The History of Interferon: Some personal thoughts and experiences in the early years of Interferon research

Joseph Sonnabend

In 1964, the world of interferon research was much different and really just beginning to blossom. There was no molecular biology and the tools available for research were much more primitive. Thus research into interferons required a thought process about the biology of the experimental systems being investigated. The following is a recollection from Dr. Joseph Sonnabend, one of the pioneers in Interferon research, accompanied by a reproduction of some thoughts he circulated for discussion at that time.

I probably wrote this in the room I shared with Alick Isaacs. It was written in response to Joyce Taylor's experiment with actinomycin suggesting that interferon's antiviral action required cell RNA synthesis. Joyce and I were the only members of the virology division using biochemical techniques at that time and I was quite close to the work she was doing, and of course Bob Friedman and I were to work together.

When Joyce first saw her results, we thought that an inactive preparation of interferon had been used. I believe I was probably the first to realize the implications of the actinomycin sensitivity of interferon action. One must remember that this was an incredibly exciting time: the time of Jacob and Monod, of derepression - in bacterial systems; the role of ribosomes in protein synthesis had just been worked out, and Sidney Brenner confirmed the Jacob/ Monod idea of the role of mRNA, I think in that same year- 1964. These were the issues that Joyce, Bob Friedman, some biochemists - particularly

(continued on page 2)
Ted Martin, and I talked about. It was also a time when virologists were venturing into biochemical approaches. However not our division, as we had no high speed centrifuge or spectrophotometer let alone a scintillation counter. Joyce and I, and then Bob, had to use equipment in other divisions. So I recognized that this was the first indication (at least to me) that maybe something similar was happening in eukaryotic systems as in bacterial systems, which was then a topic of great interest. That is, the induced synthesis of specific proteins. Alick Issacs was completely disinterested in these discussions at that time.

I wrote the few pages in this state of enthusiasm. Joyce and Bob read it - it reflected what we were talking about.

It was not intended for publication, but we sent it to interferon labs, those we knew, which may have been all there were at that time - there were so few. This was 1964. I cannot remember that there was any response.

Of course I also showed it to Alick for any comment, he made the few annotations you can see particularly adding Jean Lindenmann's name (which was so characteristic of him).

I'm sure I also discussed it with Ted Martin and maybe others in the biochemistry division. Joyce left around this time.

Not only was there no comment at the time from those I sent it to, but Joyce herself had forgotten about it when I showed it to her a few years ago.

INTERFERON : PRODUCTION AND MECHANISM OF ACTION

Since the early reports of Isaacs in 1957 on the release of a non-viral interfering agent by virus infected cells, a large number of observations have accumulated on the production and action of Interferon. A model will be presented which will attempt to correlate these observations. Essentially, both Interferon production and Interferon action will be viewed as involving a specific participation of the host genome; Interferon will be viewed both as an inducer and, itself, an induced protein.

INTERFERON ACTION

The important observations which any scheme must take into account are:

- No direct anti-viral action
- Active on both RNA and DNA viruses
- Greater protection afforded by pretreatment of cells
- Species specificity of action
- No gross effects on host cell metabolism - as far as this has been studied
- Recovery of Sensitivity to viruses
- Inhibition of virus specific RNA synthesis
- Actinomycin sensitivity of Interferon action

From the absence of a direct antiviral action, and the observation that protection is greater if infection is delayed following a period of pretreatment, it is likely that some additional step or steps are required in the acquisition of viral resistance. These steps may involve -

(1) Interferon  (2) The Cell
The first possibility means that Interferon is in some way activated so that it can express its antiviral activity only intracellular.

It is the second possibility, namely, that the antiviral action Interferon results from some change that it induces within the cell, that would seem to be most consistent with the observations. It is evident from the actinomycin sensitivity of Interferon action that host cell RNA synthesis is required for an expression of its action. Recent results suggest a similar dependence on protein synthesis. It is suggested that Interferon induces the synthesis of a specific messenger RNA determining the synthesis of a protein having antiviral activity.

Thus, resistance to viruses would increase with pretreatment. Two further observations are explained on this basis:

The persistence of protection despite removal of the Interferon, and the failure to recover Interferon from treated cells which are protected.

The Antiviral Agent and its Mode of Action

Interferon inhibits both RNA and DNA viruses. A common point of action would be on RNA synthesis. An important observation is that Interferon does not seem to inhibit the messenger function of virus nucleic acid. Thus, in the mengovirus L cell system, viral induced cut off of host cell RNA and protein synthesis is not affected, and although no new virus is produced, the cells die. It might be anticipated that the virus induced RNA-RNA polymerase is also produced. It is less likely that the action of this enzyme is inhibited, since Interferon is active on DNA viruses. It is suggested that the antiviral activity of Interferon results from the induced synthesis of an enzyme by the host cell which degrades newly synthesized...
synthesized/

RNA. From the preservation of the messenger function of the viral RNA referred to above, it is necessary to specify that it is newly synthesized RNA that is susceptible. One would also anticipate an effect on host cell RNA synthesis, and this will be returned to later.

The antiviral agent is apparently not present in crude preparations of Interferon, since the action of these preparations is sensitive to actinomycin. This implies an instability to the various treatments that Interferon preparations are subjected to to remove virus, or to the fact that it does not penetrate the cell membrane.

Species Specificity

If Interferon is viewed as an inducer, specificity of action might reside at the point of induction; in other words, only Interferon of appropriate specificity can induce the synthesis of the antiviral agent.

Action on the Host Cell

On the basis of the above model, one might predict an effect on host cell RNA synthesis. As far as this has been studied, it is clear that there is no gross effect at levels of Interferon which afford considerable protection against viruses.

It is suggested:

1. That the action of Interferon is self limiting
2. That bulk (ribosomal) RNA synthesis is unaffected
3. It is newly synthesized messenger RNA, both viral and cellular, that is susceptible to the degradative enzyme. If this enzyme is unstable, a basis is provided for a self limiting effect
The dependence of Interferon action on continued host cell RNA and protein synthesis leads to the prediction that viruses that inhibit cellular functions would be less sensitive to the action of Interferon when treated with the virus; a period of pretreatment before challenge would be expected to protect the cells.

**Summary**

It is suggested that Interferon induces the synthesis of an unstable enzyme which degrades newly synthesized RNA, both viral as well as host cell M-RNA.

This outline suggests the following work:

1. Attempts to isolate an RNA degradative enzyme from Interferon treated cells. An approach may be to look for increased activity of enzymes known to have this effect. (polynucleotide phosphorylase).
2. The effect of Interferon on cell RNA synthesis.
   1. The effect on overall RNA synthesis
   2. The effect on specific molecular species of RNA
3. The demonstration that Interferon action depends on continued protein synthesis. There are already supportive preliminary results.

J.A. Sonnabend
R.M. Friedman
Joyce Taylor

National Institute for Medical Research
The Ridgeway, Mill Hill, London. N.W.7

April, 1964.
We welcome all the new members to the ISICR and encourage their participation in the annual meeting as well as ISICR committees and initiatives.

