/staff/msimmunolglob.shtml

After completing a PhD in Immunology in Germany in 2003, Dr Martina Schroeder conducted postdoctoral research in the laboratory of Prof. Andrew Bowie at Trinity College Dublin, Ireland, from 2003 to 2008. During that time, she developed her interest in anti-viral pattern recognition receptors and in particular the signalling pathways leading to type I interferon induction, and discovered that the human DEAD-box protein DDX3 is a positive regulator of IFN-beta induction by identifying it as the host target of the vaccinia virus immune evasion protein K7 (EMBO J, 2008). In 2007, Dr. Schroeder was awarded a postdoctoral career development fellowship by the Irish Health Research Board; and in 2008, Dr. Schroeder was the recipient of a postdoctoral investigator award at the Annual Meeting of the International Cytokine Society (ICS). At the end of 2008, Dr. Schroeder started to establish her own research group in the Institute of Immunology at the National University of Ireland Maynooth. Since DDX3 appears to be a highly multifunctional cellular protein that is targeted or co-opted by several different viruses, including HIV and HCV, research in Dr. Schroeder's own lab is currently focused on understanding the biology of DDX3 and its interaction with viruses in more detail. Research in the lab is funded through grants from Science Foundation Ireland and the Irish Health Research Board.

Tominori Kimura
Professor in Microbiology and Cell Biology
College of Pharmaceutical Sciences
Ritsumeikan University
Noji-Higashi, Kusatsu, Shiga 525-8577, Japan

Tominori Kimura earned his medical degree and obtained Ph.D. in Microbiology from Kansai Medical University, Osaka, Japan. He established his independent research laboratory in 2007 at Ritsumeikan University. The research of his laboratory focuses on regulatory RNAs for gene regulation. His research team is currently interested in natural antisense transcripts that regulate cytokine gene expression post-transcriptionally.

New Member MINIBIOs

Michael Robek
Assistant Professor
Department of Pathology
Yale University School of Medicine
New Haven, CT 06520-8023
http://info.med.yale.edu/bbs/faculty/rob_mi.html

Michael Robek is an Assistant Professor in the Department of Pathology at Yale University. He received his Ph.D. degree from Washington University (St. Louis) in 2000, after which he completed his postdoctoral work at The Scripps Research Institute. His laboratory studies the host-pathogen interactions related to hepatitis B virus (HBV) infection. First, he is investigating the relationships between HBV proteins and cellular regulatory pathways, as these may be exploited pharmacologically to block virus replication. Second, he is characterizing the ability of antiviral and immunomodulatory cytokines to inhibit HBV replication and prevent liver damage. Third, he is studying new methodologies for therapeutic vaccination to boost the immune response to HBV in people who are chronically infected with the virus. In addition to his interest in HBV, he is also examining the role of interferon and the interferon-related cytokines in preventing virus spread within the brain. There is a currently a postdoctoral position open in his lab.

Lih-Hwa Hwang
Professor
National Yang-Ming University
No. 155, Sec. 2, Linong Street
Taipei, 112
Taiwan

Lih-Hwa Hwang obtained her Ph.D. degree from Princeton University, New Jersey, U.S.A. in 1985 and finished her post-doctoral training at Wistar Institute, Pennsylvania. She established her own research laboratory in Taiwan in 1987, initially at National Taiwan University Hospital, and recently she moved her laboratory to National Yang-Ming University in the Institute of Microbiology and Immunology. The research interests in her laboratory include using cytokine gene therapy to treat hepatocellular carcinoma, investigating the interferon antagonisms conferred by hepatitis C viral antigens, and studying the regulatory molecules involved in interferon responses.

Another Chapter in the History of Interferon

Essay: *Aimez-vous Brahms?* A story *capriccioso* from the discovery of a cytokine family and its regulators

Tadatsugu Taniguchi

Tadatsugu Taniguchi is in the Department of Immunology, Graduate School of Medicine and Faculty of Medicine, at Tokyo University, Tokyo, Japan.

e-mail: tada@m.u-tokyo.ac.jp

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doi:10.1038/ni0509-447

Reprinted through the kind generosity of Nature Immunology

Abstract

Do you delight in Brahms? Do you delight in immunology? Tada Taniguchi recounts the story of Type 1 interferon and its downstream regulators.

