

# 1997 ISICR MEETING

**OCT. 19-24, Sheraton Harbor Island, SAN DIEGO, CA**

## **1997 Milstein Award Winners**

James Darnell

George Stark,

sharing with Ian Kerr\*

\*Please note that Dr. Kerr was a previous Milstein Award winner for his contributions to the discovery of 2'5'A- synthetase

## **1997 Honorary Members**

Ion Gresser

Gerhard Bodo

1997 Young Investigator Awards

Michael Gale, Jr.

Univ. of Washington

Seattle, WA

Suzanne Kadereit

Cleveland Clinic Foundation

Cleveland, OH

Gero Waschutza

Fraunhof Inst. Toxikol/

Aero Res

Hannover, Germany

## **PRELIMINARY PROGRAM**

(subject to change)

**Sunday, October 19, 1997**

2:00 - 6:30 pm Registration

2:00 - 5:30 pm ISICR Committee Meetings

5:30 - 7:00 pm Opening Lectures and Awards

7:00 - 9:00 pm Get- Together Reception

**Monday, October 20, 1997**

8:00 - 11:30 am **Plenary Session 1**

Interferon and Cytokine Actions - Interferon Inducible Genes and Signals  
Transduction

Chairpersons: Dr. Nancy C. Reich

Dr. Ian M. Kerr

Selected Abstracts and Presenters:

8:00 - 8:19 am Robert H. Silverman

INTERFERON ACTION AND APOPTOSIS ARE DEFECTIVE IN MICE DEVOID OF 2', 5' -  
OLIGOADENYLATE DEPENDENT RNASE L

8:19 - 8:38 am Andrew Larner

A ROLE FOR B- RAF IN ALPHA INTERFERON SIGNALING

8:38 - 8:57 am Lawrence M. Pfeffer

STAT3 AS AN ADAPTER TO COUPLE PHOSPHATIDYLINOSITOL- 3 KINASE TO THE IFNAR1 CHAIN OF  
THE TYPE 1 IFN RECEPTOR

8:57 - 9:16 am Igna Strehlow

AMINO AND CARBOXY TERMINAL DOMAINS CRITICALLY REGULATE STAT5 ACTIVITY

9:16 - 9:35 am Aseem Kumar

DEFECTIVE TNF - **[[alpha]]** - INDUCED APOPTOSIS IN STAT1- NULL HT1080 CELLS DUE TO LOW  
CONSTITUTIVE EXPRESSION OF ICE- FAMILY PROTEASES

9:35 - 9:55 am Coffee Break

9:55 - 10:14 am Brian Weaver

INTERFERON REGULATORY FACTOR 3 IS A SUBUNIT OF THE dsRNA ACTIVATED FACTOR, DRAF1

10:14 - 10:33 am Lucienne V. Ronco

THE HPV- 16 E6 ONCOPROTEIN BINDS TO

INTERFERON REGULATORY FACTOR - 3 AND INHIBITS ITS TRANSCRIPTIONAL ACTIVITY

10:33 - 10:52 am Paula M. Pitha

CRITICAL ROLE OF KAPOSI SARCOMA VIRUS (HHV- 8)- ENCODED IRFs IN VIRUS REPLICATION AND PATHOGENICITY

10:52 - 11:11 am Amitabha Deb

INTERACTION OF INTERFERON INDUCED

PROTEIN KINASE PKR WITH STAT3: A NEW LINK FOR PKR TO DIFFERENT SIGNALING PATHWAYS?

11:11 - 11:30 am

YOUNG INVESTIGATOR AWARDEE

Michael Gale, Jr.

REGULATION OF THE INTERFERON - INDUCED

PROTEIN KINASE, PKR: MODULATION OF P58ipk INHIBITORY FUNCTION BY A NOVEL Hsp90 - RELATED PROTEIN, P52ripk

1:00 - 3:30 pm **Workshop 1**

Interferon Inducible Genes

Chairperson: Dr. Charles Samuel

1:00 - 3:30 pm **Symposium 1**

Interferon, Side Effects

Chairperson: Dr. Jeremiah Tilles

3:30 - 6:30 pm **Poster Session 1**

**Tuesday, October 21, 1997**

8:00 - 11:30 am **Plenary Session 2**

Interferon Gene Regulation Including Interferon Receptors

Chairpersons : Dr. Keiko Ozato

Dr. Menachem Rubinstein

Selected Abstracts and Presenters:

8:00 - 8:30 am Menachem Rubinstein

A STAT3 SIGNALLING PATHWAY CONTRIBUTES TO THE IFN- INDUCED ANTIVIRAL STATE

8:30 - 9:00 am Rongtuan Lin

VIRUS DEPENDENT PHOSPHORYLATION AND DEGRADATION OF THE IRF- 3 TRANSCRIPTION FACTOR

9:00 - 9:30 am Lucia Gabriele

APOPTOSIS OF MYELOID CELLS IS REGULATED BY IRF FAMILY MEMBERS

9:30 - 10:00 am Coffee Break

10:00 - 10:30 am Keiko Ozato REGULATION OF THE INTERFERON AND IL- 12 GENES

10:30 - 11:00 am Eleanor N. Fish

DEFINITION OF THE MINIMUM RECEPTOR REGIONS FOR IFN- **[[alpha]]**- INDUCIBLE JAK- STAT ACTIVATION AND AN ANTIVIRAL RESPONSE

11:00 - 11:30 am Paul Hertzog

GENETIC ANALYSIS OF THE FUNCTION OF INTERFERON RECEPTOR COMPONENTS IN IFNAR1 AND IFNAR2 KNOCKOUT MICE

1:00 - 3:30 pm **Workshop 2**

Interferon Gene Regulation

Chairpersons: Dr. John Hiscott

Dr. Raymond Kaempfer

1:00 - 3:30 pm **Symposium 2**

Interferon and Multiple Sclerosis

Chairperson: Dr. Michel Revel

3:30 - 6:30 pm Poster Session 2

**Wednesday, October 22, 1997**

8:00 - 11:30 am **Plenary Session 3**

Interferons and the Immune System

Chairpersons: Dr. Christine Czarniecki

Dr. Howard A. Young

Selected Abstracts and Presenters

8:00 - 8:20 am Vincent Vieillard

ENHANCEMENT OF HIV- SPECIFIC CTL ACTIVITIES BY IFN-  $[[\text{Beta}]]$ - TRANSDUCED CD8+ T LYMPHOCYTES DERIVED FROM HIV- INFECTED INDIVIDUALS

8:20 - 8:40 am

Patricia Fitzgerald- Bocarsly

IL- 10 IS PRODUCED IN RESPONSE TO VIRAL STIMULUS AND IS RECIPROCALLY REGULATED BY IFN-  $[[\text{alpha}]]$

8:40 - 9:00 am Sandra Gessani

BIOLOGICAL RESPONSE OF MOUSE PERITONEAL MACROPHAGES TO IL- 12: EXPRESSION OF IL- 12 RECEPTORS AND PRODUCTION OF IFN-  $[[\text{gamma}]]$