**Bernhard Baune**  
James Cook Univ - Sch of Med, Queensland, Australia

**Viviane Calabrese**  
Univ of Montreal, Montreal, Canada

**Marina Degtyareva**  
Russian State Med Univ, Moscow, Russian Federation

**Aurelio Flores-Garcia**  
Universidad Autonoma de Nayarit, Tepic, Mexico

**Simone Haeberlein**  
Univ Clinic of Erlangen, Erlangen, Germany

**Sylva/Sotiria Haralambous**  
Hellenic Pasteur Inst, Athens, Greece

**Claudia Jursik**  
Bender Medsystems, Vienna, Austria

**Archontoula Nadia Kavrochorianou**  
Hellenic Pasteur Inst, Athens, Greece

**Joseph Kuijper**  
Zymogenetics, Seattle, WA USA

**Thomas Lavoie**  
PBL InterferonSource, Piscataway, NJ USA

**James Lucas Honokaa**  
Hawaii, USA

**John Matthias**  
Roche Kulmbach Gmbh, Kulmbach, Germany

**Theresa Peterson**  
Dalhousie Univ, Halifax, Canada

**Nicholas Plotnikoff**  
TNI Pharmaceuticals, Ocean City, NJ USA

**Selena Sio**  
Nat'l Univ of Singapore, Singapore

**Irina Soldatova**  
Russian State Med Univ, Moscow, Russian Federation

**Mathieu Vernier**  
Univ de Montreal, Montreal, Canada

**Todd Wuest**  
Univ of Oklahoma - HSC, Oklahoma City, OK USA

**Hiroki Yoshida**  
Saga Univ Faculty of Med, Saga, Japan

**New Member Minibios**

**Dr. Bernhard Baune**  
Professor and Head of Psychiatry and Psychiatric Neuroscience  
James Cook University, Australia

Dr. Baune received his medical and scientific training (including PhD training) at the University of Muenster, Germany. Prof. Baune's research focuses on the relationship between cytokines and neuropsychiatric disorders with an emphasis on cognitive impairment and mood disorders. In basic research, his group investigates the physiological role of TNF in neurodevelo-
Professor of Immunology
Autonomous University of Nayarit, Tepic, Nayarit, México

Dr. Aurelio Flores obtained his medical degree from the University of Guadalajara, México. He obtained his Ph.D. in Immunology at the University of Guadalajara, Mexico in 2004. His research focuses on the role of IL-12 in both, innate and adaptive immune response to *Sporothrix shenckii* infection in an animal model of sporotrichosis, specifically, analyzing the therapeutic effect of rmIL-12 to cure this infection, as well as the pathways implicated. He is also interested in investigating the role of the IL-23/IL-17 proinflammatory axis in obesity.

**Matthias J. John, Ph. D.**
Associate Director Biochemistry
Group leader: immuno safety of RNAi-therapeutics
Roche Kulmbach GmbH, Germany

Dr. Matthias John began his research career studying biology and biochemistry at the University of Erlangen in Germany. He earned his Ph.D. for his work on mammalian transcription factors, which was conducted at the IBMC in Strasbourg, France. Afterwards he joined the lab of Kevin Struhl at Harvard Medical School and investigated interactions between signaling pathways and transcription factors in yeast. In 2001, he became one of the first employees of Ribopharma AG. This company was the first one worldwide to develop new innovative drugs based on short interfering RNA. After 4 years with Alnylam pharmaceuticals, the whole research unit was acquired by Roche in 2007. For several years, the Matthias group has been investigating the immune responses to siRNA and ways to minimize the side effects of RNA-based drugs.

Dr. Hiroki Yoshida received his medical training at Kyushu University and Tokyo Women's Medical University hospital. His Ph.D. training was conducted in the Medical Institute of Bioregulation, Kyushu University. After completing his doctoral studies, he became a post-doctoral fellow at the University of Toronto under the supervision of Dr. Tak Mak. During his time at the U of T, he generated various gene knockout mice, including NF-ATc1, Apaf1, RANKL (OPGL), and WSX-1 (IL-27R±). Investigation of WSX-1-deficient mice initiated his study of IL-12-related cytokines. He established his independent research laboratory in 2003 at Saga University. He is currently investigating the role of IL-27 and related cytokines in autoimmune diseases as well as protozoan and bacterial infections. He received prizes for his research from JSICR (2006) and the Japan Medical Association (2008).
GeneGo donates pathway slides to the ISICR slide repository

GeneGo Inc (genego.com), a leading systems biology and bioinformatics company, has recently donated 41 of their canonical pathway maps to ISICR. These maps are constructed from manually curated, experimentally validated biological and chemical pathway interactions. Each map describes multi-step signaling covering the full spectrum of cellular signaling from ligand-receptor interaction through enzymes and scaffold proteins to transcription factors. The donated maps describe the role of interferons and cytokines in the immune response, development (via a variety of growth hormones), cell cycle, apoptosis, survival, cell adhesion and chemotaxis. In addition to creating canonical pathway maps GeneGo's software analysis tools enable functions such as determining the biological enrichment and representative networks for a gene (or list of genes), associated metabolism and diseases, and therapeutic drugs complete with supportive links to the public domain literature. Additional tools include full interactome analysis and chemical analysis tools to predict metabolites and activity as well as target and related functions. For more details or a trial contact julie@genego.com and visit our web site, www.genego.com

GeneGo's unique bioinformatics technology for systems biology enables complete reconstruction of mammalian cellular functionality from interactions data at the level of ligand-receptor interactions, cell signaling and regulation and core metabolism. Whether you working with one gene or an extensive list from high throughput data, exploit the functional enrichment of a data set and build a network to depict these functional interactions. MetaCore allows for the comparison of several data sets to determine what biology is shared or unique to each, overlay and visualize expression levels of objects from the same data to help you formulate more applicable hypotheses.

For researchers with Rodent data:
The mouse and rat content in MetaCore (MetaRodent) does not derive from orthologous gene matching between rodent and human, but rather on the specific manual curation of rodent genes, proteins, protein complexes, protein function, transcriptional regulation, etc. from experimental literature. MetaRodent enables direct comparison between metabolism, signaling, and cellular processes in human and model organisms, taking full account of the differences between human and rodent biology. This is a critical feature, allowing the evaluation of multiple types of systems biology data from experiments in model species, while facilitating the appropriate interpretation of the outcome with respect to the potential effects in man.

ISICR has negotiated a 25% discount off MetaCore list price for its members. Please contact Laura Brovold <laura@genego.com> for more information.

Editor's note: GeneGo slides are in the process of being created and deposited. It will take me (Howard) some time to complete depositing all 41…..(although chocolate will help me work faster)

THE ISICR SLIDE REPOSITORY

Ever see a slide in a talk that you wish you could use for your own presentation? Well now this may be possible through the ISICR Slide Repository. Members can now go in and post slides that they have developed or download slides that others have provided to the membership. OVER 500 SLIDES ARE NOW AVAILABLE!!!!! For this member only feature, you need to have your member number so if you are not sure what that is, please contact the membership office. We urge members to upload general slides that other members can use for lectures, classes, seminars, etc. Slides are not to be changed without permission from the donor and all copyright permissions must be obtained. The repository now has a useful search capability that allows you to find slides on a particular topic. If you have trouble uploading or downloading slides, please contact Howard Young at younghow@mail.nih.gov.

PLEASE CONSIDER CONTRIBUTING YOUR SLIDES. The success of this initiative depends upon you, the membership!!!!


The Workgroup on Human Interferon Zignalling

The Workgroup on Human Interferon Zignalling (WHIZ) is a recently launched trans-NIH Center for Human Immunology Workgroup, focusing on interferons (IFNs) and their impact on IFN-affected immune processes such as, but not limited to, antiviral immune response, antitumor immunity and tissue rejection. Considering the widely recognized importance of these processes in human immunity, and the complexity and challenges of this field, we believe that WHIZ could serve as a useful common platform for exchanging ideas, improving communication and developing collaborations between both NIH intra-and extramural researchers working on IFN-related topics. WHIZ will create a new forum for such communication by organizing brief meetings, inviting expert speakers of the field, and providing the infrastructure for lectures and informal discussions between interested participants in a relaxed atmosphere. If you are interested in joining this group, please contact Dr. Zoltan Pos, posz@cc.nih.gov.

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The ISICR wishes to express its thanks and gratitude to Dr. Sidney Grossberg for his many years of service as Chair of the ISICR Standards Committee.
The Importance of Stupidity in Scientific Research

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Accepted 9 April 2008
Journal of Cell Science 121, 1771 Published by The Company of Biologists 2008
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I recently saw an old friend for the first time in many years. We had been Ph.D. students at the same time, both studying science, although in different areas. She later dropped out of graduate school, went to Harvard Law School and is now a senior lawyer for a major environmental organization. At some point, the conversation turned to why she had left graduate school. To my utter astonishment, she said it was because it made her feel stupid. After a couple of years of feeling stupid every day, she was ready to do something else.

I had thought of her as one of the brightest people I knew and her subsequent career supports that view. What she said bothered me. I kept thinking about it; sometime the next day, it hit me. Science makes me feel stupid too. It's just that I've gotten used to it. So used to it, in fact, that I actively seek out new opportunities to feel stupid. I wouldn't know what to do without that feeling. I even think it's supposed to be this way. Let me explain.

