The History of Interferon:

An Interview with Sid Pestka

Patricia Fitzgerald- Bocarsly

For this inaugural article for what we hope will be a series of articles on key individuals in interferon and cytokine research, I conducted a lengthy interview with Dr. Sidney Pestka. Although trained as a physician, Pestka's passion has always been for research, and he began his research career while still a medical student at the University of Pennsylvania where he was working on the mechanism of action of antibiotics in the laboratory of Joel Flax. Following a medical internship, he went to the laboratory of Marshall Nirenberg, who later won the Nobel Prize, at the National Institutes of Health in 1962 for his post- doctoral fellowship. In Nirenberg's lab, along with fellow post- doc Phil Leder and many others, he was part of the team which broke open the genetic code, assigning specific amino acids to each triplet codon. Sidney reports that this was a very exciting time, with new discoveries being made each day. During this time he was also studying the mechanism of action of streptomycin, which he discovered to cause altered codon recognition and protein miscoding, a discovery which was made almost simultaneously by the Harvard group of Gorini and Davies. Also during this productive postdoc, he challenged the then- current dogma (based on findings of W. Gilbert and J. Watson) that the 50 S ribosomal subunit was the binding site for tRNA, finding instead that the 30S subunit was the binding site. Because he was challenging such widely held dogma, his findings met with considerable skepticism from Nurenberg, but in the end, he was shown to be correct and the results published in what is now a classic J. Molecular Biology paper.

While at the NIH, Pestka was intrigued by the interferon work being done in the laboratories of Hilton Levy and Samuel Baron, who were also at the NIH at that time. When he moved from the NCI to the newly formed Roche Institute in New Jersey, he was looking to develop a new area of research and settled on interferon as one of those areas. At this point, little was known about the chemical structure or composition of interferon, although it was inferred to be a protein by the indirect evidence of trypsin sensitivity. PestkaOs lab tried for a few years to purify rabbit interferon, but to his dismay, in

the end, the activity would always disappear. He would later learn that a number of other groups were trying and similarly failing to purify this elusive substance. The purification techniques of the day were simply not up to yield 100,000 - fold purification of a rare protein! In the meantime, Pestka's lab had become fairly sophisticated in their handling of mRNA, being the first to isolate heavy chain immunoglobulin mRNA. Although he had intended to study immunoglobulin diversity, with interferon breaking as an important molecule, he chose to concentrate his efforts on the latter. In collaboration with Jan Vilcek who provided massive amounts of cell extracts, Pestka's lab was able to isolate interferon message and produce the proteins from message, leading to the publication of what has become another classic paper, this one in the PNAS. They then compared Namalwa vs. fibroblast derived interferon using the cell-free translation system and demonstrated that they were getting two distinct products: the fibroblasts produced an interferon which was neutralized by antiserum to fibroblast interferon, whereas the Namalwa cells produced a second species of interferon as well as small amounts of material neutralized by the anti- fibroblast interferon antiserum. In a classic example of parallel research leading to equivalent results, De Maeyer's lab did the same experiments in mouse and Paula Pitha's lab did the same experiments in an oocyte translation system at almost the same time.

When recombinant DNA technology broke around 1975, Pestka realized that they could use their expertise in IFN message work to clone the cDNA. Meanwhile, the Roche Institute President Sidney Udenfriend assigned Stan Stein (who had developed a very sensitive analyzer for amino acid analysis) and Menachem Rubinstein, then a post- doc, to work with him on the interferon purification project. They first set about trying to purify human leukocyte interferon using material obtained from 100 NDV- stimulated buffy coats of human blood/week. When they tried to purify the material on the HPLC columns, the interferon got stuck and could not be eluted with either methanol or ethanol. When Pestka suggested trying propanol for elution, the two chemists were appalled since everyone knew that proteins were not soluble in organic solvents. However, there had always been (and still is to this day!) a standing rule in the Pestka lab: if you don't take Pestka's suggestion for an experiment, he reserves the right to assign it to someone else or do it himself. Fearing for their HPLC columns, Rubinstein and Stein decided it was better to do it themselves rather than let Pestka ruin them. So, they eluted with propanol and the IFN came off! Ultimately, the HPLC work led to the

discovery that leukocyte interferon (now known as IFN- a) could be separated into 10 different peaks, each of which had a different peptide map, representing a family of closely related but individually coded proteins - an observation that the scientific community was not quite ready for when it was published in Science in 1978!

