FOSTERING COMMUNICATION AND COLLABORATION

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

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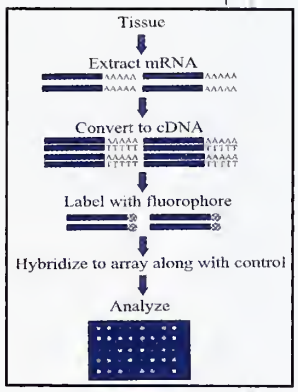
IN THE MAINSTREAM: MICROARRAY RIVULETS FOUND CAMPUS-WIDE

by Joanne Peter

Microarray technology, a technique used for the rapid screening of genes using chips containing immobilized cDNA fragments, has burst upon the NIH intramural scene.

An Array of Users

The Microarray User Group, an NIH special interest group that began in 1998, grows weekly and is now approaching 300 members, almost half of whom are intramural investigators (others hail from academia and industry in this country and around the world).



The ranks are filled with investigators from nearly every institute, with the NCI cohort currently the largest.

According to Katherine Peterson of NEI, who heads the group, the range of experience among members encompasses "Affymetrix experts, who use oligonucleotides on a silicon wafer [and] those scientists who use spotted arrays on a nylon membrane." Members use the group to exchange ideas, listen to guest speakers, and share equipment.

Another element of the research involves the Center for Information Technology here on campus. Peter Munson, acting chief of the Mathematical and Statistical Computing Lab, notes that "there has been a real

continued on page 11

LOOKING NIFTY AT 50: NIH SALUTES NEW LABS

by Fran Pollner

Add buildings 2, 3, 7, and some of 6 and you get 50—clearly the whole is greater than the sum of its parts.

Building 50—the Louis Stokes Laboratories—was officially welcomed onto the NIH campus in June in a ceremony enlivened by jazz combos, former HHS secretary Louis Sullivan, and Congressman Stokes himself. This most recent NIH edifice will be home to intramural scientists from NIDDK, NHLBI, NIAID, NIAMS, NHGRI, NIDCD, and NCI—as well as the labs of the new NEI director, Paul Sieving, and the new NIDCR director, Lawrence Tabak.

All told, there are 253 lab modules in Building 50—ranging from 37 to 44 on each of its six floors and arranged in neighborhood clusters. The essence of the research to be conducted in the building is structural and cell biology and microbiology; the essence of its design is to facilitate collaboration. The ease of interaction with colleagues who are "asking similar biological questions" was extolled by Maria Morasso of NIAMS and John Carpten of NHGRI, two tenure-track investigators who could well bump into one another in Building 50 during their respective explorations into the molecular basis of inherited disease and the molecular basis of normal development.

As of early July, floors 2, 3, and most of 4 were occupied; by September's end, the remaining floors will be filled with the estimated 650 people assigned Building 50 space, more than 600 of whom are scientists, according to the building's award-winning design and construction project officer, Frank Kutlak.

A state-of-the-art vivarium, in the basement, is managed by NIAID but used by all the institutes, with their allotted space proportional to the square footage of their lab space in the building.

'By Act of Congress
This building is designated as
THE LOUIS STOKES LABORATORIES
Congressman Louis Stokes served as a distinguished member of the United States Congress for 30 years, representing his native State of Ohio. He was elected to the House Appropriations Committee in 1971, and served on the House Appropriations Subcommittee on Health and Human Services, where he was a strong proponent of biomedical research. His dedicated service to the nation is marked by hard work and a commitment to fairness. His unwavering support of the National Institutes of Health is defined by judicious advocacy and a determination that through research NIH can help eliminate disparities in health among the country's minority, poor, underserved and disadvantaged communities.'

An NMR suite is shared by Ad Bax of NIDDK and Jim Ferretti of NHLBI, and an electron microscopy suite is shared by Alasdair Steven of NIAMS and Sriram Subramaniam of NCI. ■

For a Building 50 history, go to
<http://des.od.nih.gov/building—50>

CONTENTS

Building Infrastructure for Science at NIH: The Three Sides to Our Stories

Michael Gottesman

On June 14, NIH dedicated the Louis Stokes Laboratories (also known as Building 50)—the second new building to be opened on the NIH campus in the past year. The first was the the Vaccine Research Center, where intramural scientists started setting up shop late last summer. With the looming superstructure of the Clinical Research Center on the skyline, our hat trick will be complete: a basic science building, an applied science building, and a clinical research building.

fran pollner

Back-door veranda at the Louis Stokes Laboratories affords an open-air space to eat lunch and talk science

These structures manifest the three legs of the NIH research effort, which begins with advanced technologies and new approaches to integrative biology, involves the application of these approaches to public health problems (such as the development of vaccines against HIV and other diseases), and reaches its destination in the innovative clinical research with human participants (patients and healthy volunteers) carried out in the Clinical Center.