For almost all of us, one of the reasons that we liked science in high school and college is that we were good at it. That can't be the only reason - fascination with understanding the physical world and an emotional need to discover new things has to enter into it too. But high-school and college science means taking courses, and doing well in courses means getting the right answers on tests. If you know those answers, you do well and get to feel smart.

A Ph.D., in which you have to do a research project, is a whole different thing. For me, it was a daunting task. How could I possibly frame the questions that would lead to significant discoveries; design and interpret an experiment so that the conclusions were absolutely convincing; foresee difficulties and see ways around them, or, failing that, solve them when they occurred? My Ph.D. project was somewhat interdisciplinary and, for a while, whenever I ran into a problem, I pestered the faculty in my department who were experts in the various disciplines that I needed. I remember the day when Henry Taube (who won the Nobel Prize two years later) told me he didn't know how to solve the problem I was having in his area. I was a third-year graduate student and I figured that Taube knew about 1000 times more than I did (conservative estimate). If he didn't have the answer, nobody did.

That's when it hit me: nobody did. That's why it was a research problem. And being my research problem, it was up to me to solve. Once I faced that fact, I solved the problem in a couple of days. (It wasn't really very hard; I just had to try a few things.) The crucial lesson was that the scope of things I didn't know wasn't merely vast; it was, for all practical purposes, infinite. That realization, instead of being discouraging, was liberating. If our ignorance is infinite, the only possible course of action is to muddle through as best we can.

I'd like to suggest that our Ph.D. programs often do students a disservice in two ways. First, I don't think students are made to understand how hard it is to do research. And how very, very hard it is to do important research. It's a lot harder than taking even very demanding courses. What makes it difficult is that research is immersion in the unknown. We just don't know what we're doing. We can't be sure whether we're asking the right question or doing the right experiment until we get the answer or the result. Admittedly, science is made harder by competition for grants and space in top journals. But apart from all of that, doing significant research is intrinsically hard and changing departmental, institutional or national policies will not succeed in lessening its intrinsic difficulty.

Second, we don't do a good enough job of teaching our students how to be productively stupid - that is,
if we don't feel stupid it means we're not really trying. I'm not talking about 'relative stupidity', in which the other students in the class actually read the material, think about it and ace the exam, whereas you don't. I'm also not talking about bright people who might be working in areas that don't match their talents. Science involves confronting our 'absolute stupidity'. That kind of stupidity is an existential fact, inherent in our efforts to push our way into the unknown. Preliminary and thesis exams have the right idea when the faculty committee pushes until the student starts getting the answers wrong or gives up and says, 'I don't know'. The point of the exam isn't to see if the student gets all the answers right. If they do, it's the faculty who failed the exam. The point is to identify the student's weaknesses, partly to see where they need to invest some effort and partly to see whether the student's knowledge fails at a sufficiently high level that they are ready to take on a research project.

Productive stupidity means being ignorant by choice. Focusing on important questions puts us in the awkward position of being ignorant. One of the beautiful things about science is that it allows us to bumble along, getting it wrong time after time, and feel perfectly fine as long as we learn something each time. No doubt, this can be difficult for students who are accustomed to getting the answers right. No doubt, reasonable levels of confidence and emotional resilience help, but I think scientific education might do more to ease what is a very big transition: from learning what other people once discovered to making your own discoveries. The more comfortable we become with being stupid, the deeper we will wade into the unknown and the more likely we are to make big discoveries.

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Update to the most recent ISICR recipe: 5 minute chocolate mug cake

Based on someone who actually tried the recipe, it was noted “You should emphasize that the cup has to be big (like a soup cup) and that if you have a newer microwave, cut back on the time.”

~ Howard
Working in the Lab too long??????

Slightly adapted from Daniel Sutton's Facebook “You know you've worked too long in a lab when” and reprinted with permission from Dan (CalXdan@hotmail.com).

You know you've worked too long in a lab when:

1. You can tell what cheap and expensive lab coats look like.

2. You can't watch CSI without cursing at least one scientific inaccuracy.

3. You use acronyms for everything and never stop to elaborate.

4. Liquid nitrogen is only about a 1/3 as dangerous as you thought.

5. You always seem to use the microscope after the person with the impossible close together eyes.

6. You've wondered why you can't drink distilled water in the lab - It should be clean?

7. You give the lab equipment motivational pep talks "Work for me today or i'll reprogram you with a fire axe" is my favorite.

8. You’ve worked out that a trained chimp could probably do 90% of your job.

9. When a non-scientist asks you what you do for a living you roll your eyes and talk science at them until they've loss the will to live (mainly for fun).

10. You have to check the web to find out what the weather is outside.

11. You realize that almost anything can be classed as background reading.

12. People wearing shorts under a lab coat disturb you slightly as they look as though they might be naked underneath.

13. Although all cooking is a glorified chemistry experiment you just still can't seem to get it right.

14. Safety equipment is optional unless it makes you look cool.

15. Warning labels invoke curiosity rather than caution.

16. The Christmas night out reveals scientists can't dance, although a formula for the movement of hands and feet combined with beats per min is found scrawled on a napkin by a waiter the next day.
17. You know which part of the lab you can chill out undisturbed on Friday afternoon.

18. You decide the courses and conference you want to go on by the quality of the food served.

19. You are strangely proud of the collection of junk you've stolen from vendors at trade shows.

20. You've used dry ice to cool beer down.

21. No matter what the timings in the experiment protocol there is always time for lunch in the middle.

22. As has been pointed out to me on several occasions - You can no longer spell normal words but have no trouble with spelling things like immunohistochemistry or deoxyribonucleic acid.

23. Burning eyes, nose and throat indicate that you haven't actually turned on the fumehood/downdraft bench

24. Your slightly too fond of the smell of (pick one or many) Xylene/Agar/Ethanol/ Undergraduates/ Alcoholic handwash.

26. You've left the lab wearing a piece of PPE (personal protective equipment) because you forgot you had it on
Genetic Variations in **Toll-Like Receptors** and Susceptibility to Chronic Lung Disease in Very Low Birth Weight Babies (CLD). ClinicalTrials.gov identifier: NCT00710112. Contacts: Venkatesh Sampath, MD, 414.337.7162, vsampath@mcw.edu; Kathleen M Meskin, BSN, 414.337.7171, kmeskin@mcw.edu. Locations: Children's Hospital of Wisconsin, Milwaukee, Wisconsin, United States, 53226; St. Joseph Regional Medical Center, Milwaukee, Wisconsin, United States, 53210. Principal Investigator: Venkatesh Sampath, MD, Medical College of Wisconsin. Study ID Numbers: CHW 06/92, GC151

**AMG 655 (anti-DR 5 antibody)** in Combination With AMG 479 (anti-IGFR1 antibody) in Advanced, Refractory Solid Tumors. ClinicalTrials.gov identifier: NCT00819169. Contact: Amgen Call Center, 866-572-6436. Location: Research Site, Santa Monica, California. Study ID Numbers: 20070411


Combined Treatment of Sorafenib and **Pegylated Interferon α2b** in Stage IV Metastatic Melanoma (SoraPeg). ClinicalTrials.gov identifier: NCT00623402. Contacts: Axel Hauschild, MD, +49431597 ext 1613, AHAuschmidt@dermatology.uni-kiel.de; Michael Weichenthal, MD, +49431597 ext 1537, MWeichenthal@dermatology.uni-kiel.de. Locations: Dpt. of Dermatology; UK-SH Campus Kiel, Germany, D-24105. Principal Investigator: Axel Hauschild, MD, UK-SH Department of Dermatology. Study ID Numbers: DeCOG SoraPeg 2007, EudraCT 2007-001918-16.


A Study to Evaluate the Safety, Tolerability and Effects of **MEDI-563 (Anti-Interleukin-5 Receptor Alpha antibody)** in Adults With Asthma. ClinicalTrials.gov identifier: NCT00659659. Contacts: Angi Gillen, MICP166@medimmune.com; Danielle Quarels, 301-398-0000, QuarelsD@MedImmune.com. Locations in the US and Canada. Study Director: Nestor Molfino, M.D., MedImmune LLC. Study ID Numbers: MI-CP166


Rituximab and CVP Plus **Interferon** for Follicular Non Hodgkins Lymphoma (NHL) (LNH-Pro-05). ClinicalTrials.gov identifier: NCT00842114. Contact and Principal Investigator: Reyes Arranz-Saez, MD, +34-91-5202316. rarranzs@telefonica.net.
The Developmental Studies Hybridoma Bank at the University of Iowa
http://dshb.biology.uiowa.edu

We are happy to announce that you can now order online at the DSHB website. To register, just click on the announcement panel or on “Register” in the right hand corner of our homepage. Also take a look at our ever increasing list of monoclonal antibodies. Remember, we still sell for $25.00/ml.