For full article, see http://www.nature.com/ni/journal/v10/n5/full/ni0509-447.html

REVIEWS OF INTEREST

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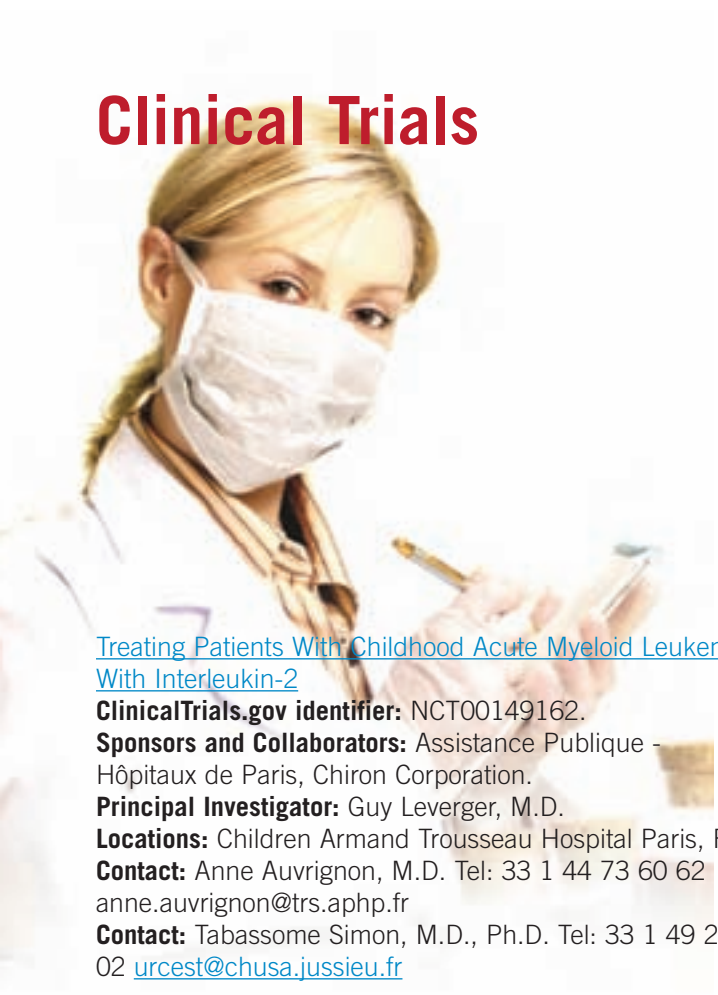
Thoughts to Ponder...

"I am only one, But still I am one. I cannot do everything, But still I can do something. And because I cannot do everything, I will not refuse to do the something I can do."
- Edward Everett Hale

"I can only please one person per day and today is not your day- tomorrow is not looking good either!"

Clinical Trials



Treating Patients With Childhood Acute Myeloid Leukemia With Interleukin-2
ClinicalTrials.gov identifier: NCT00149162.
Sponsors and Collaborators: Assistance Publique - Hôpitaux de Paris, Chiron Corporation.
Principal Investigator: Guy Leverger, M.D.
Locations: Children Armand Trousseau Hospital Paris, France
Contact: Anne Auvrignon, M.D. Tel: 33 1 44 73 60 62 anne.auvrignon@trs.aphp.fr
Contact: Tabassome Simon, M.D., Ph.D. Tel: 33 1 49 28 22 02 urcest@chusa.jussieu.fr

Relationship Between Natural Killer Cells' Ability to Kill Leukemia Cells and the Outcome of Patients With Acute Myeloid Leukemia Previously Treated With Interleukin-2
ClinicalTrials.gov identifier: NCT00896701.
Sponsors and Collaborators: Cancer and Leukemia Group B, National Cancer Institute (NCI).
Study Chair: Sherif S. Farag, MD, PhD Indiana University Melvin and Bren Simon Cancer Center.
Locations: Kinston Medical Specialists, Kinston, NC 28501.
Contact: Peter R. Watson, MD 252-559-2200ext.201. Arthur G. James Cancer Hospital and Solove Research Institute at Ohio State University Medical Center Recruiting Columbus, OH 43210
Contact: Ohio State University Cancer Clinical Trial Matching Service. Tel: 866-627-7616 osu@emergingmed.com