Although several labs were simultaneously working on cloning IFN alpha and beta, Taniguchi was the first to clone interferon- beta, and the Weissman group cloned IFN- alpha and confirmed it was a family of related genes. A couple of months later, the Pestka lab cloned interferon cDNA for both IFN- a and - b on the same plate and then contracted with Genentech to express it in a mature form, which was accomplished very rapidly, making this the first interferon to be expressed in a mature form. It then remained for the recombinant material to be purified. Theo Staehlin from the Roche Institute, Basel, had made monoclonal antibodies to the individual alpha interferon peaks and to interferon- beta and arrived in New Jersey with those on a Friday afternoon in October, 1990. Along with H- F Kung and D. Hobbs, Pestka and Staehlin worked non- sop over the weekend, using the antibodies attached to a solid support, and successfully purified the interferon around 2 a.m. on Monday morning. Pestka made souvenir vials of lyophilized material for each of the investigators, and over champagne, they presented one of them to the President of the Roche Institute USA. While sitting in the President's office, an exhausted Staehlin fell asleep. They decided to send him back to Switzerland first class so he could get a chance to sleep! In Switzerland, Staehlin presented a vial to Roche International President Gerber, who decided to have it embedded in plastic for Roche's historical archives. Gerber's office soon contacted Pestka's office for another vial of material - the IFN in the original vial had dissolved when plastic leaked into it!

Pestka is currently the Chairman of the Department of Microbiology and Molecular Genetics at the UMDNJ- Robert Wood Johnson Medical School in Piscataway, New Jersey. Over the past decade, Pestka's studies have concentrated on interferon receptor studies. They were the first to clone the IFN- g receptor and show that it had two components encoded by different chromosomes, 6 and 21. This was the first evidence for a multiple chain receptor. Multi- chain receptors are now known, of course, to be involved in signaling with most cytokines. In addition to ongoing receptor studies, the Pestka laboratory is studying IFN- a in its potential for gene therapy of

cancer.

Throughout its existence, Pestka has been a key figure in the International Society for Interferon Research (now the International Society for Interferon and Cytokine Research). He has served for secretary of the society for many years, and completed a two year term as President in 1995. His most recent (and time demanding activity) has been to raise corporate sponsors for the ISICR, and he would welcome assistance in this endeavor.

When asked about differences between doing research today as compared with his early days, Pestka replied immediately that science is as exciting now as ever before. He cited new technology and instrumentation such as confocal microscopy as providing the potential for great depth in understanding of biological processes. When asked about difficulties in doing research in todayOs environment, he cited funding as the number one detriment. Until 10 years ago, because he was at the NIH and then the Roche Institute, Pestka never had to write a grant to fund his research. Now he finds that he must spend increasingly greater amounts of time in securing funding. He stated the major problems are in funding enough research overall and in funding novel, imaginative programs. Pestka believes that funding rates should be as high as 50%, enabling scientists to concentrate on doing innovative research, rather than trying to write the OperfectO grant to reach the 10% funding mark which has recently prevailed. Another frustration of Pestka's is that the scientific community has not been able to cure cancer except for in a few specific types. He anticipates major breakthroughs if adequate funding opportunities are provided.

Finally, when asked what advice he would pass along to young scientists, Pestka had six specific comments. The first was to be perseverent: good scientists (and good science) will always be funded. Secondly, he advises scientists to keep the focus on important problems and to minimize the effort spent on trivial problems. He stated that it takes no more effort to concentrate on important problems than on trivial ones, and that the rewards are far greater with the former. Third, he advised young scientists to enjoy the effort, and fourth to collaborate. He cites the establishment of excellent collaborations as a key to much of his success. Fifth, he advises scientists to be good mentors, to nurture the next generation of scientists, and finally, to keep a focus on personal responsibilities and to keep a balance in life. Sounds like great

advice for the next generation of scientists!

MEMBERSHIP RENEWALS ARE DUE AT THE ISICR BUSINESS OFFICE

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

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9650 Rockville Pike

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ISICR Election Results

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ARGENTINA Marcelo E. Criscuolo

(1997- 99)

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R. Michael Roberts

Berish Y. Rubin

Gerald Sonnenfeld

Milton W. Taylor

Member Information

New Members

We welcome the following new members who have joined the ISICR since the last newsletter.

Mary Annam Antonysamy - Pittsburg, PA

Erzsebet Blint - Szeged, Hungary

E. Bonnefoy - Paris, France

Hakan Borg - Umea, Sweden

Bogna Domaraczenko - Wroclaw,Poland

Ferenc Farkas - Budapest, Hungary

Paritosh Ghosh - Miami, Fl

Lawrence Lachman - Houston, TX

Anna Machaj - Wroclaw, Poland

Anthony Mire- Sluis - Herts, England

Beata Orzechowska - Wroclaw, Poland

Osman Nidal Ozes - Antalya, Turkey

Gyorgy Premecz - Budapest, Hungary

Chun Shong Wang - Wuhan Hubei, P.R. China

Holly Wetzel - Miami, FL

Barbara Zdzisinska - Lublin, Poland

I LISTENED TO MY GRASS ROOTS, BUT HEARD ONLY MURMURS OF DISCONTENT*

Bob Friedman, President ISICR

The recent joint meeting of the International Society for Interferon & Cytokine Research and the International Cytokine Society in Geneva was, greatly to the credit of the organizers, a resounding success scientifically. So much so that meetings of the two groups together are planned in alternate years for the remainder of the millennium: in 1998, in Jerusalem; and in 2000, in Amsterdam.