Best Regards,
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HIV Databases
http://www.hiv.lanl.gov/content/index

The HIV databases contain data on HIV genetic sequences, immunological epitopes, drug resistance-associated mutations, and vaccine trials. The website also gives access to a large number of tools that can be used to analyze these data. This project is funded by the Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH).

Human Metabolome Database
http://www.hmdb.ca/

The Human Metabolome Database (HMDB) is a freely available electronic database containing detailed information about small molecule metabolites found in the human body. It is intended to be used for applications in metabolomics, clinical chemistry, biomarker discovery and general education. The database is designed to contain or link three kinds of data: 1) chemical data, 2) clinical data, and 3) molecular biology/biochemistry data. The database (version 1.0) contains information on over 10,000 metabolites.
2.0) contains over 6500 metabolite entries including both water-soluble and lipid soluble metabolites as well as metabolites that would be regarded as either abundant (> 1 uM) or relatively rare (< 1 nM). Additionally, approximately 1500 protein (and DNA) sequences are linked to these metabolite entries. Each MetaboCard entry contains more than 100 data fields with 2/3 of the information being devoted to chemical/clinical data and the other 1/3 devoted to enzymatic or biochemical data. Many data fields are hyperlinked to other databases (KEGG, PubChem, MetaCyc, ChEBI, PDB, Swiss-Prot, and GenBank) and a variety of structure and pathway viewing applets. The HMDB database supports extensive text, sequence, chemical structure and relational query searches. Two additional databases, DrugBank and FooDB are also part of the HMDB suite of databases. DrugBank contains equivalent information on ~1500 drugs while FooDB contains equivalent information on ~2000 food components and food additives.

HMDB is supported by David Wishart, Departments of Computing Science & Biological Sciences, University of Alberta.

**Mesothelioma**
http://www.mesotheliomaweb.org/mesothelioma.htm

Exposure to asbestos can result in malignant mesothelioma, a cancer of the lining of the lung. For more information about asbestos exposure and mesothelioma, please visit the mesothelioma website.

**Michigan Molecular Interactions**
http://mimi.ncibi.org/MimiWeb/main-page.jsp

MiMi Web gives you an easy to use interface to a rich NCIBI data repository for conducting your systems biology analyses. This repository includes the MiMI database, PubMed resources updated nightly, and text mined from biomedical research literature. The MiMI database comprehensively includes protein interaction information that has been integrated and merged from diverse protein interaction databases and other biological sources. With MiMI, you get one point of entry for querying, exploring, and analyzing all these data.

Search MiMI Using the Free Text search bar at the top of the Main Search page. You can enter a single Keyword, Gene symbol, or Gene ID and retrieve matching genes from the MiMI database. Some search examples are:

csf1r
pwp1
prostate cancer
cellularComponent:nucleus
Insulin Receptor AND Oxidation
SMAD4, MAPK, CTNNA1

**The Missouri Science & Technology cDNA Research Center**
www.cdna.org

cDNA clones for 100's of human signal transduction proteins are available from the UMR cDNA Resource Center. These includes clones for

1) heterotrimeric G proteins (alpha, beta and gamma subunits)
2) G protein coupled receptors
3) RGS proteins
4) Small GTPases (Ras, Rac, Rho, Ran, Arf, Rab)

These high quality clones are full length; sequence verified; free of extraneous 3' and 5' untranslated regions; propagated in a versatile expression vector; expression verified by coupled in vitro transcription/translation assays (documentation available online); and usually shipped within 24 hours by overnight delivery (FedEx).

**Mouse Phenome Database**
http://www.jax.org/phenome

The Mouse Phenome Database is an open source, web-based repository of phenotypic and genotypic...
data on commonly used and genetically diverse inbred strains of mice and their derivatives. MPD is also a facility for query, analysis and in silico hypothesis testing. Currently MPD contains about 1400 phenotypic measurements contributed by research teams worldwide, including phenotypes relevant to human health such as cancer susceptibility, aging, obesity, susceptibility to infectious diseases, atherosclerosis, blood disorders and neurosensory disorders. Electronic access to centralized strain data enables investigators to select optimal strains for many systems-based research applications, including physiological studies, drug and toxicology testing, modeling disease processes and complex trait analysis. The ability to select strains for specific research applications by accessing existing phenotype data can bypass the need to (re)characterize strains, precluding major investments of time and resources. This functionality, in turn, accelerates research and leverages existing community resources. A new interactive Tool Demo is available through the MPD homepage (quick link: http://phenome.jax.org/phenome/trytools).

**PMAP - The Proteolysis Map**
http://sonny.burnham.org/proteases

The Proteolysis MAP (PMAP, http://www.proteolysis.org) is a user-friendly website intended to aid the scientific community in reasoning about proteolytic networks and pathways. PMAP is comprised of five databases, linked together in one environment. The foundation databases, Protease-DB and SubstrateDB, are driven by an automated annotation pipeline that generates dynamic ‘Molecule Pages’, rich in molecular information. PMAP also contains two community annotated databases focused on function; CutDB has information on more than 5000 proteolytic events, and ProfileDB is dedicated to information of the substrate recognition specificity of proteases. Together, the content within these four databases will ultimately feed PathwayDB, which will be comprised of known pathways whose function can be dynamically modeled in a rule-based manner, and hypothetical pathways suggested by semi-automated culling of the literature. A Protease Toolkit is also available for the analysis of proteases and proteolysis.

**Reactome - a curated knowledgebase of biological pathways**
http://www.reactome.org/

Reactome is an expert-authored, peer-reviewed knowledgebase of human reactions and pathways that functions as a data mining resource and electronic textbook. Its current release includes 2975 human proteins, 2907 reactions and 4455 literature citations. A new entity-level pathway viewer and improved search and data mining tools facilitate searching and visualizing pathway data and the analysis of user-supplied high-throughput data sets. Reactome has increased its utility to the model organism communities with improved orthology prediction methods allowing pathway inference for 22 species and through collaborations to create manually curated Reactome pathway datasets for species including Arabidopsis, Oryza sativa (rice), Drosophila and Gallus gallus (chicken). Reactome’s data content and software can all be freely used and redistributed under open source terms.

**RNA Binding Sites Database**
http://bioinfo3d.cs.tau.ac.il/RsiteDB/

The database details the interactions of extruded, unpaired RNA nucleotide bases. It presents and classifies the protein binding pockets that accommodate them. It allows the recognition of similar protein binding patterns involved in interactions with different RNA molecules. Given an unbound structure of a target protein it allows the prediction of its RNA nucleotide binding sites.

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STRUCTURAL PREDICTION FOR PROTEIN FOLDING UTILITY SYSTEM - SPROUTS
http://bioinformatics.eas.asu.edu/springs/Sprouts/projectsSprouts.html

Historically, this database was designed to gather all the results from a study concerning the comparison between tools devoted to the prediction of stability changes upon point mutations. The amount of data to collect from various sources was important and the need of a database was evident. 10 structures corresponding to a total of 1211 amino acids have been processed each time by 5 different programs for the 19 possible mutations on each amino acid. Thus, the output data at the end of the experiment consisted in 138054 pieces of data. The execution of the different programs is producing one file per amino acid for a total of more than 7200 files to manipulate. It is clear that this solution is not conceivable for an open and easy access. The need of a database is mandatory and also offers the opportunity to provide this information for the whole scientific community.

As of today, this database has grown up and consists in more than 100 structures which have been computed for a total of around 16500 amino acids. The second aim of this database is to offer simple and user-friendly tools to better visualize and analyze the results obtained. We are now able to propose three ways of visualization and analysis: the first one consists in getting raw $\Delta G$ values in a table. The second one is a 2D graph representation of a computed stability score for each residue of a given sequence and for each tool. The last one is based on a Jmol applet [Jmol] with the possibility to represent the 3D structure of a given protein with symbols representing the information stored in the database. We assume that each visualization mode offers a different look on the data stored in the database and will suit to every scientists willing to query the database whether they are more used to handle 3D protein structure or 1D/2D sequence problems.