Interferon Alfa and Interleukin-6 in Treating Patients With Recurrent Multiple Myeloma.
ClinicalTrials.gov identifier: NCT00470093.
Sponsors and Collaborators: Sidney Kimmel Comprehensive Cancer Center, National Cancer Institute (NCI)
Study Chair: Carol A. Huff, MD Sidney Kimmel Comprehensive Cancer Center.
Locations: Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD 21231.
Contact: Clinical Trials Office - Sidney Kimmel Comprehensive Cancer Ctr Tel: 410-955-8804 jhcccro@jhmi.edu

Interleukin-7 in Treating Patients With Metastatic Melanoma or Locally Advanced or Metastatic Kidney Cancer
ClinicalTrials.gov identifier: NCT00492440.
Sponsors and Collaborators: National Cancer Institute (NCI),
Study Chair: Steven A. Rosenberg, MD, PhD.
Locations: National Cancer Institute, Bethesda, MD 20892.
Contact: NCI Clinical Trials Referral Office - Warren Grant Magnusen Clinical Center, Bethesda, Maryland 20892-1182 Tel:888-NCI-1937

Interleukin-7 (CYT107) Treatment of Idiopathic CD4 Lymphocytopenia: Expansion of CD4 T Cells (ICICLE).
ClinicalTrials.gov identifier: NCT00839436.
Sponsors and Collaborators: National Institute of Allergy and Infectious Diseases (NIAID).
Study Chair: Teresa M. Petrella Edmond Odette Cancer Centre at Sunnybrook.
Locations: Multiple, Canada.
Contact: Teresa M. Petrella Tel: 416-480-5248

Interleukin-12 Followed by Interferon Alfa in Treating Patients With Advanced Cancer
ClinicalTrials.gov identifier: NCT00003451.
Sponsors and Collaborators: Arthur G. James Cancer Hospital & Richard J. Solove Research Institute, National Cancer Institute (NCI).
Study Chair: William E. Carson, MD.
Locations: Arthur G. James Cancer Hospital - Ohio State University Columbus, Ohio 43210

Interleukin-12 Gene in Treating Patients With Liver Metastases Secondary to Colorectal Cancer.
ClinicalTrials.gov identifier: NCT00072098.
Sponsors and Collaborators: Mount Sinai School of Medicine, National Cancer Institute (NCI).
Study Chair: Max W. Sung, MD Mount Sinai School of Medicine.
Locations: Mount Sinai Medical Center New York, NY 10029.
Contact: Max W. Sung, MD Tel: 212-241- 7902 max.sung@mssm.edu

Combination Study Of SB-485232 (Interleukin 18) And Doxil For Advanced Stage Epithelial Ovarian Cancer
ClinicalTrials.gov identifier: NCT00659178.
Sponsors and Collaborators: GlaxoSmithKline,
Study Chair: GSK Clinical Trials GlaxoSmithKline
Locations: GSK Investigational Sites- Stanford, CA 94302, Miami, FL 33136, Philadelphia, PA 19104.
Contact: US GSK Clinical Trials Call Center Tel: 877-379-3718

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Interleukin-21 in Treating Patients With Metastatic or Recurrent Malignant Melanoma.
ClinicalTrials.gov identifier: NCT00514085.
Sponsors and Collaborators: NCIC Clinical Trials Group.
Study Chair: Teresa M. Petrella Edmond Odette Cancer Centre at Sunnybrook.
Locations: Multiple, Canada.
Contact: Teresa M. Petrella Tel: 416-480-5248

Zidovudine, Interferon Alfa-2b, and PEG-Interferon Alfa-2b in Treating Patients With Human T-Cell Lymphotropic Virus Type 1-Associated Adult T-Cell Leukemia/Lymphoma.
ClinicalTrials.gov identifier: NCT00854581.
Sponsors and Collaborators: University of Miami Sylvester Comprehensive Cancer Center.
Study Chair: Juan Carlos Ramos, MD University of Miami Sylvester Comprehensive Cancer Center – Miami, William J. Harrington, MD University of Miami Sylvester Comprehensive Cancer Center – Miami.
Locations: University of Miami Sylvester Comprehensive Cancer Center – Miami, Miami, FL 33136
Contact: University of Miami Sylvester Comprehensive Cancer Center Clin Tel: 866-574-5124 Sylvester@emergingmed.com