9:00 - 9:20 am Yulong Han

TNF-  $[[\text{alpha}]]$  SIGNALS TO THE IFN-  $[[\text{gamma}]]$  RECEPTOR COMPLEX TO INCREASE STAT- 1a ACTIVATION

9:20 - 9:40 am Ilkka Julkunen

INDUCTION OF IFN-  $[[\text{gamma}]]$  SYNTHESIS IN T CELLS BY IFN-  $[[\text{alpha}]]/[[\text{beta}]]$  AND IL- 18 PRODUCED BY INFLUENZA A VIRUS- INFECTED MACROPHAGES

9:40 - 10:00 am Manfred W. Beilharz

LOW DOSE ORAL TYPE 1 INTERFERONS REDUCE EARLY VIRUS REPLICATION OF MURINE CYTOMEGALOVIRUS IN VIVO

10:00 - 10:20 am Coffee Break

10:20 - 10:40 am

YOUNG INVESTIGATOR AWARDEE

Suzanne Kadereit

DEFECTS IN THE REGULATION OF CONTACT HYPERSENSITIVITY IN PKR DELETED MICE

10:40 - 11:00 am

YOUNG INVESTIGATOR AWARDEE

Gero Waschutza

SYNTHESIS AND PURIFICATION OF SOLUBLE CYTOSOLIC RECOMBINANT HUMAN INTERFERON-  
[[gamma]] from *E. coli* JM 105

11:00 - 11:30 am Robert M. Friedman

**Outgoing Presidential Message**

REVERSION by TRANSFORMING ONCOGENE DELETION FOLLOWING INTERFERON [[Beta]] and  
RETINOIC ACID TREATMENT

1:00 - 1:30 pm **Workshop 3**

Cytokine Interactions

Chairperson: Dr. Jan Vilcek

1:00 - 1:30 pm **Symposium 3**

Interferon and Hepatitis

Chairperson: Dr. Myron J. Tong

3:30 - 5:30 pm **Poster Session 3**

6:30 - 9:00 pm Banquet **at the Sheraton (Note: Change from previous plans)**

**Thursday, October 23, 1997**

8:00 - 11:30 am **Plenary Session 4**

Interferons and Cancer

Chairpersons: Dr. Filippo Belardelli

Dr. Susan E. Krown

Selected Abstracts and Presenters

8:00 - 8:30 am Opening from Chairs

8:30 - 8:50 am Xin- Yuan Fu

FUNCTIONS OF THE PTK- STAT PATHWAY IN CELL CYCLE CONTROL, APOPTOSIS AND HUMAN DISEASES

8:50 - 9:10 am Alan S. Lau

MECHANISMS OF TNF- INDUCED, PKR-

MEDIATED APOPTOSIS: A ROLE FOR TUMOR SUPPRESSOR GENE p53

9:10 - 9:30 am To Be Announced

9:30 - 9:50 am Filippo Belardelli

LOCAL AND SYSTEMIC ANTITUMOR RESPONSE AFTER COMBINED THERAPY OF MOUSE METASTATIC TUMORS WITH TUMOR CELLS EXPRESSING IFN-  $[[\alpha]]$  AND HSV- TK

9:50 - 10:20 am Coffee Break

10:20 - 10:40 am Stephen J. Ralph

DEFICIENCY OF INTERFERON REGULATED

TRANSCRIPTION FACTORS, ISGF3 AND IRF1 IN INTERFERON RESISTANT MELANOMA CELLS: RESTORING CELL RESPONSIVENESS BY GENE THERAPY

10:40 - 11:00 am Detlef Jakschies

REVERSIBILITY OF IFN- ALPHA RESISTANCE BY RETINOIDS IN RENAL CELL CARCINOMA IN VITRO AND IN VIVO

11:00 - 11:20 am A. Ulmer

ISOTRETINOIN PLUS INTERFERONS IN THE TREATMENT OF DISSEMINATED MELANOMA

1:00 - 3:30 pm **Workshop 4**

Interferon Receptor Interactions

Chairpersons: Dr. Oscar R. Colamonici

Dr. Bryan R.G. Williams

1:00 - 3:30 pm **Workshop 5**

Interferon Applications in Cancer and Non- Neoplastic Diseases

Chairperson: Dr. Ernest C. Borden

Dr. Luis De La Maza

1:00 - 3:30 pm **Symposium 4**

Interferon and Gene Therapy

Chairperson: Dr. Edward De Maeyer

3:30- 6:30 pm **Poster Session 4**

**Friday, October 24, 1997**

8:00 - 12:30 pm **Plenary Session 5**

Interferons: Infectious and Other Diseases

Chairpersons: Dr. Paula M. Pitha- Rowe

Dr. Gerald Sonnenfeld

Abstracts Selected and Presenters

8:00 - 8:30 am

Opening from Chairs

8:30 - 8:55 am To Be Announced

8:55 - 9:20 am Bernard Lebleu

A 2- 5A BINDING POLYPEPTIDE OF 37 kDa AS A POTENTIAL BIOCHEMICAL MARKER FOR CHRONIC FATIGUE SYNDROME

9:20 - 9:45 am Vagn Bonnevie- Nielsen

IFN-  $[[\alpha]]$  INDUCED ENZYMES IN PANCREATIC  $[[\beta]]$  AND  $[[\alpha]]$  CELLS, INFECTED WITH EMC VIRUS

9:45 - 10:10 am Otto Haller

GTP- DEPENDENT ASSOCIATION OF HUMAN MxA PROTEIN WITH THE RIBONUCLEOPROTEIN COMPLEX OF THOGOTO VIRUS

10:10 - 10:40 am Coffee Break

10:40 - 11:05 am E. Simeoni

TREATMENT OF CHRONIC HEPATITIS C WITH IFN $[[\alpha]]$ : CORRELATION BETWEEN RESPONSE TO TREATMENT AND EXPRESSION OF MX PROTEINS

11:05- 11:30 am Joan E. Durbin

INFLUENZA VIRUS TROPISM IS ALTERED IN THE ABSENCE OF INTERFERON SIGNALING

**CONCLUSION**

Member Information

International Councilors

Brazil (1998- 2000) :

Luiz Fernando Lima Reis

Italy (1998- 2000) :

Guido Antonelli

Maria R. Capobianchi

Alternates:

Elisabetta Affabris

G. Gribando

New Members

We welcome the following new members

Andrei Alexenko - Columbia, MO

Cristina Contursi - Bethesda, MD

Elizabeth Cali Cutrone - Piscataway, NJ

Yulong Han - Cleveland, OH

Deborah Hodge - Frederick, MD

Tomoaki Hoshino - Frederick, MD

Lara Izotova - Piscataway, NJ

Malin Jidenius - Stockholm, Sweden

Robert Khusainov - Boca Raton, FL

Christopher Krause - Piscataway, NJ

Witold Lawrynowicz- New Brunswick,NJ

Maite Lewerenz - Montpellier, France

Michael Milone - Newark, NJ

Ines Raineri - San Francisco, CA

Tapani Ronni - Helsinki, Finland

I- Ming Wang - Bethesda, MD

Z H Lucy Zhou - Cleveland, OH

Famous Quotes

The shortest distance between two points is always under construction

Noelie Alito

The History of Interferon: A Continuing Story

Our series on the history of interferon is meant to represent the personal reflections of those scientists involved in the earliest days of interferon research. By nature, historical accounts reflect the views of the observer, and, as such, these accounts can seldom be determined to be

totally subjective. The history of science is certainly no exception to this rule, even though we as scientists would like everything to be as objective as the science we study in our laboratories. We realize that others involved in some of the studies described may recall things

differently or place different emphases on particular findings or events, and we will consider publishing comments from the readership about the events described.