Finally, the ultimate objective is to integrate these data and their analyses with other structural bioinformatics concepts in order to improve other methods that may be related to this concept. We are currently working at adding the information extracted from our other projects related to the prediction of protein folding nucleus in order to obtain a meta server devoted to the characterization of the folding core of proteins.

VirHostNet
http://pbildb1.univ-lyon1.fr/virhostnet/

VirHostNet (Virus-Host Network) is a knowledge-base system dedicated to the curation, the integration, the management and the analysis of virus-host molecular (mainly protein-protein) interaction networks as well as their functional annotation (molecular functions, cellular pathways, protein domains). VirHostNet contains high quality and up-to-date information gathered and curated from public databases (VirusMint, Intact, HIV-1 database). An extensive literature curation process was also initiated and has significantly increased the amount of available data in the fields. Altogether VirHostNet provides to the scientist community the most complete and accurate source of virus-virus and virus-host protein-protein interactions.

The VirHostNet knowledgebase system will speed up systems biology analysis of infectious diseases and will provide new insights for antiviral drug design. We hope this unique resource will also help worldwide scientist to improve our knowledge on molecular mechanisms involved in antiviral response mediated by the cell and in viral strategies developed to evade and hijack host immune system.

VirHostNet is supported by INSERM, INRA and UCBL.
CALL TO AUTHORS
(and win prizes)

ISICR contest: WIN PRIZES!!!!! First Prize - an ELISA kit of your choice from Cell Sciences and a 1 year ISICR membership; 4 2nd prizes - 1 year ISICR memberships (if you are a current member, your membership will be extended for 1 year) - this contest is sponsored by Cell Sciences, an ISICR Silver Sponsor.

Contest Rules: Come up with a paragraph or 2 to complete this story using as many terms from COPE (http://www.copewithcytokines.org/) as you can. Winners will be decided by Horst and I, although I can possibly be bribed with chocolate.

Poems using terms from COPE are also welcome and may even be published!!!

The BIK Adventures of ELMER in Search of the Golden FLICE

By Horst Ibelgaufts

a THREAD or a yarn written in sentences with many an extra unnecessary acronym and written down for posterity in letters beginning with abdominal A or ABCD-1 and ending with Z and up to Zzzz.

Once upon a time in Acronymania a long time before the great juxtacrine wars that left the plains branchless and the people breathless there lived king 3T3. So named he was because he could have had 3 times 3 children and more had he shown less contact inhibition and given more burst promoting activity to his wife, good Diva. Thus he only had one daughter of his own who went by the name of fair Fractalkine. And her mother, whom they called mother of the son of sevenless, had become a great orphan receptor for want of children, but this is quite a different story.

King 3T3 may have been a BAD husband, and that, maybe, was one of his CARDINAL mistakes, but at least he was a good ruler. He busied himself with his 5637 lord chancellors. He boasted at least 464.1 privy counsellors. He gave large sums of money to more than 744.1 consultants in the stem cells of his palace. And he ruled wisely his less than 2E8 subjects, who died of old age rather than of programmed cell death. Lovingly the people called him dad-1 (some close relatives pronounced it deddy and spelled it DEDD).

Being no friend of cell activation and colony-forming cells the king had introduced a new cell culture and adhered to the principles of cell ablation. And for all perpetrators against the law he had abolished hanging by death effector filaments and banned detachment induced cell death. Instead of putting these people into quiescent cells where they could idle he had advanced the prosperity of his honest citizens and intrabodies by taking many a Natural Born Killer completely out of the cell cycle. He had ordered that they should work in the State Boyden chamber for the good of all until they became completely frazzled and jagged. And by being not only a great silencer of death domains but also a big defensin, protectin as it were the country against chemoinvasion and other intruders, he had sustained welfare and peace.

It then was that in the kingdom of king 3T3 there lived a poor costimulator by the name of Cripto with his wife, MaMi Livertine in the cobblestone area near the helper peak 1 in the delta of the great river Kit near the little hamlet of Da on the island of Epo.

A reaper of sorrow and a poor SOD this man was, the only feeder of his little multigene family who never struck silver or gld, let alone an AU-rich element. So poor he was that many a day the family had to live on miserable dwarf mice. No sweets, not even Mini-ICE. They lived in a little motheaten beige house which in winter was quite humig and there was not even a LIGHT as they had had to build their home without windows for lack of CASH. Even the MICE living in the dark corners were nude and shivered and some even committed harakiri. And the LICE of the MICE had died for want of food long ago..

Despite their poverty the family had mastered the difficulties of life without a major knock-out and never did they HARP long upon their miseries. They had one blessing though and that was their only son whom they called ELMER, and the following tale is all about him.
It happened that one day the local MP had come to the little hamlet to make some personal remarks to all RANK and file in the cause of which he also mentioned the great misfortune that had befallen fair Fractalkine and that had gone by RELAY all through the kingdom with the exception of the little hamlet. A strange LIGHT had been seen one night in the king's castle and the princess had not turned up to receive her conditioned medium for breakfast the next morning. The princess so it appeared had swallowed a faint little ball of some unknown mixture of an immunotoxin and green fluorescent protein. After that she was full of doom for targeted disruption. "SOS1 and SOS2", the MP had concluded his tale, suggesting that he who would restore the princess' neuroimmune network would receive 10 saka of gld, half of the kingdom, and granted unrestricted homologous recombination with HER1.

"She will not be survivin unless someone brave will be suppressin his fears and go and visit the wise son of sevenless beyond the K-4 mountains and the deep morasses of acronyms and the unchartered and unexplored bleak deserts of synonyms in the land of LETE to consult the magic BOK in his subtractive library for help" thought ELMER. And he did not care to know that many valiant knights and even heroines had already failed to find a cure (I just name K-sam Clemens, KYM-1D4 Basinger, Sheer LAK-1 Holmes, JAB Erwicky and say that each of them deserved a special COPE entry with their adventures). Be that as it may, ELMER went home and told his parents.

I bek your pardon, son, what the HEK or HEK293 do you think you will be doing? You must be MADD" his mother had cried. "YY.1 will you do this? What will your father say?" But his father had said "Nil-2-a" as he had taken a NAP and would not be disturbed and so did not hear about the high falotein plans. And then they TRANK a cup of tea and looked at each other in anticipation. Eventually, actually, in a NIK of time, his father gave HIM his blessing and said: "o, blast-1, yes, IF that is what you wnt-1 to do my son, it will be a small step for you because you are really A1, but a large LAP for the kingdom. You will find your way APAF-1 and below, even if you are without EMAP-1 and no passport to help you with customs and XICE". There were always strange words in his expression library.

The next morning when it was still DARC and the wingless LARC was singing high up in the SCYA1 ELMER was already on his TRAIL, a homeo box with a bit of LARD for food on his BAK and a small bag full of tea leaves.

He had not gone far when he heard someone shout: "Do a CAM assay, come, come HER2, hILP, me". He saw someone who looked like a TRAMP who had got stuck in a deep TRAP and could not free himself out of this limitin situation. "DAUDI", ELMER said politely in the vernacular, "HAF no fear CAS IL, HLP you out of your apelin condition. B2 or b4 you can CLARP your hands ILINCK my rope to you and by my artificial juxtacrine stimulation you shall be FINAP in no time."

"O my gadd34" cried the TRAMP whose name was actually Casper. "I already flt quite RAW264.7. It is Zif I am viable motheaten. UGIF me BAK my life and so I can pursue my profession as an astronomer and do another Comet assay although I still feel like having eaten death proteins. DEDD is nice of you to help me. ZENK you so much. How can I TANK you before I-T the low road and you the high road? And he gave ELMER a friendly pAT464. "I wnt-2 you to HAF a free WISH. (TACA so myc he said and ELMER thought it was strange that he spoke Swedish)" And before ELMER could say something Casper waved-1 his hands and disappeared with a PuF and a FIZZ-3 and a FLASH. And the place looked as if they had not met at all.