Evaluation of Birdshot Retine Choroidopathy Treatment by Either Steroid or Interferon alpha2a.
ClinicalTrials.gov identifier: NCT00508040.
Sponsors and Collaborators: Assistance Publique - Hôpitaux de Paris.
Study Chair: Christine Fardeau, MD Assistance Publique - Hôpitaux de Paris.
Locations: Hopital La Pitie Salpetriere, Paris, France, 75013.
Contact: Christine Fardeau, MD Tel: +33(0)1 42 16 32 07 christine.fardeau@psl.aphp.fr

Genetic and Biochemical Markers of Interferon-Induced Depression.
ClinicalTrials.gov identifier: NCT00252538.
Sponsors and Collaborators: Department of Veterans Affairs.
Study Chair: Peter Hauser, MD VA Medical Center, Long Beach.
Locations: VA Medical Center, Long Beach, CA 90822.
Contact: Peter Hauser, MD Tel: 562-826-8000 ext 2629 peter.hauser2@va.gov VA Medical Center, Minneapolis, MN 55417
Contact: Eric Dieperink, MD Tel: 612-725-2000 ext 2037 eric.dieperink@va.gov VA Medical Center, Portland, OR 97201
Contact: Jennifer M Loftis, MA PhD loftisj@ohsu.edu

Murphy's Other Laws

1. Light travels faster than sound. This is why some people appear bright until you hear them speak.
2. A fine is a tax for doing wrong. A tax is a fine for doing well.
3. He who laughs last, thinks slowest.
4. A day without sunshine is like, well, night.
5. Change is inevitable, except from a vending machine.
6. Those who live by the sword get shot by those who don't.
7. Nothing is foolproof to a sufficiently talented fool.
8. The 50-50-90 rule: Anytime you have a 50-50 chance of getting something right, there's a 90% probability you'll get it wrong.
9. It is said that if you line up all the cars in the world end-to-end, someone would be stupid enough to try to pass them.
10. If the shoe fits, get another one just like it.
11. The things that come to those that wait may be the things left by those who got there first.
12. Give a man a fish and h e will eat for a day. Teach a man to fish and he will sit in a boat all day drinking beer.
13. Flashlight: A case for holding dead batteries.
14. The shin bone is a device for finding furniture.
15. When you go into court, you are putting yourself in the hands of 12 people who weren't smart enough to get out of jury duty.

The Tree of Strife

Post-docs deserve their own species designation

by Helen Pickersgill

www.lablit.com/article/152
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Classify this: Pickersgill at work

Darwinian selection ensures that only the fittest specimens will undergo a successful metamorphosis

Being a post-doc – the phase of existence that kicks in after surviving a Ph.D, – is more than just making a living: it's a life. And the post-doctoral branch of life is unique – almost a separate species. In fact, it deserves its own place on the phylogenetic tree.

The life of post-docs (*Homo postdocus*) is dedicated to science, and they work almost constantly, seemingly oblivious to the many joys of the outside world. Post-docs generally appear quite unkempt, but as they rarely venture outside their laboratory environment, they pose no threat to other species. Indeed, post-docs are quite solitary, existing mostly in groups of two or less. Mating rituals are something of an enigma, as none has ever been reported (frankly, they don't have the time).

The post-doctoral life cycle is relatively short, commonly three to five years, and for a lucky few, a dramatic metamorphosis into a completely different and much more prominent species, the Principle Investigator (PI, also known as the Assistant Professor or Group Leader) follows. The first subtle sign of this impending transformation is the loss of the strained look that inevitably accompanies even the most successful post-docs as they go about their day. This change is followed by the gradual shedding of their scruffy white coats, exposing smarter attire. To balance out the transient nature of the post-doc phase, their number are constantly replenished by young and naïve specimens known as Ph.D. students.

(The fate of the large group of post-docs that fail to make this transition is unclear, as even with sophisticated electronic equipment it has been impossible to track them all. However, there have been unconfirmed reports of trans-speciation into more common strains such as consultants or industry workers.)