Just prior to the meeting of the general membership of the International Society of Interferon & Cytokine Research at the joint ISICR/ICS meeting in Geneva, which as ISICR president I was to chair, a number of gratis copies of Cytokine & Growth Factor Reviews were deposited on the desk in main hallway of the meeting site. I picked up a copy of the August, 1996 issue, which had not yet arrived at my lab and was delighted to find in it additional fodder for our already crowded meeting agenda - namely, an editorial entitled "One or Two Cytokine Societies?" in which the nameless writer boldly suggested that the leaders of the ISICR and ICS "...heed the sentiments of their grass roots." And do what? I took the anonymous author to mean to get the societies to unite. As one of the leaders of one of the societies in question, the finger was definitely pointing at me to do something !

Ethnically determined guilt being my lot in life, I doubled my pace up the stairs to the meeting room, to right the wrong that had been demonstrated so lucidly to me. Filled the spirit of the brotherhood of man, or at least of that part of woman- and mankind carrying out research on cytokines, I made an impassioned plea to all of the grass roots present that we move to unite the ISICR and the ICS to form one big, happy family. My proposition was met at first with polite silence (after all, I am the president), but then with a flood of decidedly negative responses. I shall summarize these uniformly negative comments. Caveat lector - I am here merely transmitting

comments; they are not necessarily mine.

Interferons are still a major player in cytokine research: witness for instance the recent hoard of important findings discovered in the study of interferon signal transduction and interferon receptors. In addition, interferons still are employed clinically far more than any other cytokine. Whether by commission or omission, the ICS does not give research on interferons a fair shake at its meetings.

The ISICR has over the years been able to save a significant amount of money. How are those funds to be divided, if a unification takes place ? After all, they were contributed or solicited solely by the ISICR membership.

Joint meetings in alternate years are sufficient for the needs of the members of ISICR. In the odd numbered years each society will do its own thing.

The two societies conduct their affairs quite differently. As president of ISICR I am bound by rules that establish protocols for the work of my society. I could not circumvent these, even if I chose to do so.

Apropos of the latter point, I shall relate two incidents that occurred at the Geneva meeting that starkly point out how different the procedures of the two groups are. In one instance, I was approached just before the beginning of a plenary session I was to chair by a prominent member of the ICS with a person in tow whose identity was unknown to me. I was introduced to this gentleman, who informed me that the two of them had made arrangements to hold the joint ISICR/ICS meeting in the year 2000 in a city in Europe. I pointed out that the Meetings Committees of both ISICR and ICS, after some wrangling, had just agreed to hold the year 2000 joint meeting in Amsterdam, which was not the city that the two had named. I was told that it didn_t matter; everything would be arranged. I said that indeed it did matter, and asked them to submit their proposal to the appropriate Meetings Committees.

The second instance: at another point in the meeting, I asked one of the speakers who had delivered a superior lecture at one of the plenary sessions if he wouldn_t like to submit a written summary of his talk to the Journal of Interferon & Cytokine Research, the

official journal of ISICR. I was sure its Editor, Phil Marcus, would love to publish it. The speaker replied that he_d very much like to do so, but had signed an exclusive contract (a contract!) to print a version of his talk in The Journal of Leukocyte Biology, a publication of neither ISICR nor ICS. This apparently was standard procedure at ICS meetings.

Yes, the two societies do carry out their work in different ways. Can they ever become compatible ?

* A excerpt of this article will appear in *Cytokine and Growth Factor Reviews*

REMEMBER:
ISICR STUDENT & POSTDOC MEMBERSHIPS ARE ONLY $10

Famous Quotes

Experience is the one thing you have plenty of when you're too old to get the job

WWW SOURCES

ISICR WEB SITE

http:// **bioinformatics.weizmann.ac.il/ISICR/**

Thanks to the efforts of Menachem Rubinstein, the ISICR WEB site is now up and running. Comments and suggestions regarding the contents are welcome.