In response to our first interview with Dr. Sidney Pestka, we have received the following email from Dr. Menachem Rubinstein:

Issue 4:2 of the ISICR Newsletter included an article entitled "The History

of Interferon: An interview with Sid Pestka". In this article it was written that Dr. Pestka suggested to me to use propanol as a solvent in HPLC and that his suggestion was an important step in the purification of interferon. My work on interferon started on about Nov. 1977. At that time I was a post- doctoral fellow in the lab of Sidney Udenfriend. In June 1978 I became a Visiting Scientist in the same lab and my first paper on interferon was published in Dec. 1978. During my entire stay at Roche Institute I was working under Sidney Udenfriend and the work on interferon was a collaboration between the Udenfriend and Pestka laboratories.

While I recognize the article represents the recollections of Dr. Pestka, I wish to point out that I initiated the use of propanol for the interferon purification. I used propanol previously in my work on opioid peptides in the Udenfriend lab (e.g., Rubinstein et al., (1977), Proc. Nat'l. Acad. Sci USA 74, 3052- 3055) and thought it would be reasonable to try this solvent.

The purification of interferon in 1978 required innovative thinking based on a thorough understanding of protein chemistry. In fact, the use of propanol was an important, but in my opinion, not the most critical factor in succeeding to purify interferon. Those who wish to purify interferons and other proteins by HPLC should take notice that solvents such as ethanol, methanol and even acetonitrile will work just fine.

Prof. Menachem Rubinstein

Dept. Of Molecular Genetics

The Weizmann Institute of Science

Rehovot 76100 Israel

email: lvrub@weizmann.weizmann.ac.il

Dr. Pestka responds:

When I was interviewed by Pat Fitzgerald- Bocarsly for the ISICR Newsletter, she patiently summarized a long interview well including my recollections involving a suggestion to use propanol when the interferon was not eluted from the reverse phase column. Menachem Rubinstein and I clearly have different recollections

about this specific aspect of the early interferon purification efforts. Thus, although we disagree with the recollection of these specific details, I agree that the use of propanol was only one component of the purification which itself was one part of an extensive program that involved the contributions of many individuals. Many people

contributed important and innovative steps that made the purification of and the discovery of the human interferon alpha family of proteins possible. In addition to the specific purification efforts, it involved induction and production of the interferon, development of a rapid assay, use of highly sensitive amino acid and protein detection methods by fluorescence developed by Stanley Stein and Sidney Udenfriend, and new protein microsequencing technology. I take this opportunity to thank everyone who made

this achievement possible: Menachem Rubinstein, Stanley Stein, Phillip Familletti, Sara Rubinstein, Robert Miller, Alan Waldman, Robert Hershberg, Mitchell Gross, Larry Brink, John Moschera, Louise Gerber, Jordan Gutterman, Jean Hester, Robert Bartlett,

Warren Levy, Jack Shively, U. Del Valle, Eileen Gusciora, Cynthia Rose, and, of course, Sidney Udenfriend, who as a friend and mentor for many of us provided the environment and support to

carry out the work at the Roche Institute. Only through the contributions of all the above individuals was our overall goal

accomplished. I thank all involved for their contributions to this productive and successful effort.

## MEMBERSHIP APPLICATIONS ARE DUE AT THE ISICR BUSINESS OFFICE

Address all correspondence including membership applications, renewals, address changes, corrections and change in professional degree to:

ISICR Business Office

9650 Rockville Pike

Bethesda, MD 20814- 3998

Tel: 301- 571- 8319

Fax: 301- 530- 7049

Email: [isicr@faseb.org](mailto:isicr@faseb.org)

Thought to ponder

Do radioactive cats have 18 half- lives?

### WWW SOURCES

The Virtual Lab

<http://www.novo.dk/vl/index.asp>

If you are interested in genetic engineering, and want to learn more about how actual researchers design new medicines and proteins, come visit The Virtual Lab.

The Virtual Lab is a free educational resource on the internet, which uses shockwave to provide unique multimedia lessons geared to upper level high school students and college students.

If you don't have shockwave or hate browser plug- ins, the virtual lab offers a pure HTML version which can be viewed on any browser!

Good Luck,

Tor Kristensen

Web Designer

Araneum A/S

RELIBASE at EBI

<http://www2.ebi.ac.uk:8081/home.html>

Relibase by Manfred Hendlich is the first web based non- commercial service that can access the PDB by true 2D search queries, on the 3D database. 3D queries are being developed now. However, results of the searches are delivered in 3D via VRML options that can display the requested interactions.

RELIBase is an archive for structural data about receptor/ligand complexes.

The main purpose of RELIBase is to provide a selective and efficient access to the receptor/ligand complexes currently deposited in the Brookhaven Protein Databank (PDB) and to make the enormous wealth of information contained in the receptor/ligand structures available for structure based drug design studies.

The www public access relibase data base and search tools can be used to input a sub- structure search object either by text, a smilesstring, or by an interactive java based molecule editor,

and the system can perform the following functions:

Fast identification of all ligands which contain a specific functional group

Identification of receptor/ligand complexes with specific spatial interactions

Analysis of interaction preferences of functional groups.

Mutations.

Protein modifications.

Cross links to several protein sequence databases and the Beilstein Database of small molecules (not available on the WWW).

( manfred email: [hendlich@pharmazie.uni-marburg.de](mailto:hendlich@pharmazie.uni-marburg.de))

English Language Help <http://www.ixpres.com/globalin/LanguageHelp.html>

A new web page for English language help to biologists for whom English is a second language has been established.

Also a free English Grammar Tutorial specifically written for biologists is available for the asking (specify desired application and computer system).

Gisela Hoschek

TRANSFAC 3.2

<http://transfac.gbf.de>.

On the TRANSFAC server, you will find also the sequence analysis programs

PatSearch

MatInspector

SaGa

FastM

and Thure Etzold's SRS5 with a large collection of databases.

TRANSFAC is a database about eukaryotic transcription factors and their binding sites.