There is a great deal of variation within the post-doc species – you have only to pass down the corridors of a university to see examples of each different type. In the middle of the night, the corridors are home to the *Slave worker*. Instantly recognizable by their gloved hands, they are bent over workbenches performing experiments for at least sixteen hours a day. If you're lucky, you may see one of them going home, but formal evidence of this has yet to be documented. They are extremely solitary, and they hold a monopoly on most of the communal equipment, which makes them less popular with the other post-docs.

The library and other literary establishments provide a comfortable niche for the *Visionary* post-doc. This type is usually lost in thought, identified by deep lines in the middle of the forehead. They stand or sit almost motionless, pen in hand, and to the untrained observer may appear close to death. However, wait long enough and you may catch a rare glimpse of them furiously scribbling things that are incomprehensible to the rest of the *Homo* genus – as well as to most other post-docs. The *Visionaries* are also solitary creatures, but they cause fewer disturbances than the *Slave workers* as they remain stationary for long periods of time.

If you listen carefully, you will hear that most of the noise in the corridors comes from the *Verbalisers*. These Post-docs are the most social type, and are often found engaged in animated discussions. However, they tend to aggravate the *Slave workers* by interfering with their work, and the *Visionaries* by interrupting their thinking. They are otherwise well-tolerated, as they ensure effective intra- and inter-species information transfer, which is instrumental in procuring funds for propagation of the species.

Darwinian selection ensures that only the fittest specimens will undergo a successful post-doc-to-PI transformation. And it is known that certain geographical locations provide richer environments for increased survival. However, it has proven difficult to predict the precise conditions required for a post-doc-to-PI metamorphosis. From our primitive observations, it appears to be a combination of characteristics from all three of the post-doc types, often coupled to a persistent (some might call parasitic) relationship with an established PI. But the post-doc remains a fascinating species to observe because even with its uncertainty survival and below-*Homo*-average living conditions, it remains a dynamic and thriving population. And in any major city, as with the rat, you may be surprised to know that there is a post-doc living closer than you think.

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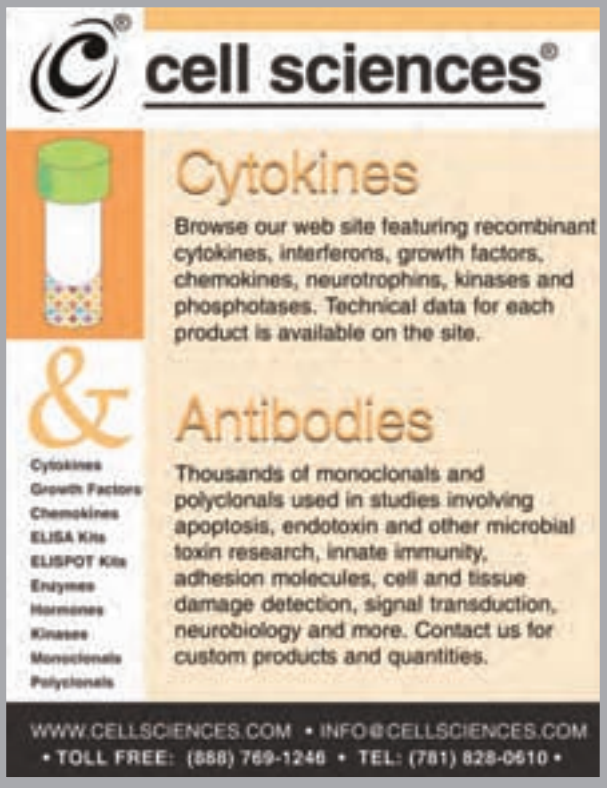

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ArrayExpress

http://www.ebi.ac.uk/microarray-as/ae/

ArrayExpress is a public archive for functional genomics data compliant with MIAME- and MINSEQE requirements in accordance with compliant data in accordance with MGED recommendations. The Gene Expression Atlas uses curated, re-annotated subset of data from the Archive to provide information about gene expression under various biological conditions.