ELMER had not gone far when he heard other sounds like "HC11, HC14, HC21, HCC1, HCC2, HCC3, HCC4, HCP, HCSF". "Somebody has a strong hck up" he thought. "I don't see a livin soul and wonder who that may be. But he did not have to stretch his imagination for long because soon he saw a poor miserable woman hu looked like a HUMSTR in a wsl-1 fur coat and whose DARK eyes were streaming with Harlequin molecules and she didn't have a nice TAN-1 at all. "L-309 am HILDA, not CARMEN" wailed the creature with a strange dictated..., BOO, BOO, BOO". "TX, TX, TX, lck here" cried ELMER, "what
(Call to Authors, cont. from page 20)

is this wailing all about? Put your CARD on the table. I can't COPE with this noise and you should be restrictin-P yourself a BID." The woman tried a targeted disruption of her tears and tried to compose herself. "Th0, Th1, Th2" she began, and stuttered. "CHO, you ARE an impatient one but T-helper in great sorrow you are." "I AMH a Catalase from far-away Spain" she continued. "Run down in the world a bit now, but I AM OP-1 noble birth and OP-2 highest RANK in a CFC family full of ART, wearing Purpurin clothes all the time. There's been an ATAC by a Cerberus and I couldn't RON away and I haven't had any Feeder for at least H89 hours". ELMER looked at the poor SODD quite awd. "ALAK of courtesy has not been my AIM" he said. ELMER thought of the LARD, apologized that he had nothing else, and gave it the lady to eat.

You should have seen the strong chemotaxis exerted by the food although it had become a little soggy. While the lady was eating, ELMER told her about his plans. "You'll be wearing off your SOCS for this, COS I see you have no boots. Sounds TAF and a bit raf to me" she said. "Be sure you get the golden FLICE to wrap the princess in with. That'll restore her in next to Nil-2-a". ELMER looked amazed and the thoughts went through his mind like Harlequin molecules. "What the HEK are you talking about? I WISH you would explain!" he cried. "Well" said the lady, "don't you know that the sone of sevenless, who lives in the white spotting locus in the mountains, where they still ride on a YAC-1, has a cure-all, a healing blanket called the golden FLICE, which is better than any wound healing formula people know of? If you should manage to get there and not succumb to any targeted deletion on your way, you may URG him to help you. But, mind you, his motto is 'UGIF me something, IGIF you something' otherwise there won't be any VIP treatment with HIM". "YFt", thought ELMER, I still have some tea leaves to give him. This doesn't grow in the branchless mountains and he will not have DRONC tea for some time. It should provide a good entrance and Xid." "Look here," said CARMEN, you have been kind to me, and I have at least some boots for you. It will ease the TRIP through the mountains. You can call yourself Ladsin boots now". ELMER looked at

the lady, then at the boots of lethal yellow, thanked her again, waved-1 and waved-2, and bid his farewell, threw her an air CISK, and showed her his derriere.

The thought to have to go all the way to the mountains did not seem particularly attractin to him, and he wished he were BAK in his AATYK ANT amida his books with a good Cop of tea before him. But before a black tremor could come over him and DRIVEDD, he hid these thoughts and tried to augment his sprouty gait with a semi-solid song.

to be continued........ (winners to be published in the next ISICR newsletter).


Dr Horst Ibelgaufs runs the COPE 'Cytokines & Cells Online Pathfinder Encyclopedia' at www.cope-withcytokines.org

COPE contains extensive subdictionaries on Angiogenesis, Apoptosis and Cell death, CD antigens, Cell lines in Cytokine Research, Chemokines, Cytokine Inter-species Reactivities, Cytokine Concentrations in Biological Fluids, Eukaryotic cell types (with expression profiles), Hematology, Hormones, Innate immunity defense peptides, Metalloproteinases, Modulins, Protein domains/sequence motifs, regulatory peptide factors, Virulence Factors/virokines/viroceptors
Mike Nichols and Dr. Huda Zoghbi to Receive 2009 Vilcek Prizes

Inaugural Vilcek Prizes for Creative Promise Go to Ham Tran and Dr. Howard Chang

Annual Awards Presentation: Thursday, April 2, 2009

New York, February 9, 2009 - Legendary stage and screen director Mike Nichols will receive the 2009 Vilcek Prize in the arts, and internationally renowned scientist Dr. Huda Zoghbi, a pioneer in the study of Rett Syndrome and related autism spectrum disorders, the prize in biomedical science. “We have been awarding these prizes annually since 2006,” said Dr. Jan Vilcek, President and Cofounder of the Vilcek Foundation, “and this year I’m proud to announce the expansion of our awards program with the Vilcek Prize for Creative Promise, to recognize the successes of foreign-born individuals in the early stages of their careers in the arts and biomedical sciences.” Filmmaker Ham Tran and biologist Dr. Howard Chang have been named the first Creative Promise Prize recipients.

Of the new prize category, Marica Vilcek, Vice President and Cofounder of the Vilcek Foundation, explained, “We have always wanted to honor and publicize the contributions of a younger generation of immigrants working in the arts and sciences, to help them maximize their potential. Jan and I were in the early stages of our careers when we immigrated to the United States, and the professional support we received here was pivotal to our success.” The Vilcek Prizes for Creative Promise are presented to foreign-born individuals, 38 years old or younger, in the fields of biomedical science and the arts.

At the awards presentation, to be held at the Mandarin Oriental Hotel in New York City, Thursday, April 2, 2009, Mr. Nichols and Dr. Zoghbi will each receive a $50,000 cash award and a commemorative trophy created by designer Stefan Sagmeister. Creative Promise Prize winners Mr. Tran and Dr. Chang will each receive a $25,000 cash award and a plaque, also designed by Mr. Sagmeister. The four prize winners were chosen by independent panels of experts.

The Vilcek Foundation, in meeting its primary purpose, to call attention to the accomplishments of immigrants currently working in United States, also serves to remind the public of the immeasurable contributions of the foreign-born to this country throughout its history. Dr. Vilcek points out, “Much of the advancement of science in the United States from the first half of the twentieth century onward rests on the achievements of foreign-born individuals. The outstanding work of this year’s science honoree, Dr. Huda Zoghbi, underscores the importance of remembering this fact. The same is true in the arts. Mike Nichols, the 2009 Vilcek Prize winner in the arts, is universally acclaimed for his film and theater work, but few realize that he, too, was born overseas, reminding us that the American movie industry in large part owes its growth and worldwide preeminence to immigrants.”

This year’s Vilcek Prize recipients demonstrate the truly global influence of America’s immigrants: Mike Nichols was born in Berlin, Germany; Dr. Huda Zoghbi in Beirut, Lebanon; Ham Tran in Saigon, Vietnam; and Dr. Howard Chang, in Taipei, Taiwan.

About the Prize Recipients

Mike Nichols

Through his groundbreaking work in improvisational comedy, theater, and film, Mike Nichols has, for almost a half-century, shown us that through honesty - in particular, the special brand of honesty conferred by humor - we can make some sense of life, and when we can’t, to laugh at it. Only the most ardent of film and theater buffs, however, knows that this virtuoso of the American entertainment landscape was not born on American soil.

Mike Nichols began life as Michael Peschkowsky, in Berlin, the son of a Russian-born father and a German mother. With the voice of Hitler still ringing in his ears, he escaped to this country in 1939. Smart and quick-witted, early on Mr. Nichols found the power in humor, and began to master its intricacies, often using his childhood experiences as seed for laughter. He worked the ground while at the
University of Chicago in the early 1950s, where luck landed him among a talented theater group; full germination occurred when he met and paired with the brilliant Elaine May. For four years, the duo refined the art of improvisational comedy.

After the pair broke up, Mr. Nichols found something he was even better at than comedy: directing. In less than ten years (1963-1972), he directed five hit plays on Broadway and won four Tonys. In 1966, he made the move to Hollywood. Directing the film version of Edward Albee's play *Who's Afraid of Virginia Woolf* earned him his first Academy Award nomination; the four leading actors were also nominated, a first in Academy history. He took an Oscar home for his second film, *The Graduate*, at the same time launching his reputation for audacious casting and an uncanny ability to bring out the best in actors.