It consists of six cross- linked tables:

SITE

CELL

FACTOR

CLASS

MATRIX

GENE

It is also cross- linked with TRRD (Transcription Regulatory Region Database) and COMPEL from the ICG, Novosibirsk (N. A.Kolchanov, A. E. Kel). It contains numerous cross- references

to external databases such EMBL, SWISSPROT, PIR, FLYBASE, EPD, and PROSITE. For further details see Wingender et al.,

Nucleic Acids Res. 25:265- 268, 1997.

NEW FEATURES are:

- Additional FACTOR and SITE entries,
- cross- references to PDB,
- comprehensive linkage of FACTOR entries with a proposed transcription factor classification system

(<http://transfac.gbf.de/TRANSFAC/cl/cl.html>).

The TRANSFAC database comes along with several sequence analysis tools such as

- PatSearch, which uses the sequence information contained in the SITE table for analysis of submitted sequences,
- MatInspector, using a library of matrices selected from the TRANSFAC MATRIX table (see Quandt et al., Nucleic Acids Res. 23:4878- 4884, 1995).

Moreover, the TRANSFAC server provides a new program (SaGa: structural analysis with genetic algorithms, developed by Stefan Meier) which can be used to identify structural characteristics in the environment of aligned functional

sites, e.g., transcription factor binding sites. SaGa uses a library of structural parameters developed by H. Sklenar and

coworkers (MDC, Berlin; see Karas et al., CABIOS 12:441- 446, 1996).

The SRS5 system implemented on the TRANSFAC server comprises the

following databases, in addition to the TRANSFAC tables:

EMBL, EMBLNEW

SWISSPROT, SWISSNEW

TREMBL

REMTREMBL

SPTREMBL

PIR

EPD

PDB

PROSITE

ENZYME

EMBLNEW is now updated daily on the TRANSFAC SRS- Site with the new files from European Bioinformatics Institute (EBI) in Hinxton.

Edgar Wingender

Dr. Thomas Heinemeyer

Ges. f. Biotechn. Forsch. mbH

Abt. Genomanalyse, Mascheroder Weg 1

D- 38124 Braunschweig

Tel.:++49(0)531 6181 295

Fax:++49(0)531 6181 266

E- Mail: thh@gbf.de

<http://transfac.gbf.de/Staff/thh.html>

WebIn - New EBI WWW Sequence Submission Tool

<http://www.ebi.ac.uk/submission/webin.html>

WebIn is the new WWW Sequence Submission Tool for submitting nucleotide sequence data and associated biological information to the EMBL Nucleotide Sequence Database at the European Bioinformatics Institute (EBI).

Database entries created by the new WWW submission tool and submitted to the EMBL Nucleotide Sequence Database at the EBI will be exchanged and shared among the International Collaboration of Nucleotide Sequence Databases (DDBJ/EMBL/GenBank).

WebIn guides the user through a sequence of WWW forms allowing the submission of sequence data and descriptive information in an interactive and easy way. All the information required to create a database entry will be collected during this process:

- 1 Submitter Information
- 2 Release Date Information
- 3 Sequence Data, Description and Source Information
- 4 Reference Citation Information
- 5 Feature Information (e.g. coding regions, regulatory signals etc.)

EBI staff will process data submissions within 2 working days and send the database accession number(s) assigned to your data to your e-mail address.

For further assistance please contact EMBL Nucleotide Sequence Submissions at:

e-mail: [datasubs@ebi.ac.uk](mailto:datasubs@ebi.ac.uk)

telephone: +44- 1223- 494499

telefax: +44- 1223- 494472

ALL THE VIROLOGY ON THE WWW UPDATE

<http://www.tulane.edu/~dmsander/garryfavweb.html>

"All the Virology on the WWW" is pleased to announce several updates of interest to our users:

- Our new AIDS/HIV links make our collection the most comprehensive available
- "The Big Picture Book of Viruses" has new VIRUS PICS from Abadina to Zirqa
- Our index of Microbiology and Virology Departments continues to grow....
- New additions to our unique JOBS page have made it a very popular addition
- We've added numerous labs to our list of VIROLOGY LABS - Do we have yours?
- Even more sites have been added to our WEIRD VIROLOGY section!

All the Virology on the WWW has also been adding to its already substantial collection of internet links of use to Virologists, Microbiologists and the general public.

If you aren't familiar with the site, or would like to add a URL to my collection, please read "About All the Virology on the WWW" below, and don't miss the TABLE OF CONTENTS.

Thanks for your continued support!

David

P.S. COMING SOON: Emerging Disease Updates and new Gene Therapy Sites

Thoughts to ponder:

Would a fly without wings

be called a walk?

PROTOCOLS ON THE WEB

<http://www.horizonpress.com/gateway/protocols.html>

The Molecular Biology PROTOCOLS ON THE WEB page is moving. Please, please make a note of the new location:

Protocols on the Web

A complete guide to molecular biology protocols available on the Web

<http://www.horizonpress.com/gateway/protocols.html>

Other sites you might like to add to your bookmarks include:

The PCR Jump Station. The ultimate site for links and information on

the Polymerase Chain Reaction. Check it out at <http://apollo.co.uk/a/pcr>

Molecular Biology Journals. A fully comprehensive list of links to

journals relevant to life scientists, in particular molecular biologists.

The URL is <http://www.horizonpress.com/gateway/journals.html>

Books for Molecular Biology

A range of books of interest to the Molecular Biologist, includes full

chapter abstracts and book reviews.

<http://www.horizonpress.com>

Molecular Biology Gateway. The ultimate gateway to Web resources for

molecular biology, genetics, microbiology, and biochemistry. Located at

<http://www.horizonpress.com/gateway>

Funding Databases

Infoed Homepage ( SPIN grant database).

<http://www.infoed.org/>

FEDIX (Database for federal grants).

<http://web.fie.com/>

Mouse and Rat research

(sites for databases, transgenics, KOs, cell- lines, etc.).

[http://www.cco.caltech.edu/~mercer/htmls/rodent\\_page.html](http://www.cco.caltech.edu/~mercer/htmls/rodent_page.html)

Thoughts to Ponder:

Why isn't there

mouse flavored cat food?

Zucchini Problem Solved

In a little known provision of the 1993 tax law changes, there was a hidden section that dictated that all US offices and laboratories must designate one individual to be the "Zucchini Provider" each summer. This individual is assigned to grow zucchini and provide it to all members of the office or lab. This law was instituted to save the zucchini seed producers from extreme financial ruin. It is recognized that this program has been widely successful and all US offices/labs are overrun with zucchini during the summer months. The problem occurs as no one seems to know what to do with all this zucchini. Fried zucchini and zucchini bread are common solutions but grow old fast and the zucchini still appear. In a continuation of our tradition of providing ISICR members with recipes "guaranteed" to make even the most sour lab member happy, we now provide the best solution ever invented to the "Zucchini Problem".

