Future ISICR Meetings

Sept. 15, 2007
(History of the Interferons)

Sept. 16-19, 2007
Oxford, UK

2008 Meeting
Joint ISICR/ICS
Montreal, Canada
Oct. 12-16

ISICR WWW Site

www.ISICR.org

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ISICR

INTERNATIONAL SOCIETY FOR INTERFERON AND CYTOKINE RESEARCH

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Editor's Note: To commemorate the 50th anniversary of the discovery of interferon, I have asked members to relate their personal experiences in the lab during those early years. If you have a willingness to reminisce, please feel free to send me anything you think appropriate. I would also refer members to the Journal of Interferon and Cytokine Research as the journal is running longer articles about the early days of interferon research.

Graduate School in the Early Years of Interferon Research

Bob Fleischmann

It was late September or early October in 1966. I was attending one of a required series of evening lectures designed to introduce us to the research programs in the Department of Biological Sciences at Purdue University. Tonight's lecture was given by Edward Simon and I was enthralled. I had known that I wanted to be a biomedical researcher,

(Continued on Page 2)

A TALE OF TWO INSTITUTES

Bob Friedman

Britain and America are said to be separated by a common language. My experience tells me that the separation involves a lot more than that.

After spending four years at NIH; two in Sam Baron's lab in what is now the FDA, and two as a pathology resident in the Laboratory of Pathology at the National Cancer Institute, I was accepted as a

(Continued on Page 4)

*(**Graduate School Early Years**, cont. from page 1)*

hopefully contributing in some way to the betterment of patients' health, since the 9th grade when I had read Arrowsmith by Sinclair Lewis. Here was Ed Simon, speaking directly to my soul. He was relating his research with and his hopes for this magical protein called interferon. I knew that I had found my life's work: I had to work on interferon.

The next day, I approached Ed about working in his laboratory. After answering a series of probing questions asking me to do dilutions in my head, to add and subtract triple digit numbers in my head, to calculate the weight of a hydrogen atom, and to determine the number of people who died last year in New York City, Ed decided to take me on. Try asking your potential new graduate student to take an oral "qualifying" test like that today. None-the-less, it was the beginning of a life-long relationship with a wonderful mentor and a dear friend. It was also my initiation into the wonders of interferon and other cytokines.

Working with interferon in those days was interesting, if labor-intensive. When I first joined the laboratory, we made all of our own media, carefully weighing out each of the more than 30 ingredients of Eagle's MEM. Many hours were spent filtering the media under pressure through a Seitz filter set up on the tabletop and collecting it one bottle at a time. We made productive use of this "babysitting" time by working on our course problem sets and course term papers. Before refrigerating the media, we left the media bottles at room temperature for two days to see if any bacteria would grow up. In 1969 or 1970, my major professor purchased a clean bench for filtering the media that eliminated our contamination problems. We also filtered calf serum and trypsin (from homogenized cow pancreases) that we had obtained from a local slaughterhouse. We were so happy when, during my last years in graduate school, we were finally able to purchase powdered Eagle's MEM in packets, commercially bottled calf-serum, and powdered trypsin. Still, a part of me misses the adrenalin rush that accompanied burst or suddenly disconnected tubes that occasionally enlivened our evenings of filtering. No dogs ever ate my homework, but there were several times when it was drowned by Eagle's.

We performed cell transfers in wooden still-air hoods that were painted with high-gloss oil-based white paint. We pipetted media and viruses using glass "shortie" pipettes from BellCo and small 10 ml and 2 ml rubber bulbs. Talk about having muscles "to die for". Hercules would still be proud of the size of the muscle between the thumb and forefinger on my right hand. Talk about a "babe magnet". When I took off my gloves in the winter, I had to fight off the women.

Of course, the pipettes had to be autoclaved, washed, and re-autoclaved after each use. Everything - or almost everything - in the hoods had to be sterilized before use by passing it's opening and neck through the flame of a "touch-o-matic" Bunsen burner. I say almost everything, because one young undergraduate laboratory assistant tried to flame the rubber hose attached to a vacuum flask and vacuum pump, only to turn the shiny white hood to a smelly black charred hulk. Through her efforts, we learned that there is at least one drawback to using oil-based paint.

The high gloss white paint did more than give a nice, fresh "laboratory look" to the hoods, it also permitted the hoods to be wiped down on a regular basis with 70% alcohol. Turning on a fluorescent UV-lamp in the hoods between uses also assisted in maintaining the sterility of the still-air hoods. One young undergraduate laboratory assistant - yes, the same one mentioned above - decided to reduce the possibility of contamination by leaving the UV-light on during her cell transfer. The graduate student who was consulted the next day about her "strange-appearing" cells instantly snapped to the cause by noting the bright red color of her hands and forearms.

Initially, cell cultures were maintained on 100 mm or 150 mm glass Petri dishes that had to be autoclaved, washed, and re-autoclaved between uses. Even plaque assays were performed on 60 mm glass Petri dishes, using a 5 ml starch-based overlay that had to be made as a fresh 200 ml batch for every 36 plates.

When I joined the laboratory, the Petri dishes were

*(**Graduate School Early Years**, cont. from page 2)*

set on wooden trays and incubated. Contamination was a serious problem. Frustrated by contamination fed by spills on the wooden trays, I personally paid for the construction of a few plexiglass trays that could be decontaminated by washing with 70% alcohol between uses. My contamination problems went to near zero, causing my famously frugal major professor to decide to invest in a sufficient number of plexiglass trays for the whole laboratory.

Oh, the joy of plaque assays. You haven't lived until you have made starch overlays. After you have made your virus dilutions but before you have made your virus overlays, you have to set the appropriate amount of water to boil on a heater/stirrer while you do the virus infections. No, there were no microwaves to give nearly instant boiling water. Then, once the water was brought to a full boil, a pre-made starch slurry had to be slowly dripped into the stirring, boiling water at a rate that would not cool the water, lest there be lumps in the starch overlay. Then, after all of the starch slurry had been added and mixed in, the starch preparation would be moved to a stirrer and allowed to slowly cool, with continued stirring. At 60°C, 5-fold concentrated Eagle's medium and calf serum that had been prewarmed to 37°C would be added slowly. As the temperature dropped to 50°, the starch/medium/serum preparation would be dripped from a wide-mouth 5 ml pipette onto the 60 mm Petri dishes. Oh yes, the starch had to be ready at 45-60 minutes after the virus overlaid plates were put into the incubator, or the plates would begin to dry. Other notes, add the starch at too fast a rate and it could peel the monolayers off of the Petri dishes; add the starch at too slow a rate, and it could set before you finished overlaying all 36 of the Petri dishes.

Then, the plaques needed to be counted. At 24 h or 30 h or 36 h or whenever the plaques were "up", the plates would be stained with neutral red and counted after an hour. The timing of the development of the plaques was dependent upon how many people went into your slowly recovering incubator while the plaques were developing, as well as the relative health of the cells, and the phase of the moon. In the end, it didn't matter whether the plaques were up at 5 pm or at 5 am, they had to be counted 1 hour after adding the neutral red or the neutral red would kill the monolayer, causing the plaques to be unreadable and the experiment to be a bust.

Calculating virus titers was by means of a slide rule, as personal calculators were not available until towards the end of my graduate studies. Believe me, I found it easier to multiply the virus count by the plating factor (5) and the dilution factor in my head than to constantly figure things out using the slide rule. It's easy: you just multiply the plaque count by 10, divide by 2, and multiply by the dilution factor.

Many of my "typical experiments required a two-week cycle. They involved setting microdrops onto Petri dishes, covering the microdrops with paraffin oil to prevent drying, counting the microdroplets to identify those that contained a single cell. In one series of experiments designed to determine whether interferon protected cells completely or partially from viral infection, cells were treated with interferon, infected with mengovirus, set in microdrops, and counted. Beginning at 9 hours, the supernatant fluids from the selected microdrops were harvested and replaced at 3-hour intervals for 24 hours. The supernatant fluids were frozen until assayed for virus. In another series of experiments designed to determine whether all or a select few cells made interferon, cells were infected with interferon-inducing Newcastle's disease virus, set in microdrops, and counted. After allowing for interferon production by the Newcastle's disease virus infected cells, approximately 30 indicator cells were added to each of the selected microdrops and counted to identify microdrops containing 30±6 cells. After allowing time for any interferon produced to protect the indicator cells, the indicator cells were challenged with light-sensitive mengovirus. After allowing an hour for virus absorption, the light-sensitive challenging mengovirus was inactivated by fluorescent white light. After 24 h, the supernatant fluids were harvested and frozen until assayed for progeny virus.

Remembering all of the work involved in growing 40-60 x 150 mm Petri dishes of cells; trypsinizing the 40-60 x 150 mm Petri dishes and setting the cells on 1,000-1,500 x 60 mm Petri dishes; infecting the 1,000-1,500 x 60 mm Petri dishes 36 at a time, and

*(**Graduate School Early Years**, cont. from page 3)*

counting them whenever they were ready gives me nightmares to this day. After hours of pipetting, I developed a near permanent case of what I called pipetter's shoulder: a muscle at the base of my right shoulder blade would contract spasmodically, causing persistent pain that no amount of rubbing would assuage. Disposable plastic Petri dishes, particularly microtiter plates, multichannel pipetters, and methylcellulose-based overlays were Godsends. Still, I can make the best, smoothest, gravy!!!

Each of the bigger experiments required 28-42 starch overlays. However, with sufficient efficiency, one could "dove-tail" the starch overlays, doing 3 starch overlays at one "sitting" and 4 sittings in one day. In my "spare" time, I would be setting up the Petri plates for the next day's virus overlays and/or counting the plaques of the previous day's overlays. Not bad, this way, I could complete the assay of an experiment in just 4-5 days by working very nearly round the clock. I just love to hear today's graduate students tell me that they can't work in the evening to finish an experiment because that's when their favorite show is on television.