Over the years, Mr. Nichols has proved to be consistently light on his directorial feet, moving deftly between stage, screen, and television; along the way, he added producer to his skill set. He is one of the elite in show business to have won all the major entertainment awards: Oscar, Tony, Emmy, and Grammy. He has twice more been nominated for the Academy Award for Best Director (*Silkwood* and *Working Girl*), and once as producer (*The Remains of the Day*). In addition to his Oscar, his awards shelf is weighed down by an astounding nine Tonys (*Barefoot in the Park, Luv, The Odd Couple, Plaza Suite, The Prisoner of Second Avenue, Annie, The Real Thing, Spamalot, and Whoopi*), one Grammy (*Best Comedy Album, An Evening with Mike Nichols and Elaine May*), and four Emmys (two for *Wit* and two for *Angels in America*). He is the recipient of the George Abbott Award, the Lincoln Center Lifetime Achievement Award, the Kennedy Center Honor, and the Directors Guild of America Lifetime Achievement Award; he also has been recognized by the American Museum of the Moving Image for his contributions to the film industry. He is a co-founder of the New Actors Workshop in New York City.

**Dr. Huda Zoghbi**

Huda Zoghbi's first semester of medical school at the American University in Beirut was shattered by civil war. Determined to finish the year, she and her fellow students and their professors lived in the basement of the medical school building, attending class in “safe” rooms, with double-thick walls. Perseverance was to become a hallmark of Dr. Zoghbi’s character, and be instrumental to the achievements of this internationally renowned child neurologist and molecular geneticist - notably, the discovery of the gene responsible for Rett syndrome.

Forced by the escalating war in Lebanon to complete her medical studies in the States, Dr. Zoghbi received her MD from Meharry Medical College in Nashville, Tennessee, in 1979. She joined the pediatric residency program at the Baylor College of Medicine and, during a rotation in neurology, became “fascinated by the brain.” A three-year residency/fellowship program in pediatric neurology followed, in 1982, at Baylor.

Intending to become a pediatric clinician, an encounter with a five-year-old girl at Texas Children's Hospital and an article on Rett syndrome in the Annals of Neurology redirected Dr. Zoghbi’s professional path. Realizing that solving the problem of this mysterious disease would require research training, Dr. Zoghbi went back to school, in molecular genetics. Rett syndrome, would have to wait, however, as too little data was available at the time to make it the launch point of her new career. Instead, she focused on spinocerebellar ataxia type 1 (SCA1), a crippling, neurodegenerative disease that affects balance and coordination. In 1988, she set up her own laboratory at Baylor College of Medicine, and began a close collaboration with Dr. Harry Orr of the University of Minnesota, who was also working on SCA1. Astonishingly, in 1993, both cloned the SCA1 gene on the same day. Behind the scenes, Dr. Zoghbi continued to work on Rett syndrome. In 1999, sixteen years after first learning of the disease, she and her collaborators identified mutations in the MECP2 gene as the cause of Rett syndrome.

Today a professor of Pediatrics, Neurology, Neuroscience, and Molecular and Human Genetics at Baylor College of Medicine, and an investigator at the Howard Hughes Medical Institute, Dr. Zoghbi...
(Vilcek Prizes, cont. from page 24)

says her ultimate professional goal is “to actually make a patient better” through treatments resulting from her discoveries in research.

Dr. Zoghbi is a member of the National Academy of Sciences and the Institute of Medicine; she is also a trustee at the American University of Beirut. She has been honored with the E. Mead Johnson Award for Pediatric Research, the nation's most distinguished pediatric research award; the Kilby Award for Extraordinary Contributions to Society through Science, Technology, Innovation, Invention, and Education; the Sidney Carter Award; and the Bristol-Myers Squibb Award for Distinguished Achievement in Neuroscience Research.

Ham Tran

In the films of Ham Tran, stories gone untold too long are unraveled, voices kept silent too long are heard. They are the stories of the Vietnamese boat people and the survivors of the reeducation camps, and they are not easy to tell.

Born in Saigon, Mr. Tran immigrated as a refugee at the age of eight to America, with his ethnic Chinese Vietnamese parents. The desire to regain memories lost during the process of assimilation“institutionalized amnesia,” he calls it“drew him to poetry, prose, playwriting, and, eventually, filmmaking. Even before leaving college, with a BA in English Literature from UCLA and an MFA from the UCLA School of Film and Television, Mr. Tran's multifaceted talent for storytelling on film became evident—he writes, directs, edits, and produces. His first two short films, The Prescription and Pomegranate were semifinalists for the Student Academy Awards; and his 28-minute thesis film, The Anniversary, about two brothers separated by the Vietnam War, qualified for an Academy Award for Best Live Action Short, in 2004, and has won more than 30 international film festival awards.

While working on The Anniversary, Mr. Tran became aware that no film had ever been made about the war years in Vietnam, from the Vietnamese perspective. His first feature film, Journey from the Fall, emerged from that realization. Inspired by a true story, it chronicles one family's struggle for freedom as they flee their country after the fall of Saigon in 1975, as well as those forced to stay behind. Journey from the Fall was an Official Selection for the 2006 Sundance Film Festival and was nominated for the FIPRESCI Award for Best ASEAN Film at the 2006 Bangkok Film Festival; it has won 16 international awards.

Mr. Tran is now working on his second feature film, Distant Country, about two Vietnamese illegal immigrants whose dreams of reaching the United States take them on a journey around the world. Another new project is a documentary film, tentatively titled, Sponsored '75, which traces the lives of Vietnamese families rescued from four American refugee camps in 1975, and their sponsors.

Mr. Tran is part of a new Vietnamese filmmaking movement called the Viet Wave, whose mission is to bring Vietnamese-content films to American movie houses through Wave Releasing, the first Vietnamese-American film distribution company. He is an active member of the Asian and Pacific Islander community and serves on the board of the Vietnamese American Arts and Letters Association. He has also directed a promotional video for the Vietnamese Overseas Initiative for Conscience and Empowerment, and worked with the Orange County Asian and Pacific Islander Community Alliance to create a curriculum around Journey from the Fall to help change the way the history of the Vietnam War is taught in high schools across America.

Dr. Howard Chang

Why do long hairs grow on our scalp, but not on our palms or the soles of our feet? How do cells decide where they should be located in the body?

Unconventional questions such as these - in particular, those with a direct connection to human diseases - drive the research of Dr. Howard Y. Chang, a practicing dermatologist and Associate Professor of Dermatology and principal investigator in the Program in Epithelial Biology at the Stanford University School of Medicine.
With a disciplined mind even as a teenager, Taipei, Taiwan-born Dr. Chang remembers well the shock of his first day in junior high school in southern California, where his family had moved when he was twelve years old. He went on to earn his AB in Biochemical Sciences, from Harvard University, in 1994. He then joined the Harvard MIT MD PhD program, and together with MIT Professor David Baltimore discovered several key biochemical control mechanisms of how cells self-destruct (a process called programmed cell death), which have important applications in the study of cancer, autoimmunity, and degenerative diseases.

Dr. Chang completed his PhD in two years, and while pursuing medical training in dermatology, began to pursue his postdoctoral research in Professor Patrick Brown's lab at Stanford University. There, he began a new research program to understand the basis of site-specific differences in human skin, resulting in novel modes of gene control that extends from cancer treatment to aging.

To understand why skin cells in diverse parts of the body have different characteristics - how cells know their “positional identities” - a fact that guides the diagnosis and treatment of many skin diseases, Dr. Chang and his colleagues are seeking to define in molecular terms how the expression of different genes in stromal cells determines their ability to affect the development of skin cells. The answers they have discovered so far reveal critical information about gene regulation; specifically, that cells are used to record the positional identity in human tissues, and that the “perturbation,” the disturbance, of such programs plays a major role in cancer progression, especially in metastasis, whereby cancer cells spread to other parts of the body. These breakthroughs may suggest new approaches for the treatment of malignant tumors.

Dr. Chang is a highly productive researcher. He has published more than 60 papers in such journals as Nature, Cell, Science, Nature Genetics, PLoS Genetics, Genes and Development, and Genome Research, with more in press. Dr. Chang has received the American Academy of Dermatology Young Investigator Award, the Damon Runyon Scholar Award, and the American Cancer Society Research Scholar Award. He is a member of the Stanford Comprehensive Cancer Center.