THE SCIENCE GUIDE

http://www.scienceguide.com

A New Internet Directory and Information Service run by Scientists and Physicians for Scientists and Physicians. After visiting the Guide, If you have any suggestion for making the Guide better please let us know. (webmaster@scienceguide.com)

The Science Guide consists of a number of different sections designed to

help the scientist and physician find information on the internet and to

sponsor communication between those interested in science:

NEWS SECTION

Every day the Science Guide compiles medical and research news from national news sources around the net. Most of the news articles are concerned with medicine, bioscience, and physics, but all other sciences from agriculture to zoology are commonly included. News sources currently listed include: CNN, EurekAlert, HMS Beagle, MSNBC Sci- Tech, Science Magazine's ScienceNow, CBS Space News, USA Today, The Albuquerque Journal, Scientific American Web Weekly, The Why Files, Discover Magazine, Scientific American, Smithsonian Magazine, and the Technology Review. The news pages also list links to news sources not compiled within the News site. We are currently working on adding a number of other sources to the site to make it even more useful.

To make getting science news even easier, we send out a DAILY NEWS

EMAILER listing the articles which have been compiled on our site. Anyone can subscribe to the Emailer by sending an email to news@scienceguide.com with the message "Subscribe"

DIRECTORY OF USENET NEWS GROUPS and DISCUSSION LISTS

The Directory of Usenet and Discussion Groups is compiled quarterly from

different sources around the net to provide the scientist and those

interested in science easy access to these invaluable sources of

discourse and information. We are currently working on finding the

proper subscription method for each of the discussion lists. This is

taking a bit longer that we thought so please pardon our dust. The

Usenet portions of this section are complete.

ON- LINE JOURNAL HYPERLINK SECTION

The Journals Section contains links to peer reviewed scientific journals

on the Internet. Each listing clearly indicates whether the journal

provides only the table of contents, TOC with abstracts, or the full text

of the journal

EMPLOYMENT SECTION

The Jobs and Positions Section contains hyperlinks to the best Scientific

Employment Databases and Classifieds on the net.

GRANTS and FUNDING SECTION

The funding section contains links to the best funding and grant databases on the Internet, making it very easy for scientists to quickly find funding opportunities. The featured site of the section is "The

Community of Science," a Johns Hopkins service designed to help scientists find and continue funding.

Howard Hughes Medical Institute's

"Blazing a Genetic Trail"

http://www.hhmi.org/GeneticTrail/

"Blazing a Genetic Trail" is now online! This wonderfully illustrated book takes you on the search for mutant genes that

cause the 4,000 hereditary disorders affecting humans. The Web version is free for all to read online.

"Blazing a Genetic Trail," edited by HHMI's Maya Pines, shows how scientists and families join in seeking the causes of baffling diseases: abnormal genes. This book is written for a general audience in magazine style, and is a great aid for anyone ranging from junior high to university levels. Its detailed and colorful

graphics make it especially attractive.

You will read about the personal struggles of a University of Michigan student who tried to find the genetic error that produced his own lethal illness, cystic fibrosis; the Human Genome Project;

"How To Conquer a Genetic Disease" (a special section); the need for animal models; and the search for new treatments. You will also learn that "Virtually all human afflictions from cancer to psychiatric disorders and susceptibility to infections are rooted

in our genes," and you will see how your family history could help scientists uncover the secrets hidden in all our genes. The book also includes a brief guide to basic genetics and a glossary of

genetic terms.

The Howard Hughes Medical Institute makes this book available online as a public service. The Institute, whose primary purpose is the conduct of basic biomedical research, is the largest

philanthropic organization in the United States. It also has a complementary grants program that supports science education at all levels. You can visit HHMI's Web site at http://www.hhmi.org.

For more information on "Blazing a Genetic Trail," contact the HHMI Office of Communications at commpub@hhmi.org or call (301) 215- 8855. For help with creating a link to the Web site, visit

http://drwebby.com/hhmi/how2link.html or contact Steffanie Lynch at link2hhmi@drwebby.com

or call (804) 739- 0165.

GenPept(R)

(GenBank Gene Products) Database

This is to announce the availability of release 100.0 of the GenPept (R)

(GenBank Gene Products) Database. GenPept is provided in a format similar

to that formerly distributed by GenBank(R) under the administration of

Intelligenetics Inc. This GenPept release IS _NOT_ AN OFFICIAL RELEASE FROM

THE NCBI- GENBANK, but an attempt to provide a data file format compatible

with existing software products.

This data format is suitable as an input data file for the GCG program

GenBankToGCG/GENPEPT. Compatibility with other software has not been tested.