I do miss the hemaglutinnation assays that we used to titer Newcastle's disease virus. It was my job to obtain RBCs from a rooster, kept specifically for that purpose. The method of obtaining RBCs was by heart puncture. Don't tell me that roosters aren't smart enough to learn. They certainly recognized me and my 5 inch long needle. I still have visible scars on my hand from the jabs of rooster spurs, delivered as I tried to catch their feet. One interesting aspect of the heart puncture technique, is that after several punctures, the skin at the base of the neck becomes very tough and difficult to puncture. As the keeper of the flock, it was my job to retire the roosters when the time came. As an underpaid graduate student, rooster retirement meant, "I guess we'll have fresh chicken for dinner."

It was an exciting time for interferon research, with important new discoveries published seemingly every week. It was a time when one could not only read every interferon article published but have met the principal authors of most of them.

Yes, those were the "good, old days." However, it is so nice, today, just to be able to focus on doing the experiments, rather than spending so much time preparing the glassware, pipettes, and media to be used for the experiments. Still, it is a bit less exciting. And, I do miss the occasional fresh chicken.

Bob Fleischmann

*(**A Tale of Two Institutes**, cont. from page 1)*

post-doctoral fellow at the lab of Alec Isaacs in the Virology Department at The National Institute for Medical Research, Mill Hill. I arrived there on October 12, 1963, a little more than 5 years after the first published description of interferon.

By Mill Hill standards, I guess I was a pretty spoiled young investigator. When I needed glassware (no plastics then) or media, I went down to central supply at NIH, and signed for them. Things were not often that simple at Mill Hill. A short description of a few of the lessons I learned during my 13 month stay in Isaacs lab follows.

1. The early bird catches trouble. I was used to getting to work at the NIH well before 8:30, because otherwise one had to park somewhere in earth orbit. Since I lived in easy walking distance of the Mill Hill lab (well, not that easy as the lab really was on a steep hill, and we lived at its bottom), in the first week of my postdoc, I arrived for work well before 8 AM. At that hour the institute was pretty deserted. The technicians began to arrive about 9, and started cleaning glassware and tidying up labs until about 10:30, when the senior investigators began to arrive, and everyone went for morning tea. Since I was a lowly postdoc, I didn't expect anyone to help me, so I was not surprised when no one paid any attention to me. That was the situation for a few days, when the Chief Tech in Virology, Mr. Busby, who looked

*(**A Tale of Two Institutes**, cont. from page 4)*

to me like the guys who serviced Spitfires in the Battle of Britain in old World War II movies, and who may actually have done just that a few years previously, pulled me aside to ask me not to come in so early, as I was just getting in the way of the technicians doing their job. So like everyone else, I started coming in around 10:30.

2. Sharing is a good thing. At NIH we usually had so much equipment that each lab had its own supply of whatever apparatus it needed. It was not so at Mill Hill. All large items of equipment were held in common, and one had to sign up to use any of them. At the end of my first week, I needed an ultracentrifuge. I noticed that every Friday, the name of the Director of Mill Hill, Sir Peter Medewar, the Nobel laureate, was listed for use of the centrifuge. I asked his technician if the Director planned to use the centrifuge that day. He said that he didn't know whether he did or not, but if I wanted to use it myself, I had better ask Sir Peter myself. I thought, "You want me to go and ask a Nobel laureate to give me his time on the centrifuge?", but I really needed it, so I pulled myself together and knocked on Sir Peter's door, and asked whether he would be using the centrifuge that day. He smiled and got up from his desk, put his arm on my shoulder, steered me back to his technician, and said, "Please let this young American scientist use the Spinco today." So I did.

During my time at Mill Hill many scientists shared their equipment and their technical expertise with me, and I learned that having a common equipment room is an efficient and economical way to run a lab.

3. There really is a virtue in silence. At the NIH one walked down the hall, looked people in the eye, and said hi or wished the passerby a good day. To do otherwise was considered rude or even hostile. At meals or coffee breaks, there was constant discussion and chatter. To my dismay, the people I passed in the halls at Mill Hill for the most part didn't acknowledge my presence in any way. The cafeteria was quite quiet at meals, and at first, at coffee or tea breaks scientists often sat silently staring out the window, looking at the beautiful greenbelt surrounding Mill Hill. So, for a long time, I thought everyone in the place disliked me. I learned, however, that the British talk plenty when they get to know you, and they have something to say; I soon found myself engaged in animated discussions of science, politics, history, theater, music, and art. It became a source of great amusement to me to observe other American scientist visiting Mill Hill during my stay there. They would start to make small talk during our breaks, and notice that no one was responding, whereupon the guest would become quite uncomfortable, and believe that something wrong had been said. Most, I think, never figured out what the drill was.

4. Hands on is best. When I arrived in Alec Isaacs' lab, he was engaged in investigating whether foreign DNA induced interferon production. Since the preparations of DNA being used were very crude, I was unable to work up much enthusiasm for the project. The ability of actinomycin D to inhibit interferon production, but not the replication of some RNA viruses had recently been discovered. I thought it might be interesting to employ these observations to distinguish between inhibition of viral growth by interference and by endogenous interferon production. Isaacs thought this might be an interesting idea and encouraged me to go at it. The experiments worked out well, and I soon had enough material for a note to Nature. When I gave Alec a draft of the paper, he promptly read it over, and returned it to me with his handwritten comments, but much to my dismay, he had crossed his name out as the co-author. I naturally concluded that he didn't think the work was up to his standard, but when I asked him about this, he laughed and said that wasn't his reason at all. I had done all of the experimental work, and he believed he should only put his name on research in which he'd done a good portion of the work with his own hands.

Although I know it's quite common to list as authors the names of anyone who has contributed to the final form of a manuscript, I have tried during my career to follow Isaacs' example.

5. Coexistence is possible. When I arrived at Mill Hill I was assigned to work in the same room as another American postdoc, David Dubnau. David's

*(**A Tale of Two Institutes**, cont. from page 5)*

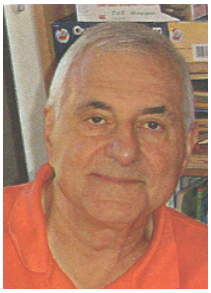
work on bacterial genetics was going well, so he had decided to finish what he was at, and it developed that we'd be working together for about 4 months in the room that had been intended for my use alone. We got along well, despite the facts that David was working on bacteria and I, on viruses using large numbers of cell cultures, and that politically I am a middle of the road liberal, while David was a flaming leftist. Since mixing bacteriology and cell cultures is usually a no, no, I was amazed that I encountered no problems with contamination of my cells during the time I shared the room with David. I had chalked up my fortunate experience to the presence of penicillin and streptomycin in my culture media. When I commented on this at David's farewell party, he agreed that it was fine that things had worked out so well, but was stranger than I had thought, because he's been using penicillin and streptomycin resistance as his genetic markers!

6. Rugged individualism isn't always the best approach. On January 2, 1964, I arrived at Mill Hill to a scene of total disarray. The previous day, I had attended a Microbiology meeting with Isaacs, at which he's performed brilliantly, discoursing on all of the major findings and treating me to lunch at his favorite pub. That evening, he'd suffered a bleeding incident due to a hemangioma at the base of his brain. He was in grave danger, and even if he recovered, it was doubtful whether he would be able to function at his previous level in the ten months left for my postdoctoral tenure. The other postdocs in the lab, Joseph Sonnabend and Joyce Taylor, and I huddled, and decided we had best pool our ideas and talents in order to come up with projects we might be able to carry out on our own. The rest of the scientists at the institute were very supportive of our efforts, since most of the work going on there was collaborative in nature.

We decided to follow up on Joyce's recent discovery that actinomycin D blocked not only interferon production, but also the development of interferon's antiviral activity. We decided to determine whether we could demonstrate that cellular protein synthesis was also necessary for interferon action, and we were successful in doing so.

This was a little different from the way I had previously worked. While I'd been in Sam Baron's lab, he'd left to work on a sabbatical with Isaacs less than a year after I had arrived. So, at that time I was pretty much on my own for over a year. During my two years as a resident, I had been the most junior member of the department, and thus got very little help. I had perforce become a rugged individualist. My experience working closely with others at Mill Hill turned out to be a very pleasant change from my previous professional life.

My time at Mill Hill was indeed critical for my subsequent development in research and clinical medicine. It certainly changed my approach to work. I like to think I was able to integrate the best of both biomedical worlds in which I'd been brought up



Bob Friedman

Vol 13.3 Corrections

1. The corrected title for the interview in the last issue (13.3) with Horst Ibelgaufts is:

PAPP-A BLyS MEA, MaMi KISS-1 MEA, COS EYE001 NOV MY10 ABC1 (or was it ABCD-1, ABCD-2, or ABCD-3?).

2. The minibio and picture that appeared for Greg Peters in the last issue under "New Member Minibios" should have instead appeared under "2006 Milstein Awardee". Greg has been a member of the ISICR for 6 years. The ISICR congratulates Greg for being selected as a 2006 Milstein Young Investigator.

The ISICR Exec Direc Corner: Welcome to John Lord

John Lord has taken over as the new ISICR Executive Director as Debbie Weinstein has left us for the University of Maryland Pathogen Research Institute. We wish Debbie much success in her new challenge and we thank her for her efforts on behalf of the ISICR. John is the manager of FASEB's Managed Society Services Department and joins us as acting Executive Director. John has ten years of experience in Association Management.

John served as Executive Director of Altrusa International, in Chicago, IL. Before that, he worked for Lions Clubs International Association, holding several positions including: Manager of Member Services; Manager of Leadership Training; and Prevention of Blindness Program Officer for Asia. John's first "job" was as a Peace Corps Volunteer in Thailand.

He has an MBA (Kellogg) with concentrations in nonprofit management and marketing. John is an avid fly-fisherman and tennis player.