Chocolate Zucchini Cake

1/2 cup margarine

1/2 cup vegetable oil

1 3/4 cups granulated sugar

2 eggs

2 cups grated zucchini, drained

2 cups unsifted all purpose flour

4 tbls. cocoa

1 tsp. salt

1 tsp. baking powder

2 cups chocolate chips

1/2 cup chopped nuts

Cream margarine, oil, sugar, and eggs. Add flour, cocoa, bk. soda, bk. powder and beat well. Add zucchini and stir. Pour into a 9 x 13 cake pan or 2 loaf pans. Top with chocolate chips and nuts. Bake 45- 55 minutes at 350F until tester toothpick comes out clean.

While some ISICR members may think the editor is 100 ml short of a liter or has done too many experiments with 32- P, it is a well published (somewhere, maybe) fact that zucchini is a potent immunomodulator. At the very least, bring this to a lab meeting and everyone will show up.

#### CONTRIBUTION TO THE INTERFERON ARCHIVE BY ROBERT M. FRIEDMAN, MD, FCAP

As a boy, I was very moved by the descriptions of the lives and research of Pasteur, of Koch, and especially of Ehrlich, as related in Paul deKruif's book *Microbe Hunters*. Added to this was the fact that, possibly because of the combined aroma of alcohol, chloroform, and iodine characteristic in those days of doctors offices, smells that I still find attractive, I enjoyed my visits to the doctor, in spite of the fact that such forays often resulted in painful injections; therefore, I very much wanted to become a physician in order someday to be able to carry out research similar to that described by deKruif. When I found myself an undergraduate at Cornell University in 1950, however, it was still very difficult for Jewish students to gain admission to medical school in the United States, most having strict "Jewish quotas". Since I was unsure how well I'd do academically, I decided it would be expedient to become a lawyer, specializing in tax problems, as my father was a senior partner in a medium- sized accounting firm in New York City.

Thus, my major field as an undergraduate came to be Economics, and I eventually graduated with honors in that subject; however, in the middle of my third year (of four) at Cornell, while waiting for a ride to go home to New York City from Ithaca after my final exams, I had an epiphany of sorts. It very suddenly became starkly apparent to me that I didn't want to become a lawyer at all; I really loved the science courses I had taken - chemistry and zoology. Moreover, I was doing well enough academically to have been elected to the university academic honor society (Phi Beta Kappa) in my junior year, so that I could well hazard applications to medical schools on the basis of that degree of scholastic success. Therefore, my last 18 months as an undergraduate, which should have been a lark, was crowded with pre- medical school subjects such as Organic Chemistry, Physics, Comparative Vertebrate Anatomy, Embryology, and Qualitative Inorganic Chemistry, that I should have taken earlier in my university career, together with seminars in Economics and courses on Advanced Economic Theory I needed to fulfill the requirements in my major area of study. I did well enough with all of this that I was admitted to the New York University School of Medicine Class of 1958.

I had made the right decision. I loved medical school, and best of all, I found my own school challenging and exciting. My favorite subject was Microbiology. At the time, NYU School of Medicine had an outstanding Department of Microbiology, and excellent faculties in all of the other preclinical disciplines; the quality of its clinical training had long been recognized. The Chairman of Microbiology was Colin McCloud, one of the discoverers of the genetic significance of DNA. Among the other members of that department were my instructor Mark Adams, an expert in bacteriophage genetics very early in its development, and Lane Barksdale, a bacteriologist who was primarily interested in medical education.

The microbiology course we took was superb. For instance, as a medical students we carried out an experiment in which we induced the transformation of one strain of pneumococcus with DNA from another, at a time (1955) at a time when friends of mine attending other medical schools were only dimly aware of what DNA was. I did a lot of reading on various aspects of microbiology, immunology, and infectious diseases; consequently, I received what I believe was the highest grade in the country on the first part of my National Medical Board Examination. Dr. Barksdale congratulated me on behalf of the members of his department on my achieving this grade, as Microbiology had come in for some criticism from students for teaching material that to many of them seemed irrelevant.

In my last two years of medical school I spent some elective time working on intermediary metabolism of amino acids in the laboratory of Dr. Elijah Adams, who was in the Pharmacology Department. The first scientific paper with my name on it was a result of our work on the metabolism of hydroxyproline, a pretty obscure subject (1). I applied for an internship, and was accepted at The Mt. Sinai Hospital in New York City, an institution with outstanding clinical facilities, but at the time, not associated with a medical school.

While I was still in my last year in medical school, however, I was puzzled about what I was going to do in the years following my internship. In the late 1950s and 60s, there was still a mandatory military draft for physicians, and most of us facing that eventuality felt it best to get our service obligation over with as soon as possible. When I spoke to Dr. Barksdale about where I might most usefully be assigned in the Uniformed Services, he told me of a program at the National Institutes of Health (NIH) in Bethesda. A selected group of young physicians, who were interested in careers in biomedical research, might spend two years in the U.S. Public Health Service (USPHS) as Commissioned Officers at NIH research laboratories. He put me in touch with Dr. Sam Baron, who had one of those positions in his unit in the Division of Biologics Standards (DBS), then part of NIH; Sam had been a student at NYU Medical School, graduating four years before me, after carrying out a commendable research program while there. Since then, he had been a fellow in the virology program in the University of Michigan, which was then the place to work in basic virology in general and influenza virus in particular. After this fellowship, Sam had taken his position at DBS, which had recently been greatly expanded as a result of problems encountered with the early use of the Salk poliomyelitis vaccine (the so- called Cutter incident of 1956).

When I called Sam, he said he'd be delighted to interview me for a job in his lab, and to arrange for me to speak to other research directors at NIH, whom he knew well, and who also had positions for people like me. I was thrilled by this offer, and drove down to Bethesda at my first opportunity. I had a delightful interview with Sam, who spoke about his plans for working on the basis for natural recovery from viral infections. I told him I'd very much like to join his group, but he insisted that I at least speak to some other lab chiefs.

The most memorable of these interviews was with the great virologist Robert Huebner, who at that time had finished his monumental work on adenoviruses, and was just taking up the study of polyoma virus, which recently had been shown to induce tumors in rodents. I was brought into his office by his secretary, who introduced me as Mr. Friedman. Dr. Huebner asked me to repeat my name, and then proceeded, non- stop, to describe the astonishing work he was doing on virus- induced cancer, and his extensive plans for future research projects in this area. I was totally bowled over. As far as I knew, cancer induction by viruses was a borderline area of science - at least until that moment for me. It was a remarkable half hour. When my time was up, Dr. Huebner's secretary reentered the room to remind him of his schedule, since I'm sure, given his enthusiasm, he'd have gone on the rest of the day with me. He asked: "What did you say your name was, son ?"

"Friedman," I replied.

"Good, Friedman. You've got some fine ideas. Maybe we can use you."

This was extraordinary, as I'd not uttered one word during the "interview", other than to give my name twice. I decided to tell Sam Baron that if he was happy with me, I'd like very much to work in his group. We shook hands on that, and a little over a year later, after a remarkable, but exhausting year as an intern at The Mt. Sinai Hospital, I reported to Sam Baron's lab to initiate research on virus infections.