Site: ftp.ncifcrf.gov

Directory: pub/genpept

Files: gprel100.txt.Z, gpdat100.seq.Z

Directory: pub/genpept/divisions

Files: gpbct.seq.Z, gpest1.seq.Z, gpest2.seq.Z, gpest3.seq.Z, gpest4. seq.Z,

gpest5.seq.Z, gpest6.seq.Z, gpest7.seq.Z, gpest8.seq.Z, gpest9.seq.Z, gpest10.seq.Z, gpest11.seq.Z, gpinv.seq.Z, gpmam.seq.Z, gppat.seq.Z, gpphg.seq.Z, gppln.seq.Z, gppri.seq.Z, gprna.seq.Z, gprod.seq.Z,

gpsts.seq.Z, gpsyn.seq.Z, gpuna.seq.Z, gpvrl.seq.Z, gpvrt.seq.Z, gpgss.seq.Z, gphtg.seq.Z

Directory: pub/genpept/updates (daily, cumulative)

Files: gpseq_updates.dat.Z

Directory: pub/genpept/updates (daily, noncumulative)

Files: gpncMMDD.seq.Z

Rel. Date: 19- Apr- 1997

Ftp mirror sites have been provided through the kind generosity of the

following institutions:

C.D. Nager (nager@fmi.ch), at the Freidrich Miescher Institute maintains:

Name: ftp.ecbi.org

Address: 147.167.128.40

Directory: ncifcrf

Dr Jaime Prilusky (lsprilus@weizmann.weizmann.ac.il), at the Weizmann Institute of Science maintains:

Name: bioinformatics.weizmann.ac.il

Address: 132.76.55.12

Directory: /pub/databases/genpept

We greatly appreciate their efforts in creating multiple points of access, and

reducing the load on our systems.

If you have questions or comments concerning this data, or you

experience any difficulty in downloading the data via ftp, please contact:

Gary W. Smythers

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Phone: (301) 846- 5778

FAX: (301) 846- 5762

LASSAP : LArge Scale Sequence compArison Package

http://www- rocq.inria.fr/genome

LASSAP is a new software package for sequence comparison. LASSAP currently implements all major sequence comparison algorithms - Blast, - Fasta, - Dynamic programming : Smith/Waterman, Needleman/ Wunsch, K- best alignments, - string matching (Mainly for redundancy problems), - pattern matching algorithms (e.g. search for PROSITE patterns).

For the time being, all algorithms in LASSAP are pairwise based. Whatever a pairwise algorithm is used in LASSAP, it shares with all other algorithms numerous enhancements such as:

(i) intra- and inter- databank comparisons

(a databank can be a set of sequences choosen among a large databank

or one sequence);

(ii) computational requests (selections and computations are achieved on the fly);

(iii) frame translations on queries and databanks (various genetic codes)

(iv) structured results allowing easy and powerful post- analysis (LASSAP provides 3 different views of a result:

. a full ASCII form, whith the alignment.

. a compacted ASCII, one line for a pairwise result, allowing easy "grep", "awk" or "perl" filters

. a structured form to perform some complex analysis such as clustering, etc.)

(v) performance improvements by parallelization and the driving of specialized hardware. (Two versions of LASSAP are available:

- one sequencial for basic needs

- one parallel to speed- up algorithms, and for large scale problems.

LASSAP implements an optimized version of Smith/Waterman algorithm

using SUN Visual Instruction Set [2])

For a programmer point of vue, LASSAP is a programmable, high-performance system designed to raise current limitations of sequence comparison programs in order to fit the needs of large- scale analysis. LASSAP provides an API (Application Programming Interface)

allowing the integration of any generic pairwise- based algorithm. (The public API is not yet available, but it will be released as soon as possible)

Results

LASSAP is both an integrated software for end- users and a framework allowing the integration and the combination of new algorithms. LASSAP is involved in different projects such as:

- the building of PRODOM

(http://protein.toulouse.inra.fr),

- the exhaustive comparison of microbial genomes (Protein Science, Vol 6, Suppl 1, April 1997)

- the subfragments matching problem of TREMBL. (Proceedings of ISMB 97 conference - June, Greece)

A LASSAP server will be set up soon through a collaborative project between INRIA, INFOBIOGEN and CNUSC.

References:

[1] E. Glemet and JJ. Codani

LASSAP, a LArge Scale Sequence compArison Package Cabios, Vol 13., No. 2, pp 137- 143 (1997)

[2] A. Wozniak

Using Video Oriented Instructions to Speed- Up Sequence Comparison Cabios, Vol 13., No. 2, pp 145- 150 (1997)

Availability:

LASSAP binaries release 1.0a are available for UNIX platforms (SGI, Solaris, AIX, Digital, ...). You can get documentation and binaries at the following address:

http://www- rocq.inria.fr/genome

For any request or feed- back please mail to: lassap@inria.fr or Eric.Glemet@inria.fr

Adress: E. Glemet and JJ. Codani

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GeneFIND

http://diana.uthct.edu/genefind.html

The Bioinformatics Research Group of the University of Texas Health Center at

Tyler is pleased to announce the availability of its GeneFIND Server for

protein family identification.