Members in the News

Dr. Michael Gale Jr. has announced his move to join the Department of Immunology in the University of Washington School of Medicine, in Seattle, WA, effective June 1, 2007. The entire Gale laboratory personnel group is making the move to Seattle, where they will add to the local expertise in the viral immunology and infectious disease research areas. The Gale laboratory specifically studies the processes of innate immune signaling and interferon actions during infection with hepatitis C virus, HIV, influenza virus, West Nile virus and other viral pathogens.

ISICR Corporate Sponsors

The ISICR wishes to thank the following companies for their 2007 corporate sponsorship of the society. Their participation as ISICR Corporate Sponsors is critical to the success of ISICR initiatives.

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SERONO INTERNATIONAL SA

NEW ISICR MEMBERS

We welcome these members to the ISICR and we look forward to their participation in the annual meeting and ISICR committees and activities.

Joined October 2006 thru February 2007

Burton M. Altura
Brooklyn, NY

Laurent P. Audoly
Gaithersburg, MD

Crystal W. Burke
Shreveport, LA

Christina L. Gardner
Shreveport, LA

Susan Goetz
Cambridge, MA

Robin d. Hatton
Birmingham, AL

Melanie Herget
Vienna, Austria

Linda M. Hibbert
London, UK

Paula Hochman
Cambridge, MA

Paula Hochman
Cambridge, MA

Xiaoyu Hu
New York, NY

Efstratios Katsoulidis
Chicago, IL

Tyler P. Kirwan
Ontario, Canada

Doranelly Koltchev
Piscataway, NJ

Shuhung Kung
Ontario, Canada

Stephen Locarnini
Victoria, Australia

Gengshi Lu
Baltimore, MD

Bei Morrison
Cleveland, OH

Frank Mueller
Cairo, Egypt

Pamela Osterlund
Mannerheimintie, Finland

Vladimir V. Parfenov
Moscow, Russia

(*New Members*, cont. from page8)

M'Bark Sadouk
Quebec, Canada

Federico Serana
Brescia, Italy

Jaleel Shujath
Piscataway, NJ

Xiaoping Song
Cambridge, MA

Katie Su
Beijing, China

Marija A. Tonnos
Ontario, Canada

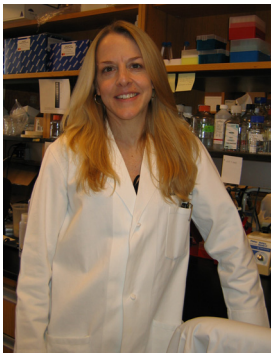
Daniela Verthelyi
Potomac, MD

Rui Wang
Liaoning, China

Chenyang Zhao
Cleveland, OH

Wenli Zhao
New York, NY

New Member Minibios



Robin D. Hatton, Ph.D.
Assistant Professor
Department of Pathology
University of Alabama at Birmingham
Birmingham, AL

Dr. Robin Hatton received her Ph.D. from the department of Microbiology at the University of Alabama At Birmingham in 1996. Her thesis work in the laboratory of Max D. Cooper involved studies on the evolution of the immune system and focused on the identification of T cell receptor component homologues in the African clawed toad, Xenopus laevis. After completing her degree, post-doctoral studies were undertaken in the laboratories of Rick Hockett and Casey Weaver investigating the molecular mechanisms that drive Th1 specific expression of Fas ligand. These studies evolved into the investigation of the transcriptional regulation of the Th1 hallmark cytokine, IFN-γ. Continuing to work with Casey Weaver, Robin identified a highly conserved non-coding sequence element approximately 22 kilobases upstream of the mouse IFN-γ promoter (CNS-22) that appears to be critical for IFN-γ expression in T cells and NK cells. Her current work is devoted to understanding how CNS-22 functions to regulate IFN-γ expression at the chromatin level throughout T cell development.

Reasons for joining the ISICR: "I joined to get to know more people in the cytokine and interferon field and to have another avenue to both present my own data and hear about others' work."

Mini Bios, cont. from page 9)

Frank Mueller
Biotechnology-Eng.
Minapharm Pharmaceuticals/
Rhein-Minapharm Biogenetics
Research & Technology
Manager
Process Development
Mina Street, 3rd Industrial Zone
A2
10th of Ramadan City
Egypt

I graduated with a degree in Chemical Engineering from the University of Applied Science in Krefeld, Germany. Since the early days at my first company, Rhein Biotech GmbH (now Dynavax Europe) in Duesseldorf, I've been involved with one of the most exciting fields in Biotechnology; the process development for therapeutic protein expression in yeast, especially Hansenula polymorpha, or mammalian cells. During my time at Rhein Biotech, I was involved in the process development for the production of the anticoagulant Hirudin and the first yeast derived Interferon-α2a - both processes were successfully transferred to Minapharm Pharmaceuticals in Egypt and launched in the market during the last three years. In 1999, I participated in a successful technology transfer to South America of the large scale production of Hepatitis B surface antigen.

From 2003-2006, I was with ProBioGen AG in Berlin, a company specializing in mammalian cell-line development and well known for the manufacturing of monoclonal antibodies and therapeutic glycoproteins. I was Head of Protein Purification and I continued my work with another member of the "interferon-family", this time a modified version of the Interferon-α molecule.

Since the beginning of 2006, I'm responsible for building up a new R&D department at Minapharm Pharmaceuticals and it's subsidiary, Rhein Minapharm Biogenetics, the leading Biotechnology company in Egypt. Minapharm recently introduced PEGylated Interferon-α2a into the market, based on its' own PEGylation technology.

Besides the challenging aspect of the work, it's very exciting for me to "infect" my team with the viruses "enthusiasm and motivation" in order to develop new production processes for therapeutic proteins in a country where the Biotechnology era has just started.

Reasons for joining the ISICR: "If a molecule becomes a good fellow for you, as Interferon has been for me, I think it's a good idea to join a community in which you can exchange stories and news with colleagues who have similar interests. I'm really looking forward to attend the annual ISCIR meeting this year in Oxford."

Pamela Österlund, PhD
Research Scientist
Department of Viral Diseases
and Immunology
National Public Health Institute
Helsinki, Finland

Dr. Pamela Österlund graduated in the Genetics Department at the University of Helsinki, and received her PhD in Experimental Allergy and Immunology from Skin and Allergy Hospital of Helsinki University Central Hospital in 2003. Her thesis work was dealing with immunological factors in cow milk allergic infants and immunological composition of the breast milk of their mothers. She evaluated the possible relation of immunological divergence in mothers' milk to the development of food allergy in the breastfed infant. Dr. Österlund started in the Allergy program at National Public Health Institute in Helsinki in 2002. She continued at the Department of Viral Diseases and Immunology as a postdoctoral research fellow in the laboratory of Prof. Ilkka Julkunen by studying the immune responses in human dendritic cells infected with influenza A and SARS viruses. Dr. Österlund has been interested in the interferon responses during virus infection, and recently she has carried out the promoter analyses of the novel type III IFN-lambda genes. Her future work will continue on the molecular biology of host cells and viruses, such as avian influenza-induced signaling cascades that regulate the expression of antiviral cytokine genes. She will also attend to national vaccination trials by analyzing the cell-mediated immune responses induced by

Mini Bios, cont. from page 10)

vaccination against avian flu.

Reasons for joining the ISICR: "I joined the ISICR because it is an excellent forum to get to know the people working in the same field. The participation in the ISICR meetings will give me a good opportunity to interact with colleagues on cytokine research especially in the view of the future collaborations. This society will provide me an appropriate channel to present my own studies and hopefully to get some feedback from the leading investigators and scientific experts of the cytokine field."

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 280 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!!!!

Clinical Trials

Hannah Nguyen

More information on this list can be obtained at http://clinicaltrials.gov [CT], http://www.centerwatch.com/search.asp [CW], or http://clinicalstudies.info.nih.gov [CCNIH].

The Efficacy and Safety of ITF2357 in Autoinflammatory syndromes (AIS) (ITF2357 is an orally active histone deacetylase inhibitor with a potent anti-inflammatory effect due to inhibition of pro-inflammatory cytokines IL-1β, TNFα, IFNα, IL-6).
ClinicalTrials.gov ID: NCT00442182
Contacts: Evelien J Bodar, MD 0031 24 3617276 e.bodar@aig.umcn.nl ;
Jos WM van der Meer, MD PhD 0031 24 3618819 j.vandermeer@aig.umcn.nl
Location: Radboud University Medical Centre Nijmegen, Nijmegen, 6500 HB, Netherlands
Principal Investigator: Jos WM van der Meer, MD PhD., Radboud University
Study ID Number: 2006/112

Cyclophosphamide and Fludarabine Followed By White Blood Cell Infusion and High-Dose Aldesleukin in Treating Patients With Metastatic Cancer That Overexpresses p53
ClinicalTrials.gov ID: NCT00393029
Contact: Steven A. Rosenberg, MD, PhD 866-820-4505 sar@nih.gov;
NCI Clinical Trials Referral Office 888-NCI-1937
Location: NCI - Surgery Branch, Bethesda, Maryland, 20892-1201, USA
Warren Grant Magnuson Clinical Center - NCI Clinical Trials Referral Office, Bethesda, Maryland, 20892-1182, USA
Principal Investigator: Steven A. Rosenberg, MD, PhD, NCI - Surgery Branch
Study ID Numbers: CDR0000514353; NCI-07-C-0003; NCI-P6850

Study to Evaluate the Safety and Efficacy of Adeno-IFN Gamma in Cutaneous B-Cell Lymphoma
ClinicalTrials.gov ID: NCT00394693
Locations: Locations in USA, France, Switzerland
Study ID Number: 12928

(*Clinical Trials* continued from page 11)

Proteinase 3 PR1 Peptide Mixed With Montanide ISA-51 VG Adjuvant and Administered With GM-CSF and Peginterferon Alfa-2b [PEG-INTRON(R)]
ClinicalTrials.gov ID: NCT00415857
Contact: Jorge E. Cortes, MD 713-794-5783 jcortes@mdanderson.org Location: U.T. M.D. Anderson Cancer Center, Houston, Texas, 77030, USA
Principal Investigator: Jorge E. Cortes, MD, U.T. M.D. Anderson Cancer Center
Study ID Number: 2006-0360
Last Updated: December 23, 2006