Sam's aim was to find the mechanisms which were operative in recovery from primary viral infections in animals. He was intrigued by reports that patients with hypogammaglobulemia were able to recover from most viral infections, although they produced little or no antibody. From these observations he reasoned that antibodies, while important in preventing viral diseases, could not be critical in recovery from many primary infections. This seemed reasonable to me, so together we set about to develop a system that would mimic the hypogammaglobulinemic state. If we were successful, and our animals recovered just as did human patients with hypogammaglobulinemia, we hoped to move on from there to block other immune and non-immune responses in our experimental animals, thus dissecting out what would be the critical factors in recovery from primary virus infections. Our ultimate aim, naive in retrospect, was to find a single response, the inhibition of which would make experimental animal susceptible to overwhelming viral infections.

We decided to start out by investigating infection with vaccinia virus in guinea pigs. At the time (1959) the immune responses of these experimental animals were better understood than were those of most others. Vaccinia virus also seemed a good choice since it was easy to obtain, and represented no great danger to the investigator. Furthermore, cases of vaccinia gangrenosa indicated that the virus could become lethal in patients with then unrecognized impairments of their antiviral responses. Our first step was to irradiate our experimental albino Hartley guinea pigs with a dose sufficient to block their antibody response. We were successful in achieving this goal, so that we were able to produce animals that seemed good models for humans with hypogammaglobulinemia. Our irradiated guinea pigs did not produce antibody to vaccinia virus after infection with the agent, but recovered from the infection just as well as did unirradiated controls (2).

The next step was to find some way to block cellular immunity in our animals. At this stage in the development of our research, Sam gave me quite a shock when he announced that he was planning to spend the next year, the last of the two I was to work at DBS with him, as a guest scientist in London at The National Institute for Medical Research in Mill Hill with a scientist named Alick Issacs, whom until then I had never heard of. Sam was planning to carry out research with Issacs on interferon, a new antiviral substance he had discovered three years earlier. This was also the first I had ever heard of interferon. Sam's original plan had been to work with Sir Christopher Andrews, but Sir Christopher had decided to retire.

Sam's incipient defection left me with several very big problems. It seemed that at the ripe old age of 26, with then six months of cumulative experience working regularly in a first class lab, I was both to take over our joint research project, and also to carry out Sam's responsibilities in the regulation of vaccines and other biologicals, that arose as a consequence of his important position at DBS. His lab consisted of a chief technician, Chuck Buckler, who was about my age, and four senior technicians, all experienced, and each quite old to be my parent. It didn't seem likely to me that I could do all of this.

But somehow, I did. The moment Sam said good- bye to us and left for London with his family, Chuck Buckler and I looked at one another and started laughing. When we had recovered sufficiently to speak, we simultaneously asked the same question: "Well, what do we do now?", whereupon we both again started laughing, this time convulsively, and kept it up well after Sam was out of the building and on his way to London.

When I recovered from my panic, I spent time in the NIH library researching how I might block cellular immune responses. I ran across some articles by Victor Haas, an NIH scientist who worked right across the street from me. Vic had found that he was able to make mice tolerant to infections with lymphocytic choriomeningitis virus (LCMV) by treating them with methotrexate. Even way back then, it was recognized that the disease associated with LCMV infections was somehow related to a cellular immunity response. Therefore, with valuable advice from Vic Haas, Chuck Buckler and I treated our guinea with methotrexate and observed their cellular and humoral immune responses. We very quickly found that we were able to block the development of both types of immunity with this treatment, and even to inhibit established cellular immunity (3). When we infected the methotrexate- treated animals with vaccinia virus, they also recovered just as well as untreated controls; therefore, a response that was not blocked by radiation or by methotrexate was responsible for their recovery from vaccinia virus infections (4).

All during this time, I was in close touch with Sam Baron, who was, of course, very interested in the uses to which we were putting his research facility. He wrote extensively to me about his work with Isaacs on interferon and recovery from primary virus infections. Both Sam and I became interested in discovering whether interferon might play a role in the recovery of the guinea pigs in our system, but we had no clue as to how we could confirm our theory that it had an important part in their response to vaccinia virus infection. No one at that time had worked with guinea pig interferon, and very few papers had been published about how to demonstrate interferon activity in skin.

Just before Sam was scheduled to return to the NIH, my two year appointment at the DBS was up. I had decided that I wanted to take medical specialty training in Pathology. With the help of Dr. Ruth Kirschstein, then a pathologist at DBS, I discovered the perfect training billet for myself. The National Cancer Institute in its Laboratory of Pathology, under Dr. Harold Stewart, had an approved residency program for USPHS officers at the NIH Clinical Center. If I were to be accepted for this program, I would be able to continue my research much more easily than had I to move to another medical center. One big help in my being accepted to Dr. Stewart's program was that I was already friendly with one of the members of his department, Dr. Alan Rabson, who is Ruth Kirschstein's husband. I started my two year residency training in July, 1961.

Sam returned to NIH a few weeks later. He surprised everyone by asking that he be transferred out of DBS into Carl Habel's laboratory in the National Institute of Allergy and Infectious Diseases, a move that turned out to be good for me, since it put his laboratory in close proximity to the Laboratory of Pathology in the Clinical Center of the NIH. With the help of Alan Rabson, I was able to set up some research space to work in not far from the desk I had been assigned as a pathology resident. Together with Robert Steinmuller, another NYU Medical School graduate, who had taken the billet I had just vacated at DBS, Sam and I tried various approaches to finding out whether methotrexate- treated guinea pigs produced interferon at the site of an infection with vaccinia virus. After several months of frustration, Steinmuller hit upon the simple expedient of slicing our skin samples with a sterilized razor blade, grinding up the resulting fragments in a mortar, and suspending the resulting material in tissue culture medium. We solved the problem of how to assay our samples for interferon activity by making cultures of guinea

pig heart cells. Much to our satisfaction and relief, we found that the animals were indeed producing quite high titers of interferon at the site of the virus infection. I believe this was, at the time, one of the most convincing suggestions that interferon plays an important role in the recovery of animals from at least some viral infection (4).

As a resident in pathology, I had one distinct advantage over my peers in other types of clinical specialty training programs - except for my rotations on surgical pathology two months a year, I was free to carry out a research program, although I had at this time no associate or technician to work with. Consequently, I was able during my residency (1961- 63) to perform experiments on interferon induction by two closely related strains of polyoma virus developed by Alan Rabson, one of which did not induce tumors in C3H mice (M- strain), the other, causing rapidly fatal thymic lymphomas (S- strain). Both *in vitro* and *in vivo* the S- strain was a poorer inducer of interferon; moreover, mice infected with both strains together failed to develop tumors (5). Interferon production, therefore, might have played a role in determining the result of infection with each of these polyoma virus strains.