GeneFIND (Gene Family Identification Network Design) is an integrated database search system that combines several search/alignment tools and ProClass database (http://diana.uthct.edu/proclass.html) to provide rapid and sensitive search results with enriched family information. Multi- level filters are used, starting with the fastest MOTIFIND neural networks, followed by BLAST search, SSEARCH (Smith-Waterman) sequence alignment, and motif pattern search.

The server currently provides large- scale on- line identification of

query

sequences for 942 protein families. Search results are returned as HTML

documents showing global and motif scores, alignment to best matched members of all possible ProSite protein groups and PIR superfamilies, motif pattern match, as well as links to corresponding ProClass family records.

Please cite the following reference in publications that benefit from the

GeneFIND family identification system:

Wu, C. H., Zhao, S., Chen, H. L., Lo, C. J. and McLarty, J. (1996). Motif identification neural design for rapid and sensitive protein family search. CABIOS, 12(2), 109- 118.

Please visit our site and send suggestions and comments to me at wu@uthct.edu.

Also contact me directly if you are interested in obtaining a copy of the

GeneFIND software program. I am looking forward to hearing from you!

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E- Mail : wu@uthct.edu

Fax : (903) 877- 5914

Phone : (903) 877- 7962

WWW URL : http://diana.uthct.edu/~wu

ProClass Database

http://diana.uthct.edu/proclass.html

The Bioinformatics Research Group of the University of Texas Health Center at

Tyler is pleased to announce the availability of its ProClass Database Server

for protein family information.

The ProClass database is a non- redundant protein database organized according to family relationships as defined collectively by ProSite patterns and PIR superfamilies. The ProClass database can facilitate protein family information retrieval, unveil domain and family relationships, and classify multi- domained proteins, by combining global and motif similarities into a single family

organization scheme.

The server provides on- line ID/keyword search for ProClass record retrieval,

with hypertext links to SwissProt, ProSite and PIR databases. Free copies of

the ProClass database can be obtained via anonymous FTP to:

ftp://diana.uthct.edu/pub/ProClass/

Please cite the following reference in publications that benefit from the

ProClass database:

Wu, C. H., Zhao, S. and Chen, H. L. (1996). A protein class database organized with ProSite protein groups and PIR superfamilies. Journal of Computational Biology, 3(4), 547- 561.

Please visit our site and send suggestions and comments to me at wu@uthct.edu. I am looking forward to hearing from you!

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Procrustes Gene Recognition Software

http://www- hto.usc.edu/software/procrustes/

Procrustes 4.0 is geared towards computational support of experimental

gene identification and annotation- quality gene predictions. The new distinctive features of Procrustes 4.01 are:

- identification of genes and exons for which the predictions are guaranteed to be correct (Las Vegas gene predictions)

- error- tolerant gene recognition

- construction of primer cover for PCR- based gene identification in large- scale sequencing projects (GenePrimer software)

- highly specific recognition of exons for selection of probes and PCR primers to cDNA (CASSANDRA software)

- recognition of incomplete genes in unfinished cosmid- size genomic

sequences via local spliced alignment

- new graphical outputs for multiple gene predictions and experimental gene identification

- assignment of confidence levels to gene predictions

- multiple gene predictions via suboptimal spliced alignment

- gene recognition based on similar domains rather than entire proteins

- gene recognition in different species.

PROCRUSTES is now available in commmand line version for incorporation in DNA sequence analysis pipelines.

The previous version of Procrustes is described in

Gelfand, M.S., Mironov, A.A.,Pevzner, P.A.

"Gene recognition via spliced sequence alignment", Proc. Natl. Acad. Sci. USA (1996), 93, 9061- 9066

and is protected by U.S. patent application "Combinatorial Gene Recognition" 60/035,720.

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!

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

CancerWEB

http://

www.graylab.ac.uk/cancerweb.html

CancerWEB is a cancer information resource site based in the UK. It has been running for 2 years and provides information and resources for patients, clinicians and scientific researchers. The site is well organised and has a fast search engine to locate documents. We hope that you will visit the site and that you find the information of benefit. There are NO access restrictions and NO charges whatsoever.

CancerWEB is also the UK redistributor of the NCI PDQ database, including the CancerNET and CancerLIT files.

All sections can be easily found from the home page, but we also have:

Information for clinicians

(http://www.graylab.ac.uk/cancerweb/clinical.html)

Information for patients

(http://www.graylab.ac.uk/cancerweb/patients.html)

SiteNET

A comprehensive listing of cancer and academic institutions, hospitals and anonymous FTP sites. The entries are located geographically.

(http://www.graylab.ac.uk/cancerweb/sitenet.html)

CancerWEB Library

Pointers to the CancerLIT files and other resources to aid research and reference information.

(http://www.graylab.ac.uk/cancerweb/library.html)

Educational Resources

Links to other sites that contain quality information relevant to education of a number of medical specialities, including oncology.