ABR-217620 With Interferon-Alpha (IFN-Alpha) Compared to IFN-Alpha Alone in Patients With Advanced Renal Cell Carcinoma
ClinicalTrials.gov ID: NCT00420888
Locations: Locations in Norway, Russian Federation, United Kingdom
Study Director: Thore Nederman, PhD, Active Biotech Research Study ID Number: 06762004

Lopinavir/Ritonavir Monotherapy vs Standard HAART in HIV/HCV Coinfected ARV Naive Patients Starting Treatment With Anti HCV Therapy
ClinicalTrials.gov ID: NCT00437476
Contacts: Adriano Lazzarin, MD +39/02/26437939 adriano.lazzarin@hsr.it
Caterina Uberti-Foppa, MD +39/02/26437938 caterina.uberti@hsr.it
Location: San Raffaele Hospital Dep. Infectious Diseases, Milan, 20127, Italy
Principal Investigator: Adriano Lazzarin, MD, IRCCS San Raffaele Hospital
Study ID Numbers: Kamon 1

Can Cytokines Predict the Severity of Acute Mucositis and the Need for PEG
ClinicalTrials.gov ID NCT00431925
Contact: Arik Tzukert, DMD 00 972 2 6777111 arik@hadassah.org.il
Location: Hadassah Medical Organization, Jerusalem, 91120, Israel
Principal Investigator: Amichay Meirovitz, MD, Hadassah Medical Organization
Study ID Number: MucoCyt- HMO-CTIL

Comparison of the Level of Connective Tissue Growth Factor Protein (a fibrogenic cytokine) and Related Cytokine in Pleural Effusion
ClinicalTrials.gov ID NCT00313066
Contact: Shen Gwan Han, MD +886-4-23592525x3217 911B@vghtc.gov.tw
Location: Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, 407, China
Principal Investigator: Shen Gwan Han, MD
Study ID Numbers: 940513/C05092

Trial of GM-CSF Given in Combination With Ketoconazole and Mitoxantrone in Patients With Progressive Prostate Cancer
ClinicalTrials.gov ID: NCT00447473
Contact: Diana Lema 713-441-7934 dlema@tmh.tmc.edu
Location: The Methodist Hospital Research Institute, Houston, Texas, 77030, USA
Principal Investigator: Robert J Amato, DO, The Methodist Hospital Research Institute
Study ID Numbers: PC-Keto-Mito.2006; 0106-0010

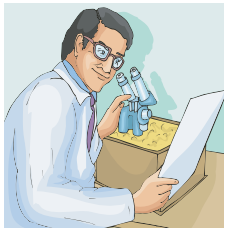
A Phase I Study of Ovarian Cancer Peptides Plus GM-CSF and Adjuvant (Montanide ISA-51) as Consolidation Following Optimal Debulking and Systemic Chemotherapy for Women With Advanced Stage Ovarian, Tubal or Peritoneal Cancer
ClinicalTrials.gov ID: NCT00437502
Contacts: Liz Anderson, RN 919-668-6406 ander094@mc.duke.edu
Emily Privette 919-668-5591 emily.privette@duke.edu
Location: Duke Comprehensive Cancer Center, Durham, North Carolina, 27710, USA
Principal Investigators: Michael Morse, MD, Duke University
Angeles A Secord, MD, Duke University
Ramila Philip, PhD, Immunotope, Inc.
Study ID Number: BB-IND 12605

Efficacy, Safety and Tolerability of ACZ885 (Anti-Interleukin-1beta Monoclonal Antibody) in Patients With Active Rheumatoid Arthritis
ClinicalTrials.gov ID: NCT00424346
Contact: Novartis Pharmaceuticals, Basel Switzerland +41 61 324 1111

(*Clinical Trials* continued from page 12)

Locations: Locations in USA, Austria, Belgium, Canada, Finland, Germany, Spain
Study ID Number: CACZ885A2201

TNF Blockade With Remicade in Active Lupus Nephritis WHO Class V (TRIAL)
ClinicalTrials.gov ID: NCT00368264
Contact: Martin Aringer, MD +43-1-40400x4300 martin.aringer@meduniwien.ac.at
Locations: Locations in Netherlands, Austria, Germany
Principal Investigators: Josef S Smolen, MD, Head, Department of Rheumatology, Internal Medicine III, Medical University of Vienna, Austria
Martin Aringer, MD, Department of Rheumatology, Internal Medicine III, Medical University of Vienna, Austria
Falk Hiepe, MD, Rheumatology, Charite, Berlin, Germany
Marc Bijl, MD, Clinical Immunology, Groningen University Hospital, Netherlands
Study ID Numbers: TRIAL V; Eudract-Nr. 2005-004067-30; Protocol EU-116; EK Nr:110/2006



Read 'em and wonder????

Can you cry under water?

How important does a person have to be before they are considered assassinated instead of just murdered?

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

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

Why does a round pizza come in a square box?

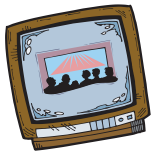
What disease did cured ham actually have?

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

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

If a deaf person has to go to court, is it still called a hearing?

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



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

Why do doctors leave the room while you change? They're going to see you naked anyway.

Why is "bra" singular and "panties" plural?

Why do toasters always have a setting that burns the toast to a horrible crisp, which no decent human being would eat?

Can a hearse carrying a corpse drive in the carpool lane?

If the professor on Gilligan's Island can make a radio out of a coconut, why can't he fix a hole in a boat?

Why does Goofy stand erect while Pluto remains on all fours? They're both dogs!

If Wiley E. Coyote had enough money to buy all that ACME stuff, why didn't he just buy dinner?

If corn oil is made from corn, and vegetable oil is made from vegetables, what is baby oil made from?

Do the Alphabet song and Twinkle, Twinkle Little Star have the same tune?

Why did you just try singing the two songs above?

Biotech News

Clips from the *Daily Drug News*
Hannah Nguyen

[March 16, 2007] Snapshots on AMD-11070, a novel small-molecule CXCR4 inhibitor. AMD-11070 is a chemokine CXCR4 antagonist that has been in early clinical trials at Genzyme for the oral treatment of HIV infection. Recently, the U.S. Food and Drug Administration has placed AMD-11070 on hold due to liver histology changes observed in longer term preclinical toxicity experiments. These findings are currently being investigated. At last month's Conference on Retroviruses and Opportunistic Infections, AMD-11070 was the subject of a number of presentations reporting recent preclinical and clinical results. A summary of these studies is presented below.

The interaction between the HIV coreceptor CXCR4 and AMD-11070 was studied using human CXCR4 receptors carrying single amino acid mutations. Binding studies revealed a pattern of interaction between AMD-11070 and the CXCR4 receptor similar to that exhibited by its predecessor AMD-3100, except for an aspartic acid residue at position 97 on the receptor that interacts specifically with AMD-11070. These results may be useful for developing newer CXCR4 inhibitors (Wong, R. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-28, Los Angeles) 2007, Abst 495).

Pharmacokinetic interactions between AMD-11070 and ritonavir were evaluated in healthy male volunteers who received a single 200-mg dose of AMD-11070 on the first study day. Ritonavir treatment (100 mg b.i.d.) was given from day 3 to day 18. Additional simultaneous doses of AMD-11070 on days 3 and 17 were given. Treatment was generally well tolerated with all reported adverse events being grade 2 or less. At steady state, concomitant ritonavir treatment increased AMD-11070 Cmax by 47%, AUC0-48 by 48% and elimination half-life by 16%, while decreasing tmax by 29% and apparent oral clearance by 38% (Cao, Y.-J. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-28, Los Angeles) 2007, Abst 570).

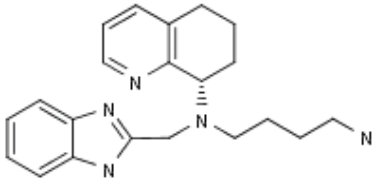
Previous *in vitro* experience revealed that AMD-1170 was a moderate inhibitor of cytochrome P450 (CYP) 2D6 and a time-dependent inhibitor of CYP3A4. Therefore, the potential for pharmacokinetic interactions was evaluated in healthy volunteers who received CYP3A4 and CYP2D6 substrates, namely midazolam and dextromethorphan, in the presence and absence of AMD-1170. The mean AUC0-24 and Cmax of dextromethorphan were elevated by 265% and 262%, respectively, by concomitant AMD-1170 treatment. AMD-1170 increased mean AUC0-24 for midazolam by 32%, with no apparent effect on other pharmacokinetic parameters (Nyunt, M. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-28, Los Angeles) 2007, Abst 569).

Further pharmacokinetic evaluation was conducted in a single-arm, open-label, dose-escalating study in HIV-infected patients carrying X4-tropic virus who received AMD-11070 at doses of 100 mg b.i.d. or 200 mg b.i.d. for 10 days. Good oral absorption with accumulation following AMD-11070 repeated administration was observed. Dose doubling induced a 3.6- and 4.8-fold increase in Cmax and AUC0-12, respectively. Plasma steady-state AMD-11070 concentrations were not achieved after 10 days of twice-daily administration in all patients. At the 200 mg dose, AMD-11070 plasma concentrations exceed the *in vitro* IC90 value for protein binding, indicating that it may be associated with antiviral activity. These results suggest that AMD-11070 pharmacokinetic parameters are similar in HIV-infected patients and healthy subjects (Boffito, M. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-28, Los Angeles) 2007, Abst 571).