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Biosystems

http://www.ncbi.nlm.nih.gov/biosystems

A biosystem, or biological system, is a group of molecules that interact in a biological system. One type of biosystem is a biological pathway, which can consist of interacting genes, proteins, and small molecules. Another type of biosystem is a disease, which can involve components such as genes, biomarkers, and drugs.

A number of databases, such as KEGG and BioCyc, provide diagrams showing the components and products of biological pathways along with corresponding annotations and links to literature. The NCBI BioSystems Database was developed as a collaborative and complementary project to (1) serve as a centralized repository of data; (2) connect the biosystem records with associated literature, molecular, and chemical data throughout the Entrez system; and (3) facilitate computation on biosystems data.

The NCBI BioSystems record for arachidonic acid metabolism, for example, displays the name and description of the biosystem along with a thumbnail image of the pathway diagram that links to the full size illustration on the source database's web site. In addition, the BioSystems record lists and categorizes the genes, proteins, and small molecules involved in the biological system, along with related biosystems and citations, and allows instant retrieval of the those data sets through a wide range of Links. Integrating the data in this way makes it possible to search across all the pathways to answer broad questions such as the "how to" examples shown below.

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The NCBI BioSystems Database currently contains biological pathways from two source databases, KEGG and the EcoCyc subset of BioCyc, and is designed to accommodate other types of biosystems such as diseases as data about them become available. Through these collaborations, the BioSystems database facilitates access to, and provides the ability to compute on, a wide range of biosystems data. Detailed diagrams and annotations for individual biosystems are then available on the web sites of the source databases.

The European Searchable Tumour Line Database

http://www.ebi.ac.uk/ipd/estdab/

The European Searchable Tumour Line Database (ESTDAB) Database and Cell Bank provide a service enabling investigators to search online for HLA typed, immunologically characterised tumour cells as part of the European Commission Fifth Framework Infrastructures Program.
The following tools and pages are available in ESTDAB:

- Search ESTDAB on primary search determinants
- Search ESTDAB on all search determinants
- Dictionary of markers and techniques used

For further information regarding the ESTDAB project please visit http://www.medizin.uni-tuebingen.de/ESTDAB/index.htm.

GESBAP: GEne Set Based Analysis of Polymorphisms

http://bioinfo.cipf.es/gesbap/

Genome-wide association studies have become a popular strategy to find associations of genes to traits of interest. Despite the high-resolution available today to carry out genotyping studies, the success of its application in real studies has been limited by the testing strategy used. As an alternative to brute force solutions involving the use of very large cohorts, we propose the use of the Gene Set Analysis (GSA), a different analysis strategy based on testing the association of modules of functionally related genes. We show here how the Gene Set-based Analysis of Polymorphisms (GeSBAP), which is a simple implementation of the GSA strategy for the analysis of genome-wide association studies, provides a significant increase in the power testing for this type of studies.

Hematopoietic Fingerprints: an expression database of stem cells and their progeny

http://franklin.imgen.bcm.tmc.edu/loligag/

The Hematopoietic stem cell (HSC) continuously regenerates the hematologic system, yet few genes regulating this process have been defined. To elucidate factors involved in differentiation and self-renewal, we have generated the first in-depth expression database of hematopoietic stem cells and their differentiated progeny, including erythrocytes, granulocytes, monocytes, NK cells, activated and naive T-cells, and B-cells. Bioinformatic analysis revealed HSC were more transcriptionally active than their progeny and shared a common activation mechanism with T-cells. Each cell type also displayed unique biases in the regulation of particular genetic pathways, with Wnt signaling particularly enhanced in HSCs. We identified ~100 to 400 genes uniquely expressed in each cell type, termed lineage fingerprints. In overexpression studies, two of these genes, Zfp105 from the NK cell lineage, and Ets2 from the monocyte lineage, were able to significantly influence differentiation toward their respective lineages, demonstrating the utility of these fingerprint genes for controlling differentiation of stem and progenitor cells.