I hope you will all get a chance to visit the new Louis Stokes building. It is an attractive structure with a spacious plaza that beckons to visitors and employees coming onto campus from the Metro stop. And its beauty is well beyond façade-deep. The edifice has won several awards for unique designs that conserve energy.

The labs are open and sunlit, with ample space for storage and equipment. They are arranged in neighborhoods to encourage interaction among scientists, both horizontally (same floor) and vertically (adjacent floors). Use of interstitial space between the floors for utilities means that as science changes, new requirements can easily be met without disrupting the labs below and above. This will extend the usable lifetime of the building by many years.

The basement of the building houses a state-of-the-art vivarium and two unique spaces: a large chamber for big magnets used in NMR structural studies and a vibration-free slab with high-end electron microscopes for use in cryomicroscopy and electron crystallography.

With the looming superstructure of the Clinical Research Center on the skyline, our hat trick will be complete: a basic science building, an applied science building, and a clinical research building

This building replaces buildings 2, 3, and 7—and none too soon!

The Vaccine Research Center has been open for business since last fall (see *The NIH Catalyst*, September–October 2000, "VRC Takes Its Place in Campus Skyline," page 1).

It has an inviting atrium and two-story cyber cafe, as well as an electronically enabled conference center and terraces on the second floor. The labs are open with large windows. The many break areas encourage scientific interactions. The top floor has facilities to produce small amounts of material for early-phase vaccine tests, and there's a small rodent vivarium below ground.

Recruitment to the VRC is well under way, and it should be fully staffed within the next few months. Staffing will emphasize the paradigm that drove the formation of the center: the resynthesis of immunology, virology, and vaccinology into a modern science that allows creation of effective vaccines against diseases that have proven resistant to traditional approaches. According to Gary Nabel, VRC director, the very first HIV vaccine trial based on a construct made in the VRC will soon start in the Clinical Center.

Work continues on the Clinical Research Center, which is scheduled to open in the late summer or fall of 2003. These new facilities will provide research beds and support for a modern clinical research facility and lab support for the clinical researchers who work there. Once the new CRC has opened, the original Building 10 will be renovated in phases, beginning with the central core of the building, to provide modern laboratory spaces for our scientists. We anticipate this process will begin in 2004.

Kudos to all of the people who have contributed to the concept, design, and construction of these magnificent new buildings, and to the scientists who will convert this infrastructure into biomedical progress.

—Michael Gottesman
Deputy Director for Intramural Research

Shared Training Programs In the Intramural Research Program

Program	*Participants*	*Number of Participants/Contacts*	*Type of Program/Selection*
Undergraduate Scholarship Program	Undergrads from disadvantaged backgrounds	67 <http://ugsp.info.nih.gov>	Scholarships. Laboratory training at NIH during summers; postgraduate training one year for each year of scholarship award. Selection competitive and central.
Loan Repayment Programs	Ph.D.s, M.D.s, and D.D.S.s in AIDS, clinical, or other research	108 <http://lrp.info.nih.gov>	Student loan repayment. Candidates recruited by ICs for research positions, but competitively, centrally selected for loan repayment benefits
NIH/FAES Summer Student Program	Area high school students	25 new, 15 returning Adrian Martinez, FAES	Summer lab research experience with weekly presentations. Central selection; support from ICs
HHMI/NIH/FAES teacher training	Area high school teachers	17 Adrian Martinez, FAES	Lab experience; weekly meetings with the director of the Office of Science Education and the deputy director for intramural research. Central selection
HHMI Research Scholars	2nd or 3rd year medical and dental students	42 (5–10 returnees)	Laboratory research experience. Central selection by mentors' panel
Clinical Research Training Program	M.D.s and D.D.S.s with one year of clinical rotations	17 <http://www.training.nih.gov>	Training in the conduct of clinical research. Selection by central committee
NIH Academy	Recent college graduates	10 <http://www. training.nih.gov>	Postbaccalaureate training with emphasis on health disparities. Central selection with support from ICs
Biomedical Engineering Summer Internship Program	Juniors in engineering	12 R. Lutz, director	Laboratory research experience in biomedical engineering. Central selection. Foundation for the NIH support
Graduate Program Partnerships	Ph.D. and M.S. students	154 <http://gpp.nih.gov>	Doctoral and masters-level research training. Students selected by university in partnership with NIH
IRTAs: 1. Postbac 2. Technical 3. Postdoctoral	1. Postbacs 2. Postbacs and Masters 3. Postdocs	1. 250 2. 100 3. 3,200 <http://www.training.nih.gov>	1. Training to cultivate interest in science careers 2. Training for technicians 3. Training to support research careers
Clinical electives program	2nd or 3rd year medical and dental students	35 <http://www.training.nih.gov>	Rotations in 23 areas, including individualized research tutorials
Summer internship program	High school, college, and grad students	700 <http://www.training.nih.gov>	Laboratory research training, with selections made by individual investigators
Summer research fellowship program	Medical and dental students	100 <http://www.training.nih.gov>	Laboratory research training, with selections made by individual investigators
Office of Education website	All levels of trainees for all institutes	<http://www.training.nih.gov>	Information and online applications for training programs; positions available