A phase Ib/IIa open-label, dose-escalating, proof-of-concept study was conducted in patients with more than 5000 copies/ml of plasma HIV RNA who had been off antiretroviral therapy for at least 14 days at study entry. AMD-11070 at 200 mg b.i.d. for 10 days was well tolerated and caused reductions of 1log10 relative luminiscence units (rlu) or more in X4-tropic virus in 3 of 6 subjects (Saag, M. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-Feb 28, Los Angeles) 2007, Abst 512). AMD-11070 was

*(**Biotech News**, cont. from page 14)*

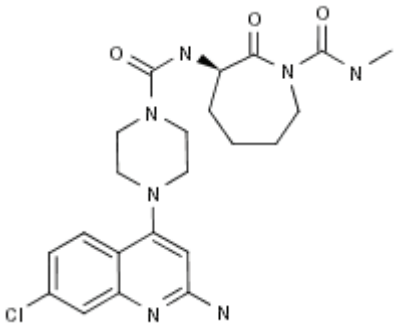
further evaluated in the X4 Antagonist Concept Trial (XACT), a multicenter, dose-finding, safety and activity study in patients carrying X4-tropic virus who received AMD-11070 monotherapy at 200 mg b.i.d. for 10 days. After this treatment period, the primary endpoint, namely an X4 rlu reduction of 1log10 or more was met by 4 of 9 patients. Responders achieved a median 1.5log10 reduction in X4 rlu. No significant changes in CD4, lymphocyte counts or HIV viral load were observed. AMD-11070 was well tolerated with no serious drug-related adverse events reported. No hepatotoxicity or clinically significant abnormal laboratory values were noted (Moyle, G. et al. 14th Conf Retroviruses Opportunistic Infect (CROI) (Feb 25-28, Los Angeles) 2007, Abst 511). AMD-11070 has been identified in the patent literature (WO 2005090308, WO 2003055876 and WO 2004106493).



[April 04, 2007] Berlex reports on novel CCR5 antagonists

Besides its role as coreceptor for the entry of HIV-1 strains into host cells, the CC chemokine receptor 5 (CCR5) has also been found in activated microglial cells and infiltrating T-cells in multiple sclerosis (MS) brain lesions. CCR5 antagonists may be useful in reducing chronic inflammation present in MS, according to researchers at Berlex Biosciences. [I] was identified as a potent CCR5 antagonist (IC50 = 22 nM) with excellent oral bioavailability in rats (73%) and dogs (91%). It showed low in vitro liver microsome metabolism across species and low inhibition of cytochrome P450 enzymes (Wei, R.G. et al. 233rd ACS Natl Meet (Mar 25-29, Chicago) 2007, Abst MEDI 66). The compound has been claimed in the patent literature (WO 2004002960).

Another compound from these quinolyl amide derivatives, [II], also exhibited antagonist activity at the CCR5 (IC50 = 42 nM) and oral bioavailability (41%) in rats (Lu, S-F. et al. 233rd ACS Natl Meet (Mar 25-29, Chicago) 2007, Abst MEDI 67). This compound has also been identified in the patent literature (WO 2004113323).



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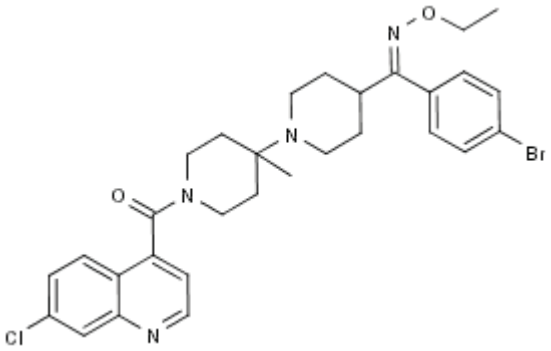
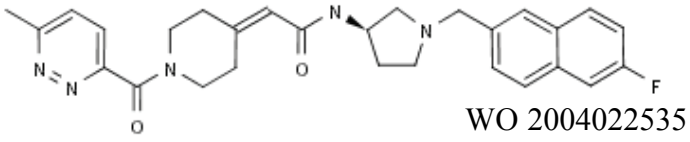


[April 18, 2007] Ccr2 protective in Alzheimer's disease. The effects of microglial accumulation in senile plaques in patients with Alzheimer's disease has been clarified in studies in mice deficient in CCR2, a chemokine receptor expressed on microglia which mediates the accumulation of mononuclear phagocytes at sites of inflammation. In research undertaken by investigators at Massachusetts General Hospital, Okayama University Medical School and Beth Israel Deaconess Medical Center, transgenic Tg2576 mice (which represent an established model of Alzheimer's disease) were generated which were deficient in CCR2. Such animals accumulated beta-amyloid earlier and died prematurely. The effect was correlated with CCR2 gene dosage. Thus, CCR2-dependent microglial accumulation promotes beta-amyloid clearance, without which mortality is increased. Agents enhancing microglial accumulation may be beneficial in Alzheimer's disease, but the research also sounds a cautionary note on the use of CCR2 antagonists for the treatment of chronic inflammatory diseases (El Khoury, J. et al. Nature Med 2007, 13(4): 432-8; Massachusetts General Hospital News Release).

*(**Biotech News**, cont. from page 15)*

[March 12, 2007] Positive preclinical results for novel dual CCR3 and histamine H1 receptor antagonist. Collaborative research between Astellas Pharma and Toray Industries has led to the development of YM-344484, a novel compound with potential utility for the treatment of allergic inflammatory diseases, such as asthma, allergic rhinitis and atopic dermatitis. In vitro, YM-344484 was found to potently block intracellular calcium elevation induced by chemokine receptor CCR3 ligands, including CCL11 (Kb = 1.8 nM), in CCR3-expressing cells. Moreover, YM-344484 inhibited histamine H1 receptor-mediated intracellular calcium increase (Kb = 47 nM) in histamine-treated PC3 cells. YM-344484 also counteracted CCL11-stimulated chemotaxis of human CCR3-expressing cells (IC50 = 6.2 nM) and inhibited eosinophil-derived neurotoxin release from human eosinophils (IC50 = 19 nM). Interestingly, the compound displayed potent and dose-dependent histamine H1 receptor antagonism in vivo when orally given to mice at 3, 10 and 30 mg/kg. In the ovalbumin-induced asthma mouse model, YM-344484 significantly prevented eosinophil infiltration by 74% and 100% at 300 and 600 mg/kg t.i.d. p.o., respectively (Suzuki, K. et al. Eur J Pharmacol 2007, Advance publication). YM-344484 has been claimed in the patent literature (WO 2004022535).



WO 2004022535

[March 15, 2007] T-cell increases seen in HIV-infected patients given recombinant interleukin-7. Recombinant interleukin-7 (rIL-7; Cytheris) was evaluated for biological effects in two dose-escalation studies in patients with HIV infection with CD4 T-cell counts > 100 cells/mcl and viral load < 50 copies/ml. In one study, 6 patients received a 3 mcg/kg dose three times a week on days 1-18. Median CD4 counts increased from 210 mcl to 405 mcl at day 21, while plasma HIV RNA values remained < 50 copies/ml. Two patients completing treatment with 10 mcg/kg had a higher increase in CD4 counts, suggesting a dose-dependent treatment effect. There were no adverse events above grade 2 (Levy, Y. et al. 14th Conf Retroviruses Opportunistic Infect [CROI] [Feb 25-28, Los Angeles] 2007, Abst 127). Patients included in the second study were randomized in double-blind fashion to single doses of rhIL-7 3, 10, 30 or 60 mcg/kg s.c. or placebo. In 16 patients, there were 2 dose-limiting toxicities at the 60 mcg/kg dose level. The most common adverse events were local reactions, LFT elevation and fatigue. Biologic activity was seen with all tested rhIL-7 doses, with a significant increase in CD4 cells. Evidence of dose-dependent effects on T-cells was noted. rhIL-7 is also being assessed in patients with a viral load < 50,000 copies/ml in this study (Sereti, I. et al. 14th Conf Retroviruses Opportunistic Infect [CROI] [Feb 25-28, Los Angeles] 2007, Abst 128; Cytheris News Release).

[March 21, 2007] Multimodal therapy with TNFerade suggested for cholangiocarcinoma. TNFerade(TM) (GenVec), a replication-deficient adenoviral vector containing the human tumor necrosis factor-alpha (TNF-alpha) gene, was evaluated in combination with bevacizumab (Avastin(R); (Genentech, Roche) in cell cultures and in a murine model of cholangiocarcinoma. Incubation of KMC and OZ cholangiocarcinoma cells with TNFerade(TM) alone or combined with bevacizumab resulted in production of TNF-alpha, followed by cytotoxicity upon irradiation. In mice bearing cholangiocarcinoma KMC or OZ xenografts, triple therapy with TNFerade(TM), bevacizumab (5 mg/kg) and irradiation produced a significantly stronger inhibition of tumor growth than monotherapy or other treatment combinations. Based on these results, this multimodal therapy could represent a potential strategy to downstage locally advanced cholangiocarcinoma (Bickenbach, K.A. et al. Ann Surg Oncol [60th Annu Cancer Symp (Mar 15-18, Washington D.C.) 2007] 2007, 14(Suppl. 2) Abst P14).

[April 04, 2007] Topical interferon alpha-2b shows clinically efficacious response in LSIL. Helix BioPharma reports positive results from its phase II study of its topical interferon alpha-2b in women with human papilloma virus (HPV)-induced, low-grade cervical lesions. A total of 41 women with cytologically confirmed HPV-induced, low-grade

*(**Biotech News**, cont. from page 16)*

cervical lesions. A total of 41 women with cytologically confirmed HPV-induced, low-grade squamous intraepithelial lesions (LSIL) of the cervix received either topical interferon alpha-2b, self-administered intravaginally 3 times per week for 6 weeks with a follow-up evaluation at 12 weeks, or no treatment over the same study period. Nearly half (46.7%) of the women in the treated per-protocol population had their abnormal Pap smears revert to normal during the 12-week period compared with only 15.8% of the untreated women, representing nearly a 3-fold improvement. Of these women, one treated patient's LSIL cytology returned following the end of treatment, uggesting that a longer dosing regimen may be advisable in future studies. Upon stratification of the patients according to the North American definition of LSIL cytology, the relative difference in the Pap response rate between the treated and untreated patient groups increased substantially. Using this approach, only those women who entered the study belonging to the Pap smear group IIID classification (the more advanced/serious Pap smear diagnosis) were evaluated. Of the women in the stratified per-protocol treatment population, 41.7% experienced normalization of their Pap IIID smear, whereas none (0.0%) of the untreated Pap IIID women experienced improvement. All other efficacy parameters evaluated showed the same tendency in favor of treatment. For example, 60% of the treated women experienced resolution of their associated abnormal cervical findings upon colposcopic diagnosis versus only 9.5% of the untreated women (Helix BioPharma News Release).