Although the usual requirement for being admitted to the examination of The American Board of Pathology is three years of training in an approved residency program, in my case one year was waved, because of the period I had spent in the DBS research program. When Dr. Stewart expressed interest in giving me a permanent place on his NCI staff in the Laboratory of Pathology, the USPHS agreed to grant me a sabbatical assignment, since laboratory space for me in the Clinical Center would not be available until the end of 1964. When I contacted Alick Isaacs to ask whether he would be willing to have me as a visiting scientist in his laboratory at Mill Hill in 1963- 64, I received an enthusiastically affirmative reply from him, complete with preliminary plans concerning what projects he wanted me to give some thought to.

Imagine my surprise at receiving a hand written note from him a few weeks later telling me he would not be able to accommodate me for the time he had promised, because he had run out of ideas for research and was exhausted. Perplexed by Isaacs' letter, I brought it to Sam Baron for some guidance about the apparent change in Isaacs' commitment. Sam informed me that Alick Isaacs was subject to periods of severe depression; he advised me to ignore the letter for a few weeks, since Isaacs was likely to snap out of his mood within that period. Sure enough, that came to pass, and I received another enthusiastic letter from Isaacs saying his current work on interferon induction by foreign DNA was going well, and he was looking forward to working with me on the project.

I finished my formal training as a resident in June, 1963, and spent that summer as a Fellow with Dr. George Brecker, then the hematologist at the NIH Clinical Center, since my background in reading bone marrow sections and smears was not strong. During this period, I first met Dr. Lois Epstein, who was also a fellow with Dr. Brecker. She later initiated an outstanding research program on interferons and cytokines; we have remained good friends since that time together in hematology.

I reported at the Mill Hill lab to work with Isaacs on October 12, 1963. At the time, he was still very excited about interferon induction by foreign DNA. I somehow could not become as enthusiastic about this subject as Isaacs, so he allowed me to work in other areas of interferon research. The ability of actinomycin D to block interferon production had just recently been reported, so Isaacs suggested that I investigate whether inhibiting interferon production might also inhibit viral interference by RNA viruses. Indeed it did. A paper based on this work was very quickly accepted and published by Nature (6). Since he had been very helpful in outlining how I could tackle this problem, I had put Isaacs name as a co- author on the original draft of this manuscript. I received it back from him

quite promptly with very nice comments on the work, but with his name crossed out as co- author. I naturally concluded that he did not think the work good enough to merit his name on it, but to my relief he explained to me that, while he thought the research was indeed interesting and well executed, he never put his name on a paper unless he had done at least 30% of the actual experimental manipulations with his own hands (which I thought was a very correct policy).

Things were going along very well for me at Mill Hill. I enjoyed living in London, and it was delightful working with Isaacs. I spent Christmas day, 1963 with the Isaacs family. On New Year's day, which was then not a holiday in England, I attended a virology meeting with Isaacs in London. I remember the virologists from Scotland, who attended this meeting, complained bitterly about British tyranny in forcing them to work on 1 January, which was for them a festive holiday. Isaacs was in fine form, brilliant, incisive, and amusing.

The next day I sensed that something was very wrong as soon as I arrived at Mill Hill. I was told that during the preceding night, Isaacs had suffered a subarachnoid hemorrhage, as a result of a congenital aneurysm; he was on the critical list at the hospital. I thought it might well have been that his history of mood shifts was related to intermittent blood leakage from this aneurysm, and was basically not a psychiatric condition.

Clearly, Alick Isaacs would not be able to act as my mentor for a long time, if ever. Indeed, while he did recover from the hemorrhage, during the balance of my stay at Mill Hill (until November, 1964) he was not able to carry out any research at all, and lapsed into a profound depression. After only two months at Mill Hill, therefore, I was on my own again. At that point, the other two fellows working under Isaacs, Joseph Sonnabend and Joyce Taylor, and I, pooled our collective experience to come up with projects we could work on together in Alec's absence. Our selection of what to do was facilitated by a remarkable discovery that Joyce was just getting ready to report: actinomycin D treatment, in addition to inhibiting interferon production, also blocked the antiviral activity of interferon. This was the first indication that DNA- dependent RNA synthesis was necessary for interferon action.

Since Joyce was about to be married and to move to Greece very soon after, Joseph and I, with her approval, decided to follow up her finding by determining whether protein synthesis also was required for development of the interferon- induced antiviral state. Together, we determined that both p- fluorophenylalanine and puromycin could also inhibit this activity (7). I worked alone on a project on the potentiation of interferon production by treatment of chick cells with very low concentrations of interferon, before exposure to a viral inducer (8), and with Joseph and Hugh McDevitt, another visiting fellow from the US, on a radioautographic study that demonstrated that interferon treatment inhibited cytoplasmic DNA accumulation in vaccinia- virus infected cells (9).

The most exciting thing to happen to me during this year, however, was the initiation of experiments employing techniques in molecular biology. Joseph Sonnabend and I used incorporation of radioactive nucleosides and sucrose density gradients to demonstrate that the production of replicative intermediate RNA virus forms was inhibited in interferon- treated cells (10). This project involved techniques I was to employ over the next seven years in studying the mechanism of interferon's antiviral action.

Just before I returned to Bethesda, I attended my first international interferon meeting, which was held in Bratislava. It was very exciting to meet other scientists working in the same area I was, and to share our results. I formed several lifelong associations that over the years grew into friendships with some

of those attending this meeting, among them Jan Vilcek, Edward and Jaqueline DeMaeyer, Tom Merigan, Ilona Beladi, and Kurt Paucker.

When I returned to Bethesda, I found many things had changed. First of all, a year in London had altered my outlook; my approach to research was now to employ techniques in molecular biology in my own laboratory to discover what I could about how interferon induced antiviral activity. I also had my very own technician, Dorothy Hughes, who had worked with me in Sam Baron's lab, before I began my residency. My country had also changed. The assassination of President Kennedy, while I was living in London, had altered the atmosphere in Washington. There was greater and greater involvement in Viet Nam under President Johnson. Finally, things seemed to have changed at NIH. Sam Baron was working closely with a biochemist, Hilton Levy, and seemed to me to be no longer very interested in collaboration with me.

This was not so bad, as by then I had become accustomed to working pretty much on my own. What was unfortunate, however, was that Sam and Hilton also were engaged in research on the potentiation of interferon induction following treatment with low concentrations of interferon, research similar to a project I had started when I was still in London (8), making us for a time competitors.