HotSpot Wizard: a web server for identification of hot spots in protein engineering

http://loschmidt.chemi.muni.cz/hotspotwizard/

HotSpot Wizard is a web server for automatic identification of 'hot spots' for engineering of substrate specificity, activity or enantioselectivity of enzymes and for annotation of protein structures. The web server implements the protein engineering protocol, which targets evolutionarily variable amino acid positions located in the active site or lining the access tunnels. The 'hot spots' for mutagenesis are selected through the integration of structural, functional and evolutionary information obtained from: (i) the databases RCSB PDB, UniProt, PDBSWS, Catalytic Site Atlas and nr NCBI and (ii) the tools CASTp, CAVER, BLAST, CD-HIT, MUSCLE and Rate4Site. The protein structure and e-mail address are the only obligatory inputs for the calculation. In the output, HotSpot Wizard lists annotated residues ordered by estimated mutability. The results of the analysis are mapped on the enzyme structure and visualized in the web browser using Jmol. The HotSpot Wizard server should be useful for protein engineers interested in exploring the structure of their favourite protein and for the design of mutations in site-directed mutagenesis and focused directed evolution experiments.

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LitInspector

http://www.litinspector.org/

LitInspector is a literature search tool providing gene and signal transduction pathway mining within NCBI's PubMed database. The automatic gene recognition and color coding increases the readability of abstracts and significantly speeds up literature research. A main challenge in gene recognition is the resolution of homonyms and rejection of identical abbreviations used in a 'non-gene' context. LitInspector uses automatically generated and manually refined filtering lists for this purpose. The quality of the LitInspector results was assessed with a published dataset of 181 PubMed sentences. LitInspector achieved a precision of 96.8%, a recall of 86.6% and an F-measure of 91.4%. To further demonstrate the homonym resolution qualities, LitInspector was compared to three other literature search tools using some challenging examples. The homonym MIZ-1 (gene IDs 7709 and 9063) was correctly resolved in 87% of the abstracts by LitInspector, whereas the other tools achieved recognition rates between 35% and 67%. The LitInspector signal transduction pathway mining is based on a manually curated database of pathway names (e.g. wingless type), pathway components (e.g. WNT1, FZD1), and general pathway keywords (e.g. signaling cascade).

The MIQE Guidelines Minimum Information for Publication of Quantitative Real-Time PCR Experiments

http://miqe.gene-quantification.info/

Stephen A. Bustin, Vladimir Benes, Jeremy A. Garson, Jan Hellemans, Jim Huggett, Mikael Kubista, Reinhold Mueller, Tania Nolan, Michael W. Pfaffl, Gregory L. Shipley, Jo Vandesompele, & Carl T. Wittwer. Clinical Chemistry 2009, 55(4): 611-622

BACKGROUND: Currently, a lack of consensus exists on how best to perform and interpret quantitative real-time PCR (qPCR) experiments. The problem is exacerbated by a lack of sufficient experimental detail in many publications, which impedes a reader's ability to evaluate critically the quality of the results presented or to repeat the experiments.

CONTENT: The Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) guidelines target the reliability of results to help ensure the integrity of the scientific literature, promote consistency between laboratories, and increase experimental transparency. MIQE is a set of guidelines that describe the minimum information necessary for evaluating qPCR experiments. Included is a checklist to accompany the initial submission of a manuscript to the publisher. By providing all relevant experimental conditions and assay characteristics, reviewers can assess the validity of the protocols used. Full disclosure of all reagents, sequences, and analysis methods is necessary to enable other investigators to reproduce results. MIQE details should be published either in abbreviated form or as an online supplement.

SUMMARY: Following these guidelines will encourage better experimental practice, allowing more reliable and unequivocal interpretation of qPCR results.

MirZ: an integrated microRNA expression atlas and target prediction resource

http://www.mirz.unibas.ch/

MicroRNAs (miRNAs) are short RNAs that act as guides for the degradation and translational repression of protein-coding mRNAs. A large body of work showed that miRNAs are involved in the regulation of a broad range of biological functions, from development to cardiac and immune system function, to metabolism, to cancer. For most of the over 500 miRNAs that are encoded in the human genome the functions still remain to be uncovered. Identifying miRNAs whose expression changes between cell types or between normal and pathological conditions is an important step towards characterizing their function as is the prediction of mRNAs that could be targeted by these miRNAs. To provide the community the possibility of exploring interactively miRNA expression patterns and the candidate targets of miRNAs in an integrated environment, we developed the MirZ web server, which is accessible at www.mirz.unibas.ch. The server provides experimental and computational biologists with statistical analysis and data mining tools operating on up-to-date databases of sequencing-based miRNA expression profiles and of predicted miRNA target sites in species ranging from Caenorhabditis elegans to Homo sapiens.