[March 28, 2007] MEDI-545 begins clinical evaluation in psoriasis. MedImmune has initiated a phase I trial with MEDI-545, its monoclonal antibody targeting interferon alpha, in patients with psoriasis. Designed to evaluate safety and tolerability, the dose-escalation trial will be conducted at three sites in North America. Patients will be dosed once and subsequently evaluated for a period of 126 days, including blood and skin analysis at regular intervals. The psoriasis trial marks a second clinical study under way with MEDI-545, which is also being evaluated in an ongoing phase I trial in patients with systemic lupus erythematosus (SLE). The single-dose study was initiated by MedImmune in April 2006 based on preclinical research conducted in collaboration with its partner Medarex. In addition to preclinical data suggesting that elevated levels of interferon alpha may be associated with lupus disease activity, preclinical study results also indicated that MEDI-545 may suppress the abnormal immune activity associated with lupus by binding to multiple interferon alpha subtypes seen in the serum of lupus patients. MedImmune also recently filed an application with the FDA for MEDI-545 to be granted orphan drug status in a third indication, idiopathic inflammatory myositis (MedImmune News Release).

[March 22, 2007] Interferon/gemcitabine-based adjuvant therapy improves survival, toxicity remains a concern. Investigators from the Washington University School of Medicine, the University of Pennsylvania Health System and the University of Pittsburgh Medical Center reported their findings in a phase II trial of adjuvant therapy with interferon alpha and gemcitabine (Lilly) after resection for pancreatic adenocarcinoma. Patients with adenocarcinoma of the pancreas who underwent resection were administered 5-FU (175 mg/m2 continuous infusion), cisplatin (25 mg/m2 weekly i.v. bolus) and IFN-alpha (3 million units s.c. 3 times/week) simultaneously with radiation for 5 weeks and were then switched to gemcitabine (1000 mg/m2 i.v. 3 weeks on/1 week off schedule for 2 cycles). Fifty patients were enrolled in this study, of whom two were lost to follow-up (median follow-up was 32 months) and sixteen (25%) failed to complete adjuvant therapy due to disease progression or toxicity; the dose was reduced for 72% of patients who stayed on study. Median overall survival was 26 months and actuarial overall survival for the first, second and forth year periods were 73%, 53% and 44%, respectively, indicating that interferon-alpha/gemcitabine-based chemotherapy improves survival when compared to standard GITSG 5-FU-based therapy and is comparable to the novel protocol of interferon-alpha/5-FU-based therapy; however, toxicity still remains a major concern (Tan, M. et al. Ann Surg Oncol [60th Annu Cancer Symp (Mar 15-18, Washington D.C.) 2007] 2007, 14(Suppl. 2): Abst 2).

[March 08, 2007] Interleukin-12 gene therapy safe

*(**Biotech News**, cont. from page 17)*

in phase I ovarian cancer study. In a phase I study, Expression Genetic's interleukin-12 (IL-12) therapeutic, **EGEN-001**, consisting of an IL-12 gene plasmid formulated with a lipopolymeric gene carrier (TheraPlas[TM], polyethylene glycol-polyethyleneimine-cholesterol), was administered in doses of 0.6, 3, 12 and 24 mg/m2 i.p. in 4 weekly infusions to patients with chemotherapy-resistant, advanced, recurrent ovarian cancer. Plasmid delivery after therapy administration was localized at the delivery site, with IL-12 plasmid detected in peritoneal fluid while very little plasmid DNA was found in the blood. IL-12 plasmid activity was also restricted to the delivery site, with interferon gamma levels increased in peritoneal fluid but not in blood samples. There was no grade 3 or 4 toxicity. Adverse events included abdominal cramping, nausea and mild elevation of body temperature (Alvarez, R.D. et al. 38th Annu Meet Women's Cancer [March 3-7, San Diego) 2007, Abst 114).

More Biotech briefs

Press Release
02 April 2007 - Nautilus Biotech begins Phase I clinical trial in the USA for subcutaneous Belerofon®, its long-lasting, Interferon-alpha drug.

Paris, France, 2 April 2007, Nautilus BiotechParis, France, 2 April 2007 - Nautilus Biotech has announced that it has initiated a Phase I clinical trial for subcutaneous Belerofon®, its long-lasting human Interferon (IFN) alpha. Belerofon has therapeutic potential for the treatment of a number of conditions, including chronic Hepatitis C. Following recent approval by the US Food and Drug Administration, the Phase I clinical trial is being held in Austin, Texas in the USA and involves six treatment groups of eight male and female volunteers, aged 18 to 50 years. The trial is an open-label, ascending dose study of four doses of subcutaneous (SC) Belerofon, which will be compared to SC administered IntronA® (a Schering-Plough product) and Pegasys® (pegylated Interferon alfa-2a (40KD), a Roche product).

The primary objective of the trial is to evaluate SC Belerofon in healthy adult subjects, for safety, tolerability and pharmacokinetics in comparison with IntronA and Pegasys. The second objective is to evaluate the comparative pharmacodynamics of the three products. Nautilus Biotech expects initial results from the trial to be available during Q3 2007.

Belerofon is an engineered variant of IFN-alpha. It has a single point mutation for lower sensitivity to protease-mediated degradation, unchanged molecular weight and specific antiviral activity compared to non-pegylated IFNs. Following subcutaneous administration in animals, SC Belerofon shows a longer half-life and subsequently improved exposure profile compared to native IFN-alpha and pegylated derivatives. "We are confident that Belerofon has the potential to set a new Gold Standard Interferon in the treatment and management of Hepatitis C", said Nautilus Biotech's CEO, Manuel Vega. "The start of a clinical trial for subcutaneous Belerofon is a major milestone in our move to become a leading drug development company".

"The commencement of a Phase I clinical trial for SC Belerofon represents an important development in our pipeline of novel engineered protein drugs", said Paul Martin, Nautilus Biotech's Vice President Strategy. "It demonstrates Nautilus Biotech's ability to move novel engineered proteins from design to the clinic quickly and efficiently". In addition to the injectable Belerofon evaluated in this clinical study, Nautilus Biotech has formulated lyophilized Belerofon together with inactive ingredients to produce enteric-coated tablets for oral administration and filed an IND for oral Belerofon in February 2007. All currently marketed Interferon alpha drugs are administered by injection.

About Hepatitis C
Hepatitis C (HCV) is the most prevalent liver disease in the world. HCV infection causes chronic inflammation in the liver that can lead to cirrhosis, liver failure, liver cancer or death. HCV infection represents a significant medical challenge worldwide. Currently, there is no vaccine that can prevent hepatitis C.

*(**Biotech News**, cont. from page 18)*

According to the World Health Organization, more than 170 million people worldwide suffer from chronic HVC. With only half of all HCV patients benefiting from current therapy, there is considerable market potential for new medical solutions. The HCV market is expected to grow from $2.2 billion in 2005 to $4.4 billion in 2010 and $8.8 billion in 2015 due to improved market penetration and better diagnosis rates (source: *Datamonitor*).

About Nautilus Biotech
Nautilus Biotech is a drug discovery and development company with a pipeline of next-generation therapeutic proteins with superior pharmacological profiles that address unmet clinical needs. The company's protein engineering technology can significantly improve the pharmacological characteristics of important blockbuster protein drugs, offering improvements in drug stability and administration. The company is also creating proprietary 'third generation' therapeutic proteins which are, per se, suitable for oral administration. The therapeutic proteins market is currently valued at over $35bn, and growing at a rate of 10-15% per annum. Nautilus Biotech has created a portfolio of next-generation therapeutic proteins with improved profiles, including long-lasting Interferon alpha (Belerofon), hGH (Vitatropin®), Interferon beta, Erythropoietin, Interferon gamma, Clotting Factor IX (in collaboration with Wyeth Pharmaceuticals) and HMGB1 (in collaboration with Creabilis Therapeutics). Nautilus Biotech has established a strong intellectual property position covering enhanced versions of these multibillion dollars molecules and is rapidly moving these products into clinical development. Nautilus Biotech is a private company with headquarters in Genopole® biopark, (Evry, France). For more information about Nautilus Biotech visit http://www.nautilusbiotech.com

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Email: mvega@nautilusbiotech.com

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Introduction to Glycolysis is an interactive textbook supplement that will help you learn human biochemistry.

Cyberbotanica, a virtual chapter in medicinal botany, describes various botanical compounds used in cancer treatment and the plants that produce them.

In Science Resources, you'll find annotated lists of biomedical Web sites for scientists, educators and students alike.

Our Professional Resources section will point you to jobs, funding, grad schools, biotechnology regulations, and more.

Bioinformatics will introduce you to this fascinating hybrid of computer science and biology and will lead you to the best bioinformatics sites on the Web.

Also be sure to check out BioMedLink, a mega-database of biomedical sites we developed for BioMedNet.