In 1965, the antiviral activity of interferon was its only universally acknowledged biological effect. There were, however, two major problems at that time about studying the mechanism of the antiviral action of interferon. The first was that there was very little known in detail about how viruses replicated; the second, that the interferon preparations available were very impure. Karl Fantès, then at Glaxo, solved the latter difficulty by giving me some fairly clean chick interferon; later, Kurt Paucker was to give me purified mouse interferon. As for the first problem, the only recourse then available was to investigate how at least one virus replicated, so that each time anything new was discovered, the effect of interferon treatment on that step could be checked. I chose to work on Semliki Forest virus (SFV), a group A arbovirus I had started studying while I was at Mill Hill. In the period between 1966 and 1971, I carried out several studies on the replication of SFV, and on whether these were altered by pretreatment with interferon (11). The general result of these studies was the finding that interferon treatment inhibited protein synthesis by the viral messenger RNA function of the positive-stranded, input SFV. Since in this situation, the RNA of the infecting virus is an mRNA, the action of interferon was manifest very early in the virus replication cycle. Another area of interferon research that interested me during the period between 1965 and 1970 was interferon binding to cells as a first step in the establishment of antiviral activity. The paper I published as a result of this study was the earliest indication that interferon bound to sites on the plasma membrane of cells (12).

Another notable international interferon meeting, held 6- 8 January, 1969 in Lyon, closed out my first decade of research on interferons. It had been organized by Charles Chany with the support of the Foundation Merieux. This meeting featured an excellent scientific program. In addition, some noteworthy events transpired outside of the meeting place. I suppose that because I had worked in London several years before, I was housed in a hotel with the British delegation to that meeting. One of my coworkers in Bethesda, who had previously worked for the UN in Lyon, had given me some dining tips for Lyon. He recommended that I be sure to eat at a restaurant called "Tant'Elise" and to take lunch at Booth 12 at the food market.

On our first night in town, I proposed we try Tant'Elise, a suggestion to which everyone agreed. When we arrived at the restaurant, however, a quick perusal of the menu indicated that the prices were beyond the budget of most of my British colleagues. Just as we were about to leave, Charles Chany, appeared with Mr.

Merieux in tow. They enthusiastically congratulated us on our finding the best restaurant in Lyon, in Merieux's estimation no mean feat, since he believed his town to be the gourmet capital of France.

Merieux was in such good spirits, that I had a strong feeling he would pick up our check, which indeed he eventually did do. So, with my assurance on that score, my British friends and I proceeded to order. Of eight of us, four ordered beef tartar, which they ate with great relish. The next day, those unfortunate four failed to report for the opening session of the meeting, not surprisingly as they all had been felled by violent gastroenteritis.

Undaunted by my unfortunate choice of restaurant, I proceeded to pass my friend's recommendation about where to eat lunch in Lyon on to Joseph Sonnabend; so at the first break for lunch, we made for Booth 12 at the food market, which turned out to purvey fresh shell fish. Joseph ordered a huge plate of mussels, and I, an equally large portion of oysters. I managed to finish my oysters, but Joseph could not get through his mussels; so, he generously offered to let me finish them off, but I couldn't eat even one, which turned out to be just as well for me, as about a month later Joseph came down with an acute hepatitis A infection.

I have never since offered suggestions about where to eat to my British friends.

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#### Clinical Trials

GOG- 9602 Phase I study of Paclitaxel, Cisplatin, and Topotecan with vs without G-CSF for newly diagnosed advanced ovarian cancer. Contact: Seamus O'Reilly, Baltimore, MD TEL: 410- 614- 4461

NCCTG- 906951 NCI- P91- 0010 Phase III randomized study of Interferon alpha plus laser therapy ablation vs ablation alone in patients with CIN grades I- III. Contact: Michael J. O'Connell, Rochester, MN TEL: 507- 284- 3903

E- 1495 Phase III study of topical therapy of psoralen with phototherapy (PUVA), nitrogen mustard (Mechlorethamine HCL) chemotherapy, or total skin electron beam (TSE) alone or one topical therapy combined with Interferon Alpha- 2b for Cutaneous T- cell Lymphoma (CTCL). Contact: Robert L. Comis, Philadelphia, PA TEL: 215- 955- 4652

T94- 0125 Recombinant human interferon- beta in recurrent glioma: Phase II. Contact: Alfred Yung, Houston, TX TEL: 713- 794- 1285

CALGB- 9661 A pilot study of low- dose interleukin- 2 plus recombinant human anti-her2 monoclonal antibody in solid tumors. Contact: Joanne Coburn, Lebanon, NH TEL: 603- 650- 6720

STLMC- BRM- 9503 NCI- V96- 0902 Phase I/II study of infusion of activated T cells and low dose interleukin- 2 combined with autologous peripheral blood stem cell transplantation for women with metastatic adenocarcinoma of the breast. Contact:

Lawrence George Lum, Milwaukee, WI TEL: 414- 649- 5818

E5Y92 Phase II study of IL- 4 in advanced indolent B- cell non- Hodgkin's lymphoma and B- cell Chronic Lymphocytic Leukemia. Contact: Usha Venkatraj, Bronx, NY TEL: 718- 904- 2754

S9711 A phase II study of interleukin- 4 in patients with B lineage acute lymphoblastic leukemia in first or second relapse. Contact: Marj Godfrey, San Antonio, TX TEL: 210- 677- 8808

UCCRC- 8381 NCI- G97- 1162 Phase I/II study of immunization with MAGE- 3 peptide pulsed autologous peripheral blood mononuclear cells (PBMC) plus recombinant human Interleukin- 12 (IL- 12) in patients with metastatic melanoma. Contact: Nicholas Vogelzang, Chicago, IL TEL: 773- 702- 6743

RPCI- DS- 96- 24 NCI- G97- 1153 Randomized phase II study of Filgrastim (G- CSF) and Stem Cell Factor (r- metHuSCF) in priming of bone marrow for autologous transplantation in patients with relapsed or refractory Hodgkin's disease (HD) or Non- Hodgkin's lymphoma (NHL). Contact: Steven H. Bernstein, Buffalo, NY TEL: 716- 845- 7611

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#### FAMOUS QUOTES

For the man whose knowledge is not in order, the more which he has of it, the greater will be his confusion.

Inspired by Herbert Spencer

(1820- 1903)

CORRECTION TO THE DIRECTORY

There is a mistake on p. xiii of the Membership Directory. The ISICR meeting in 2000 is in Amsterdam, and in 2001, in Cleveland, not the opposite as stated in the Directory.

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EDITORS OF

THIS NEWSLETTER

**Howard Young**

**Lab. of Experimental Immunology**

**NCI- FCRDC, 560/31- 23**

**Frederick, MD 21702- 1201**

**Fax: 301- 846- 1673**

**Email: [youngh@ncifcrf.gov](mailto:youngh@ncifcrf.gov)**

**Patricia Fitzgerald- Bocarsly, Ph.D.**

**UMDNJ - New Jersey Medical School**

**Dept. of Pathology and Lab. Med.**

**185 So. Orange Ave**

**Newark, NJ 07103**

**Fax: (973) 972- 7293**

**Email: [bocarsly@umdnj.edu](mailto:bocarsly@umdnj.edu)**

**Paul D. Drew**

University of Arkansas for Medical Sciences

Dept. of Anatomy - Slot 510

4301 West Markham St.

Little Rock, AR 72205

FAX: (501) 686- 6382

Email: DrewPaulD@exchange.uams.edu

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