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Pscan: finding over-represented transcription factor binding site motifs in sequences from co-regulated or co-expressed genes

http://159.149.109.9/pscan/

The first step in gene expression, transcription, is modulated by the interaction of transcription factors with their corresponding binding sites on the DNA sequence. Pscan is a software tool that scans a set of sequences (e. g. promoters) from co-regulated or co-expressed genes with motifs describing the binding specificity of known transcription factors and assesses which motifs are significantly over-or under-represented, providing thus hints on which transcription factors could be common regulators of the genes studied, together with the location of their candidate binding sites in the sequences. Pscan does not resort to comparisons with orthologous sequences and experimental results show that it compares favorably to other tools for the same task in terms of false positive predictions and computation time. The website is free and open to all users and there is no login requirement.

UniPrime2

http://habanero.ucd.ie/uniprime2/

UniPrime2 is an experimentally validated, fully automated program that generates successful cross-species primers that take into account the biological aspects of the PCR. UniPrime2 automatically retrieves and aligns orthologous sequences from GenBank, identifies regions of conservation within the alignment and generates suitable primers that can amplify variable genomic regions. UniPrime2 differs from previous automatic primer design programs in that all steps of primer design are automated, saved and are phylogenetically limited. We have experimentally verified the efficiency and success of this program.

Meeting of Interest

Immunology in the 21st Century: Defeating Infection, Autoimmunity, Allergy and Cancer

http://www.ici2010.org/index.html

10 Interesting Facts About Lisbon, Portugal

By Orson Johnson

Pictures from http://www.naic.edu/~pfreire/paulo/lisboa.html

Lisbon is the capital of Portugal and is full of beauty and charm. However, don't scrape the surface thinking it's just like any other place. Lisbon has it's list of interesting secrets too.

★

1. In Lisbon, the streets are pretty much all black and white. People say the reason for this centers around the patron Saint of Lisbon; Saint Vincent. It's said that the black represents the attire worn by Saint Vincent whereas the white represents the white outfit of the Christian Crusaders who vanquished the Moors.

2. The main river basin of the Tagus Estuary in Lisbon stretches up to 14km across and is said to be large enough to contain all the warships in the world.

3. Beneath the streets of Lisbon's downtown shopping area lies a hidden Roman Underworld with chambers, rooms, bridges and corridors. The entrance to this fascinating world is marked by a block of metal at the top of Rua da Conceicao which is only open to the public two days a year due to the dangerous conditions lurking below.

4. Lisbon was practically destroyed on 1st November 1755 as a massive earthquake tipping the scales at 8.9 took the lives of 40,000 people and could be felt as far away as Scotland and Norway.

5. Visit on of Lisbon's favorite attractions; the Torre de Belem. The tower's first purpose was to safeguard the harbor but from the late 16th century up till the 19th, the tower served as a prison. Today however, it serves as a monument to Portugal's Age of Discovery and it provides a beautiful panoramic view of the city.

6. Lisbon is also known as "the town of seven hills" which are compromised of the seven hills: Castelo, Graca, Monte, Penha de Franca, S.Pedro de Alcantara, Santa Catarina and Estrela.

7. Instead of hiking, why not take a one of a kind The Ascensor de Santa Justa (street elevator). This is another beloved landmark which takes passengers 45meteres from the Baxia elevator to the Chiado district.

8. A very large statue of Cristo Rei (Christ the King) stands on the left bank of the river. This statue was erected to commemorate Portugal's survival of World War II without its direct involvement.

9. Ironically, The Alfama, which is the oldest section of Lisbon, was spared by the 1755 earthquake and is one of the places to really go if you want to see Lisbon full of history.

10. Lisbon is home to the Stadium of Light, one of Europe's biggest and famous soccer venues in which the main sporting team Benfica play their home games.

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While experts remain at odds over the issue of when life begins, most agree it's sometime after work.

Cartoon courtesy of escienceinfo@comcast.net

Special Thanks to PBL InterferonSource for their support in the development of the new ISICR *Signals* newsletter

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