If this is your first BioTech visit, try the Guided Tour

WWW (continued)

Cancer Immunome Database

http://www.licr.org/D_programs/d4_immunology.php

Note that you must register before having access to this database. The reality of the human immune response to cancer is now beyond question. The accumulated experimental evidence is overwhelming, documenting both humoral and cellular responses to an increasing number of specific antigens. Because the amount of available information is increasing at such a dizzying rate, it is clear that a well-organized and professionally curated repository has become indispensable for scientists in the field.
The Academy of Cancer Immunology, with support from the Ludwig Institute for Cancer Research (LICR), has taken up the task to setup a database that will present through a single point of access information about all of the gene products against which an immune response has been documented in cancer patients. This project is a continuation, in a more comprehensive and organized form, of the SEREX database maintained by the LICR since the fall of 1997. It will be linked to the online Journal of the Academy, Cancer Immunity, as well as to continuing efforts to characterize in more detail the antigens discovered by the SEREX program. The project has also received support from the European Union, through the funding of the European Cancer Immunome Program (EUCIP). The aim of EUCIP, which extended from 2000 to 2004, was to provide new insights into cancer-associated alterations by analyzing a panel of genes and gene products identified based on their immunogenicity in cancer patients. The microarray and epigenetic data collected within the framework of the EUCIP have been deposited in this database. Recommended by Kevin Ahearn in Genetic Engineering News

Clinical Proteomics Map

http://www.cprmap.com/clinical-proteomics/

CPRMap provides latest information on clinical proteomics and brings together scientists and clinicians to investigate the potential uses of proteomic discoveries from the bench to the bedside. Recommended by Kevin Ahearn in Genetic Engineering News

European Hepatitis C Virus Database

http://euhcvdb.ibcp.fr/euHCVdb/

The development of the European Hepatitis C Virus database (euHCVdb) started in 1999 as the French HCV Database (HCVDB, Combet et al.,2004). The euHCVdb is mainly oriented towards protein sequence, structure and function analyses and structural biology of HCV (Penin et al., 2004). In order to make the existing HCV databases as complementary as possible, the current developments are coordinated with the other databases (Japan and Los Alamos) as part of an international collaborative effort (Kuiken et al., 2006).

It is monthly updated from the EMBL Nucleotide sequence database and maintained in a relational database management system (PostgreSQL). Programs for parsing the EMBL database flat files, annotating HCV entries, filling up and querying the database used SQL and Java programming languages. Great efforts have been made to develop a fully automatic annotation procedure thanks to a reference set of HCV complete annotated well-characterized genomes of various genotypes.

This automatic procedure ensures standardization of nomenclature for all entries and provides genomic regions/proteins present in the entry, bibliographic reference, genotype, interesting sites (e.g. HVR1) or domains (e.g. NS3 helicase), source of the sequence (e.g. isolate) and structural data that are available as protein 3D models.

ExPASy Life Science Directory

http://www.expasy.ch/links.html

A comprehensive list of links for all aspects of biomedical research.

Gene Seeker

http://www.cmbi.ru.nl/GeneSeeker//

With the GeneSeeker you can search in different databases simultaneously, given a known human genetic location and expression/phenotypic pattern.

The GeneSeeker returns any found gene names wich are located on the specified location and expressed in the specified tissue. To search for more expression location in one search, just enter them in the textbox for the expression location and separate them with logical operators (and, or, not). You can specify as many tissues as you want, the program starts 20 queries simultaneously, and then waits for a query to finish before starting another query, to keep server loads to a minimum.

You can also search only for expression, just leave the cytogenetic location fields blank, and do the query. If you only want to look for one cytogenetic location, only fill in the first location field, and the GeneSeeker will search with only this one. Housekeeping genes, found in Swissprot can be excluded, or genes that are to be excluded can be specified. Human chromosome localizations are translated with an oxford-grid to mouse chromosome localizations, and then submitted to the Mgd.

Human Protein Atlas

http://www.proteinatlas.org/

The human protein atlas displays expression and localization of proteins in a large variety of normal human tissues and cancer cells. The data is publically available and presented as high resolution images of immunohistochemically stained tissues and cell lines. Available proteins can be reached through searches for specific genes or by browsing individual chromosomes. The human protein atlas is periodically upgraded and new data is added to the database annually.

Mouse Genome Informatics

http://www.informatics.jax.org/

Mouse Genome Informatics (MGI) provides integrated access to data on the genetics, genomics, and biology of the laboratory mouse.

Natural Antisense Transcripts Database

http://natsdb.cbi.pku.edu.cn/

Natural Antisense Transcripts (NATs) are RNAs that partially complementary to other endogenous RNAs. They might be transcribed in cis from opposing DNA strands at the same genomic locus or in trans at separate loci. NATs have already been found to function at several levels of eukaryotic gene regulation including translational regulation, alternative splicing, RNA stability, trafficking, genomic imprinting, and X-inactivation. Changes in antisense transcription have been implicated in pathogenesis such as cancer or neurological disease.

- Browse cis-NATs according to the species, overlapping pattern, overlapping length, coding potential and chromosome location
- Search cis-NATs according to the species, gene name, accession number, description, chromosomal location and sequence
- Download representative cis-NATs and some related annotation information

Updates: Isoforms predicted by SVAP (Splicing Variant Analysis Platform) have been added into NatsDB as a supporting track. An example is Xist/Tsix genomic locus of Mouse. Users interested in alternative splicing could search isoforms using search modules of NatsDB.

- Yong Zhang, XS Liu, Qing-Rong Liu and Liping Wei. Genome-wide in silico identification and analysis of cis-natural antisense transcripts (cis-NATs) in ten species. Nucleic Acids Res., 34: 3465-3475, 2006.
- Yong Zhang, Jiong-Tang Li, Lei Kong, Ge Gao, Qing-Rong Liu and Liping Wei. NATsDB: Natural Antisense Transcripts DataBase. Nucleic Acids Res., 35: D156-165, 2007.

NCI-Nature Pathway Interaction Database

http://pid.nci.nih.gov

Over the past year and a half a number of scientists have helped us with the curation of pathways that populate the Pathway Interaction Database (PID). The database is now open to the public and lets you explore signalling pathways in human cells, either asking simple questions about your favourite signaling molecule or more complex questions involving

numerous molecules and pathways.

In addition to the database, the NCI-Nature PID website presents commissioned articles on noteworthy topics in bioinformatics. These 'Bioinformatics Primers' are written about similar online resources and highlight the many uses of the online tools they describe. The NCI-Nature PID website also contains a 'Research Highlights' section that lists key review articles in the cell signalling field.

Please sign up for the email updates so we can inform you about recently added pathways and other new content. Please also provide any feedback on the site. This will enable us to make it that much more useful to the cell signalling community. Finally, a heartfelt thank you from the NCI-Nature Pathway Interaction Database team for your continued support.

With best regards,
Kira Anthony
Database Editor, Web Publishing
Nature Publishing Group
Email: k.anthony@boston.nature.com
URL: http://pid.nci.nih.gov

SuperHapten

http://bioinformatics.charite.de/superhapten

An Immunogenic Compound Database: The immune system protects organisms from foreign proteins, peptide epitopes and a multitude of chemical compounds. Among these, haptens are small molecules, eliciting an immune response when conjugated with carrier molecules. Known haptens are xenobiotics or natural compounds, which can induce a number of autoimmune diseases like contact dermatitis or asthma. Furthermore, haptens are utilized in the development of biosensors, immunomodulators and new vaccines. Although hapten-induced allergies account for 6-10% of all adverse drug effects, the understanding of the correlation between structural and haptenic properties is rather fragmentary. We have developed a manually curated hapten-database, SuperHapten, integrating information from literature and web resources. The current version of the database compiles 2D/3D structures, physico-chemical properties and references for about 7500 haptens and 25,000 synonyms. The commercial availability is documented for about 6300 haptens and 450 related antibodies, enabling experimental approaches on cross-reactivity. The haptens are classified regarding their origin: pesticides, herbicides, insecticides, drugs, natural compounds, etc. Queries allow identification of haptens and associated antibodies according to functional class, carrier protein, chemical scaffold, composition or structural similarity.

This database contains currently 7257 haptens, 453 commercially available related antibodies and 24 carriers

Guenther S., Hempel D., Dunkel M., Rother K., Preissner R.: SuperHapten: a comprehensive database for small immunogenic compounds. Nucleic Acids Research 35: D906-910, 2007.

The Science Show

http://www.abc.net.au/rn/scienceshow/

The Science Show with Robyn Williams on Radio National is one of the longest running programs on Australian radio. Scientific issues, debates, events, personalities, exposing scientific fraud, discoveries and broadcasting pranks have been the hallmarks of the Science Show.

The unique content of the Science Show has given Australians fascinating insights into all manner of things from the physics of cricket to prime ministerial biorhythms. According to Robyn Williams, the Science Show has consistently achieved what it originally set out to do in 1975: 'To produce a science program about ideas, not simply facts or bits of boffinry'.

Recommended by Kevin Ahern in Genetic Engineering News

Reviews of Interest

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A TEST

At the end of this message, you are asked a question.

Answer it immediately. Don't stop and think about it.

Just say the first thing that pops into your mind.

This is a fun "test"... AND kind of spooky at the same time! You'll understand what that means after you finish taking the "test."

Now - just follow the instructions as quickly as possible.

Do not go to the next calculation before you have finished the previous one.

You do not ever need to write or remember the answers, just do it using your mind.

You'll be surprised.

Start:
How much is:

15 + 6

3 + 56

89 + 2

12 + 53

75 + 26

25 + 52

63 + 32

I know! Calculations are hard work, but it's! nearly over..

Come on, one more! ...

123 + 5

QUICK! THINK ABOUT A COLOR AND A TOOL!

(NOW GO TO THE BOTTOM OF PAGE 25)

American Association of Immunology Guest Symposia

International Society for Interferon and Cytokine Research (ISICR) Symposium

Cytokine Mediated Signal Transduction in Innate Immunity
Saturday, May 19 at 2:45 PM, Miami Beach Convention Center, Room B210/211

Chair: **Xiaoxia Li**, Cleveland Clinic Research Foundation

Speakers
Sarah L. Gaffen, SUNY at Buffalo, *Structure-function relationships in the IL-17 receptor*

Xiaoxia Li, Cleveland Clinic Research Foundation, *The essential role of Act1 in IL-17 signal transduction*

Thomas A. Hamilton, Cleveland Clinic Research Foundation, *IL-17 promotes chemokine expression through stabilization of mRNA*

Michael David, Univ. of California San Diego, *A novel anti-viral mechanism of IFNs*

Society for Leukocyte Biology (SLB) Symposium

Type I Interferon and Chronic Infection: Good, Bad or Both?
Tuesday, May 22 at 8:00 a.m., Miami Beach Convention Center - Room B118/119

Chair: **Luis J. Montaner**, Wistar Institute

Speakers
Christine A. Biron, Brown University, *Regulating the biological effects of type I interferons*

Jean-Philippe Herbeuval, Université Paris V, Hôpital Necker, *HIV immunopathogenesis: when good IFN turns bad!*

Stephen J. Polyak, University of Washington, *Interferons and hepatitis C virus*

Luis J. Montaner, Wistar Institute, *Anti-HIV-1 effects of type I interferons: glass half-full or half-empty?*

A TEST

(continued from page 24)

You just thought about a red hammer, didn't you?