About the Vilcek Foundation

The Vilcek Foundation aims to raise public awareness of the contributions of immigrants to the sciences, arts, and culture in the United States. The Foundation was established in 2000 by Jan and Marica Vilcek, immigrants from the former Czechoslovakia. The mission of the Foundation was inspired by the couple's careers in biomedical science and art history, respectively, as well as their personal experiences and appreciation for the opportunities offered them as newcomers to the United States. In addition to awarding annual prizes in the biomedical science and the arts, the Vilcek Foundation showcases the work of innovative artists, filmmakers, and others, many of them immigrants who have yet to achieve critical or financial success, at its headquarters at 167 East 73rd Street, New York City.

Former recipients of the Vilcek Prize in the arts include: architect/urban planner Denise Scott Brown; artists Christo and Jeanne-Claude; and classical music composer Osvaldo Golijov. Previous recipients of the Vilcek Prize in biomedical science are: Dr. Rudolf Jaenisch, founding member of the Whitehead Institute at MIT; Dr. Joan Massagué, Chairman of the Cancer and Biology Genetics Program at the Memorial Sloan-Kettering Cancer Center; and Dr. Inder Verma, a professor and researcher at the Salk Institute.

For more information about the Foundation, please visit www.vilcek.org
McGill University has embarked on a new era of interdisciplinary research in the life sciences with the opening of more than 150,000 sq ft of start-of-the-art research facilities in the newly constructed Bellini Life Sciences Centre and the Goodman Cancer Center. These new buildings create an interconnected McGill University Life Sciences Complex that houses a dynamic research community of over 200 biomedical researchers. In addition to spectacular laboratory space, this new infrastructure includes modern core facilities for flow cytometry, high throughput and high content small molecule screening, hybridomas, imaging, mass spectrometry, NMR, X-ray crystallography and histology. They also include a new state of the art mouse facility that is equipped for transgenic studies and for working with BSL-2 and BSL-3 level pathogens. The purpose of this expansion is to create an interdisciplinary research environment that will push the boundaries of research in a number of areas.

The Complex Traits Program is one of the 5 research themes of this new research complex. This program explores the causes of human illness by examining the interplay between genetic and environmental influences in disease onset, progression and outcome. Areas of particular interest include but are not limited to host/pathogen interactions, inflammation, metabolic disorders and cancer. The Complex Traits Program has privileged access to unique genetic (recombinant congenic strains, ENU mutagenesis) and phenotyping platforms for studies of mouse models of human diseases. We invite applications from well-qualified candidates at all stages of their careers who have enthusiasm for multidisciplinary research and are eager to develop novel collaborative approaches for investigating complex diseases of critical importance for global health. The successful candidate will be provided competitive start up packages and will contribute to the research and teaching missions of one or more of the Departments of the Faculty of Medicine including Genetics, Biochemistry, and Microbiology and Immunology. We also offer an exceedingly high quality of life in Montreal, one of North America's greatest and most lively cities.

Applicants should have an MD, a PhD or the equivalent and at least three years of postdoctoral research training. Please submit your application electronically at the following website: (http://www.medicine.mcgill.ca/academic/rec_applicationform.htm). In order to complete the application process, you must also send to facultyaffairs.med@mcgill.ca a letter outlining your current and future research interests, a copy of your CV and the names and addresses of three references.

In accordance with Canadian Immigration requirements, priority will be given to Canadians and permanent residents of Canada. McGill University is committed to equity in employment.
Male or Female?

You might not have known this, but a lot of non-living objects are actually either male or female. Here are some examples:

FREEZER BAGS: They are male, because they hold everything in, but you can see right through them.

PHOTOCOPIERS: These are female, because once turned off, it takes a while to warm them up again. They are an effective reproductive device if the right buttons are pushed, but can also wreak havoc if you push the wrong buttons.

TIRES: Tires are male, because they go bald easily and are often over inflated.

HOT AIR BALLOONS: Also a male object, because to get them to go anywhere, you have to light a fire under them.

SPONGES: These are female, because they are soft, squeezable and retain water.

WEB PAGES: Female, because they're constantly being looked at and frequently getting hit on.

TRAINs: Definitely male, because they always use the same old lines for picking up people.

EGG TIMERS: Egg timers are female because, over time, all the weight shifts to the bottom.

HAMMERS: Male, because in the last 5000 years, they've hardly changed at all, and are occasionally handy to have around.

THE REMOTE CONTROL: Female Ha! You probably thought it would be male, but consider this: It easily gives a man pleasure, he'd be lost without it, and while he doesn't always know which buttons to push, he just keeps trying.
http://www.trisociety2009.org/

Cellular and Cytokine Interactions in Health and Disease


October 17-21, 2009
Lisbon Convention Center
Lisbon, Portugal

Focus
The organizers cordially invite you to participate in the Joint Annual Meeting of the International Cytokine Society, the International Society for Interferon and Cytokine Research and the Society of Leukocyte Biology to be held October 17 to 21, 2009 in Lisbon, Portugal. Our Conference will harness the biomedical expertise and energies of these major societies to provide a comprehensive update of recent insights into basic and clinical aspects of Cytokines in Cancer, Inflammation and Infectious Diseases. The overall theme of this Conference is Cellular and Cytokine Interactions in Health and Disease, and is chosen to emphasize the integration of basic, pre-clinical, pharmaceutical and clinical research in the areas of cancer, immune modulation, inflammation and infectious diseases.

Topics to be covered will include cytokine/interferon structure and function, gene regulation, signal transduction, regulation of cell survival, microenvironment, new cytokines, as well as the multiple roles of cytokines in immunology, inflammation, angiogenesis, host defense and tumor biology. A significant part of the conference will be devoted to cytokine-based therapies in malignancy and other disorders as well as emerging therapies targeting cytokines in autoimmune, inflammatory and malignant diseases. Senior scientists, young investigators, physicians, postdoctoral fellows, graduate students and representatives of the pharmaceutical industry all stand to profit from the interactions available at this venue. We believe that this Conference - set in the beautiful historic city of Lisbon will reflect the best of current cytokine research and will provide a vital impulse for further development.

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Luis Montaner - Chair
Wistar Institute USA

Scott K. Durum
National Cancer Institute USA

Michael Tovey
Inserm, France

International Program Committee
Alberto Mantovani
Humanitas, Italy

Giorgio Trinchieri
National Cancer Institute, USA

Thomas Decker
University of Vienna, Austria

Ana Costa-Pereira
Imperial College, London

David Levy
NYU, USA

Local Organizers
Michael Parkhouse
Instituto Gulbenkian de Ciência, Portugal

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NYU, USA

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Instituto Gulbenkian de Ciência, Portugal

Rui Victorino  
Hospital Santa Maria, Portugal

**Abstracts**
Deadline: **July 15, 2009**

**Tri-Society Annual Meeting 2009**

**Official Hotel**

**Lisboa Marriott Hotel**
Avenida dos Combatentes, 45  
1600-042 Lisboa

Telephone: (+351) 217 235 400

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**International Society for Interferon and Cytokine Research (ISICR) Symposium:**

*Cytokines and Interferons in the Immune Response at the American Association Of Immunology 2009 annual Meeting*

Monday, May 11, 10:15 AM - 12:15 PM WSCTC Room 6A

*Chair: Robert M. Friedman, USUHS*

**Speakers**

Patricia Fitzgerald-Bocarsly, UMDNJ, New Jersey Medical School, *Interferons and plasmacytoid dendritic cells*

Grant Gallagher, HUMIGEN LLC, *Modulation of the Th2 response by IL-19 and interferon lambda*

Thomas A. Wynn, NIAID, NIH, *Dissecting alternative and classical activation: the role of macrophage subsets in the pathogenesis of Th2-mediated disease*

Kendall A. Smith, Weill Medical College of Cornell University, *How mutations in cytokine signaling pathways can lead to autoimmunity and leukemia*
New        Renewal  

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I certify that ________________________________ is a candidate for an advanced degree or a post-doctoral fellow
in a field related to Interferon and Cytokine Research

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Department________________________________________

(Signature of applicant's major research advisor)
REMEMBER TO RENEW YOUR ISICR MEMBERSHIP FOR 2009 OR BEYOND (3 AND 5 YEAR MEMBERSHIPS ARE AVAILABLE) OR THIS WILL BE YOUR LAST ISSUE OF THE NEWSLETTER!!!!!!!