(http://www.graylab.ac.uk/cancerweb/educate.html)

Global Cancer Links

A listing of other WWW resources relating to cancer, all arranged by tumour type. (http://www.graylab.ac.uk/cancerweb/further.html)

Dr. Graham Dark

CancerWEB , The UK Cancer Resource Site , Gray Laboratory

Northwood, Middlesex HA6 2JR, UK.

Phone: Int +44 (0)1923 828611

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cancerweb@www.graylab.ac.uk

webwizard@www.graylab.ac.uk

http://

www.graylab.ac.uk/cancerweb.html

Biological Data Transport Bioinformatics Resource

http://www.data- transport.com

From this resource, several kinds of bioinformatics related searches can be

executed - to GenBank, the MEDLINE molecular biology subset, OMIM, Entrez,

the BCM Search Launcher, PDB, BLAST, GDB, etc. Direct searching of several life sciences vendor resources are available as

well, all in one centralized location.

We've simplified the UI to these free public resources significantly - you

may find the Query Depot useful when you want to quickly scan for info at

the start of your search for information on the Internet.

Looking forward to your continued suggestions for additions and changes.

Help us to continue making this resource a high value time saver for you,

R. Scott Jokerst (510- 648- 8229) scott_jokerst@data- transport.com

Biological Data Transport http://www.data- transport.com

Bringing FOCUS to life sciences informatics, product, & services resources

WHAT HAPPENED TO THE FARSIDE CARTOON?????

A common feature of this award winning newsletter (didn't know we won an award? Well we awarded ourselves the first annual ISICR newsletter award for newsletters deserving an award) has been The Farside by Gary Larson. It turns out United Press Syndicate made a little error when it told us we could use 4 cartoons/year. It seems that was only permitted if you published a monthly newsletter. Quarterly newsletters are only permitted 1/year. Since we ran our cartoon in March, we CAN'T USE ANYMORE THIS YEAR. Now if any ISICR members know Mr. Larson personally, please get him to do a cartoon just for us!. Then we can syndicate it and sell lots of T shirts. In lieu of a cartoon, we are offering a FAMOUS QUOTE from Mr. Larson:

Great moments in Science: Einstein determines that time actually is money

Now for any budding cartoonists we may have, here is a box to be filled in with an original cartoon, suitable for all audiences. Fill it in and send it back so we can use it in one of the next 2 issues.

Title here YOUR Name Here

Funny caption here

Developmental Studies

Hybridoma Bank

Under the auspices of the National Institute of Child Health and Human Development, a hybridoma bank has been established to supply

investigators with monoclonal antibodies at cost which are useful for developmental studies. Monoclonal antibodies may be ordered in the form of tissue culture supernatant, partially purified Ig, or ascites fluid; selected hybridomas are also available. All materials distributed by the Bank are to be used for research purposes only and are not to be distributed to any third party. The Bank is actively engaged in acquiring and developing additional hybridomas to augment the current collection.

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Developmental Studies Hybridoma Bank

University of Iowa

Department of Biological Sciences, 436 BB

Iowa City, Iowa 52242- 1324

Telephone: (319) 335- 3826

Clinical Trials

ITA- GICAT- C/890301 EU- 96054. Phase II pilot study of Epirubicin/ Bleomycin/

Vinblastine/Prednisone with G- CSF and either Zidovudine or Didanosine in HIV- associated Hodgkin's disease. Contact: Umberto tirelli, Aviano, Italy. TEL: 0434- 659284

CCG- 0935. Phase I study of MOAB Ch 14.18 with GM- CSF immediately following autologous marrow or PBSC transplantation in children with neuroblastoma or other GD2- positive malignancies. Contact: M. Fevzi Ozkaynak, Valhalla, NY. TEL: 914- 285- 7997

SWOG- 8790 INT- 0083. Phase III randomized comparison of adjuvant intraperitoneal Interferon alpha vs no further treatment in patients with stage III ovarian carcinoma with no evidence of disease at second- look laparotomy following platinum- based chemotherapy.

Contact: David Samuel Alberts, Tucson, AZ. TEL: 520- 626- 7685

T96- 0056H. Phase I trial of oral 9- cis- retinoic acid and interferon - alfa in patients with AIDS- associated Kaposi's sarcoma. Contact: Carolyn Wasserheit- Lieblich,New York, NY. TEL: 212- 263- 6485

JMC- V96- 1104 NCI- V96- 1104. Phase I study of intraprostatic injections with leukocyte interleukin for advanced hormone- refractory prostate cancer. Contact: Michael Mastrangelo, Philadelhia, PA. TEL: 215- 955- 8875

DUMC- 93122 NCI- H96- 1111. Phase I study of interleukin- 2 gene- modified autologous tumor cell vaccine in advanced breast cancer. Contact: H. Kim Lyerly, Durham, NC. TEL: 919- 681- 8350