If this is not your answer, you are among 2% of people who have a different, if not "unique", mind.

98% of the folks would answer a red hammer while doing this exercise.

THE INTERFERON ANNIVERSARY MEETING

September 16-19 2007

The Annual ISICR Meeting will take place in 2007 in the historic city of **Oxford, UK.** This will be a special occasion for the Society as it will mark the 50th anniversary of the discovery of interferon by Alick Isaacs and Jean Lindenmann.

The **Interferon Anniversary Meeting** will take place from **16th - 19th September 2007.** There will also be a one day History of Interferon pre-meeting on 15th September 2007, for which separate registration will be required.

The scientific sessions of **The Interferon Anniversary Meeting** will be held in the prestigious Oxford University Examination Schools. A wide range of posters and commercial exhibits will also be on display throughout the meeting.

The meeting will provide opportunities to celebrate the discovery of interferon, to review the many important scientific developments founded on interferon research, together with successful clinical applications of interferons, and to catch up with all the latest developments in the field. Several distinguished interferon researchers, leading scientists and clinicians from all over the world have agreed to participate in this event.

Deadline Dates

May 18 - Abstract Submission
September 6 - Registration Deadline

Local Organizing Committee

Graham Foster (Chairman)
Derek Burke
Mike Clemens
Norman Finter
Linda Hibbert
Giovanna Lombardi
Tony Meager

PRELIMINARY PROGRAMME
(may be subject to change)

"History of Interferons"

SATURDAY
15 September (separate registration is required for this one day pre-meeting)

"The Interferon Anniversary Meeting"

SUNDAY 18.00-18.20 Welcome address - The President
16 September 18.20 -19.30 Prizes and awards
History of Interferons
(Chair: John Skehel)
19.30-19.50 Jean Lindenmann
19.50-20.30 Charles Weissmann

MONDAY 08.30 - 10.30 **Plenary Session: Interferon Induction**
17 September Chair: John Hiscott
Speaker: Michael Gale
10.30 - 11.00 **Coffee Break**
11.00 - 13.00 **Break-out sessions:**
Receptor interaction
Chair: Sidney Pestka
Speaker: Giles Uze
Apoptosis
Chair: Mike Clemens
Speaker: Harald Wajant
13.00 - 14.30 **LUNCH & POSTERS**
14.30 - 16.30 **Break-out Sessions:**
Non-classical effects of interferons
Chairs: Giovanna Lombardi/Richard Flavell
Speaker: To be announced
Interferon inducible genes
Chair: Linda Hibbert
Speaker: Ganes Sen
16.30 - 17.00 **Tea Break**
17.00 - 19.00 **Plenary Session: Signalling**
Chair: George Stark
Speakers: George Stark
Uwe Vinkemeier

TUESDAY 08.30 - 10.30 **Plenary Session: Interferon Induction**
18 September and Immune Response
Chairs: Caetano Reis e Sousa
Giovanna Lombardi
Speaker: David Tough
10.30 - 11.00 **Coffee break**
11.00 - 13.00 **Break-out sessions:**
Novel Interferons and New Developments
Chair: Sandra Pellegrini
Speaker: Phil Patten
Cancer
Chair: John Kirkwood
Speaker: Ernie Borden
13.00 - 14.30 **LUNCH**
14.30 - 16.30 **Break-out Sessions:**
Interferon and Autoimmunity
Chair: Tony Meager
Speaker: Christine Biron
Inhibitors of interferons
Chair: Paul Hertzog
Speakers: Paul Hertzog
Antonio Alcami
16.30 - 17.00 **Tea break**
17.00 - 19.00 **Plenary Session: Clinical roles of Interferons - antiviral and MS**
Chair: Stefan Zeuzem
Speakers: Stefan Zeuzem
Richard Ransohoff

WEDNESDAY 08.30 - 10.30 **Plenary Session: Antiviral effects of**
19 September the interferons
Chair: Otto Haller
Speakers: Bob Silverman
To be announced
10.30 - 11.00 **Tea Break**
11.00 - 13.00 **Plenary Session: Life, Death and Growth Control**
Chair: Adi Kimchi
Speakers: Adi Kimchi
Jim Darnell
CLOSE OF CONFERENCE

Top Ten Things to Do (other than studying) in Oxford

By Thomas Tan

OK, we know you don't need us to convince you to attend this year's ISICR Annual Meeting in Oxford, the flagship of one of the world's greatest academic institutions, as we celebrate the 50th anniversary of the discovery of interferon by Alick Isaacs and Jean Lindenmann. In addition to the generations of great scholars and writers it has produced, Oxford is also known for its picture-perfect college courtyards, riverside walks, and timeworn honey-colored stone buildings set around ivy-clad quadrangles. Blah, blah, blah… But we feel obligated anyway to at least attempt to help you plan ahead and feed your intellectual and cultural curiosity. So, here are some suggestions for must-dos while you're in the city dubbed as the "City of Dreaming Spires".

1. Sure, the Ashmolean Museum is Britain's oldest museum and a must-see and there are numerous great colleges to check out (frankly, aren't you sick of colleges by now?), but you may want to bring your kids (or the kid in you who still refuses to grow up) to check out the **Christ Church**, where some Harry Potter scenes were filmed and where Albert Einstein studied. The Christ Church Picture Gallery has over 2,000 drawings and old masters tucked away underground.

Christ Church Picture Gallery

Four Musical Angels (about 1340) Bernardo Daddi

2. Yes, if you must go Shakespearean on us, catch a performance in the Oxford Playhouse (www.oxfordplayhouse.com).

We would rather hang out at the **Bullingdon Comedy Club** or **Jongleurs** (www.jongleurs.com).

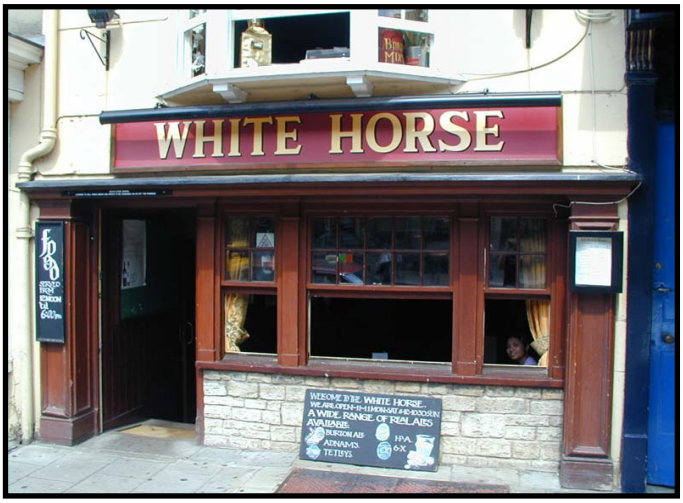
3. Need to get some fresh air, especially after sitting through long hours of oral presentations? Rent a bike to pedal out to the birthplace of Sir Winston Churchill, **Blenheim Palace** (www.blenheimpalace.com), along a pleasant, scenic route and only about 8 miles away.

Top off this with a round of golf at **Hinksey Heights** (www.oxford-golf.co.uk)-famed for its views of the Oxford skyline.

4. Go punting: What could be more romantic, more scholarly, more Oxford than boating on the **Thames**? Warning: People have been known to fall in.

5. Take afternoon tea in the **Randolph Hotel**. English style.

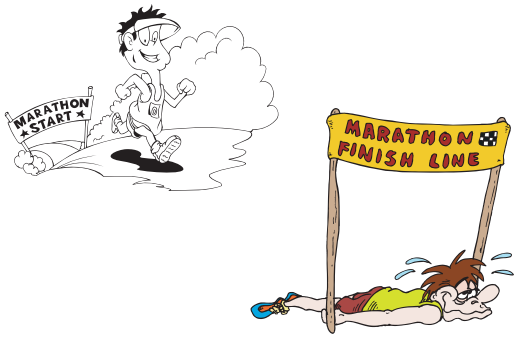
6. Have lunch at the **White Horse**, a 600 year old country pub. Forget about watching your carb intake, order fish and chips with a Deuchars IPA (at 5.8% ABV)



7. Looking for last minute shopping for souvenirs? **The Covered Market** (www.oxfordcity.co.uk/shops/market) may be your best bet.

8. If you are feeling energetic, climb the 99 steps of the 14th century **Carfax Tower** to get an excellent bird's eye view of the city.

9. Looking for something more challenging or need some real cardio workout? Sign up to race in the **New Forest Marathon** scheduled for Sept 16 (www.nfma.org.uk), and help raise funds for charities by doing so. Then wear your finisher medal proudly during the entire ISICR meeting.



10. Take a trip to Wiltshire to see the **Stonehenge** (www.stonehenge.co.uk). Some speculate the Stonehenge was built for astronomy, while others believe it was for human sacrifice. Bring along your least productive graduate student and emphasize the latter.

Cytokines 2008

Oct. 12-16, 2008

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International Society for Interferon and Cytokine Research & the
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The future of our society depends upon members maintaining an active membership status. Don't let us down, RENEW TODAY at www.isicr.org.

Access to the latest newsletter and the slide repository will be blocked if memberships are not renewed and you will not be eligible for ISICR awards. Remember 3 year regular memberships are available and Postdoctoral fellows can join/renew for only $10/year.

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