CALGB- 9621. Phase I study of MDR (multidrug resistance) modulation with PSC- 833 with a pilot study of cytogenetic risk- adapted consolidation followed by a phase II pilot study of immunotherapy with recombinant interleukin- 2 (RIL- 2) in previously untreated AML patients less than 60 years old. Contact: Joanne Coburn, Lebanon, NH. TEL: 603- 650- 6720

T96- 0036. Interleukin- 12 and EPOCH chemotherapy in untreated and interleukin- 12 in previously treated AIDS- related lymphoma. Contact: Wyndham H. Wilson, Bethesda, MD. TEL: 301- 435- 2415

FAMOUS QUOTES

Always take a job that is too big for you

Harry Emerson Fosdick

Teaching Help Needed

This Fall I will start a new position as Assistant Professor of Microbiology in which I will be teaching Immunology plus an Immunology Laboratory to senior- level

college students. I am in the process of gathering information on various resources for 1) experiments for the

immunology laboratory and 2) laboratory manuals for the immunology laboratory.

Does any ISICR member have this information or know of someone or

someplace where I may obtain this kind of information? Iwould be very grateful for any information regarding this. I look forward to hearing from you. Thank you very much!

Manuel F. Varela, Ph.D.

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Reviews of Interest

Billiau, A. Interferon- g in Autoimmunity. *Cytokine and Growth Factor Reviews* 7: 25, 1996.

Burdin, N., Rousset, F., and Banchereau, J. B- cell- derived IL- 10: production and function. *Methods: A Companion to Methods in Enzymology* 11: 98, 1997.

Decker, T., Kovarik, P., and Meinke, A. GAS elements: a few nucleotides with a major impact on cytokine- induced gene expression. *J. Interf. and Cyt. Res.* 17: 121, 1997.

Gonda, T.J. and D'Andrea, R.J. Activating mutations in cytokine receptors: implications for receptor function and role in disease.

Blood 89: 355, 1997.

Hall, G. L., Compston, A., and Scolding, N. J. Beta- interferon and multiple sclerosis. *Trends Neurosci.* 20: 63, 1997.

Liu, L., Damen, J. E., Ware, M., Hughes, M., and Krystal, G. SHIP, a new player in cytokine induced signalling. *Leukemia* 11: 181, 1997.

Murray, H.W. Interferon- gamma in infection and immunoparalysis. *Intensive Care Med.* 22: S455, 1996.

Pallone, F. and Monteleone, G. Regulatory cytokines in inflammatory bowel disease. *Aliment. Pharmacol. Ther.* 10(Suppl. 2): 75, 1996.

Tsokos, G.C. Lymphocytes, cytokines, inflammation, and immune trafficking. *Curr. Op. in Rheum.* 8: 395, 1996.

COMMON QUESTIONS TO THE EDITORS

In the spirit of full disclosure, we thought we would reprint some of the most common questions to the editors.

Q. Do you get paid for being editors?

A. Well, there is a small ISICR budget item providing $150,000/year for the editors that we hope has been overlooked. The only small problem is that it is not payable until 2096 and must be collected in person between 11- 11:10 PM at the White House.

Q. Sometimes I can't even understand the words in the web site descriptions. Do you all really know what those sites are really good for?

A. You think with a 14.4 modem and an old 486 we have the patience to download all that stuff? Actually, if it has the word "protein" or "nucleotide" in the description we figure somebody might find it useful.

Q. How do you find the time to dig up those reviews? I've never heard of some of those journals.

A. It;'s amazing the time one has after a site visit committee has gone over one's research program.

Q. Why do you all do this newsletter? What's in it for you?

A. It;'s amazing the time one has after a site visit committee has gone over one's research program. Actually, I'm shocked that you would ask this question. It's not our fault that the society is opening a new headquarters office in Maui and that the newsletter editorial board has found quartly meetings absolutely essenti8al for producing this award winning document.

Q. What would it take to get something I write in the newsletter?

A. We are willing to consider all submissions from ISICR members. It does help however, if submissions are accompanied by something green containing a famous US historical picture. Alternatively, chocolate helps a lot.

HELP US WITH THIS NEWSLETTER

Is there anything you would like to see in the newsletter? Remember we welcome complaints as well, provided that they are sent care of the ICS. If you have anything constructive for us or if you want to send us food or money, contact:

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BE A SPORT, PAY YOUR STUDENT/POSTDOCS MEMBERSHIP FEE OF $10! DON'T LET THEM MISS OUT ON FUTURE ISSUES OF THE SOCIETY NEWSLETTER!

1997

ISICR MEETING

OCT. 19- 24

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HOUSING RESERVATION DEADLINE

SEPTEMBER1