Research Festival Poster Deadline, August 6!

The NIH Research Festival will be held October 2–5. The deadline for online poster submission is Monday, August 6 at 5:00 p.m. For a preliminary schedule and online poster registration form, visit **<http://festival01.nih.gov>**.

For more information about poster submission or the festival, contact Paula Cohen at 496-1776 or **<pc68v@nih.gov>**.

Major Shared and Multi-Institute Research Resources In the Intramural Research Program

Research Resource	*Location*	*Governance/Contact/Participants*	*Research Services/Review*
Legacy Resources—Available to All Institutes and Centers			
Veterinary Resources Program (VRP)	Building 14–28 complex, Bethesda; Poolesville	Office of Research Services (ORS). M. Eckhaus, acting director <http://www.nih.gov/od/ors/dirs/vrp/vrphome.htm>	Veterinary services (surgery, radiology, pharmacy, nutrition, rodent genetic repository, animal behavior and enrichment); animal husbandry, procurement, quarantine, and health surveillance; diagnostics (pathology, bacteriology, parasitology, serology); embryo cryopreservation and rederivation. Review: Shared Resources Subcommittee (SRS), ICs
Bioengineering (Division of Bioengineering and Physical Sciences)	Building 13	ORS. R. Leapman. acting director <http://www.nih.gov/od/ors/dbeps/index.htm>	Drug delivery, molecular interactions, image analysis, instrumentation, supramolecular structure, ultramicroscopic immunochemistry. Review: SRS, ICs
Scientific Equipment and Instrumentation Branch	Building 13	ORS. J. Robbins, chief <http://seib.od.nih.gov>	Maintain scientific equipment and computers; design and fabricate custom instruments; lease and sell scientific and medical equipment
Medical Arts and Photography Branch	Building 10, B2 level	ORS. L. Canady, chief; <http://www.nih.gov/od/ors/dirs/mapb/mapbhome.htm>	Medical illustration, photomicroscopy, photomacroscopy, scientific posters
NIH Library	Building 10	ORS. S. Grefsheim, director <http://nihlibrary.nih.gov>	Full-service library, including electronic journals, electronic document desktop delivery and translations. Review: Users committee, ICs
Center for Information Technology (CIT) Division of Computational Bioscience	Building 12 complex	CIT. R. Martino, acting director <http://www.cit.nih.gov/science.html>	Image processing, bioinformatics, computational methods and algorithms, computer engineering, bioscience, molecular modeling, mathematical and statistical computing. Review: SRS, ICs
Multi-Institute Shared Services			
NIH Magnetic Resonance Imaging Facility	Building 10, In Vivo NMR Center	Lead IC: NINDS. A. Koretsky, director, and steering committee. Participants: All ICs but NIEHS	Human and animal MRI; other IC MRI instruments available. Review: ICs, SRS, steering committee
Mouse Imaging Facility	Building 10, In Vivo NMR Center	Lead ICs: NINDS, NHLBI. A. Koretsky, director, and steering committee. Participants: All ICs but NIEHS are paid charter members	Mouse radiologic imaging (from fall 2001); 7T rodent MRI, microCT, high-frequency ultrasound, laser Doppler. Review: SRS, ICs, steering committee
Structural Biology NMR	Buildings 5, 6A, and 50	Lead ICs: NINDS, A. Bax NHLBI, J. Ferretti NIDCR, D. Torchia Also: NCI	Molecular structural imaging: 500MHz cryoprobe NMR spectrometer; 750 MHz NMR spectrometer; 800 MHz NMR spectrometer; now shopping for 900 MHz NMR spectrometer. Review: ICs
Center for Inherited Disease Research	Bayview Research Campus, Baltimore	Lead contracting IC: NHGRI, D. Valle, Johns Hopkins University PI. Access Committe: <http://www.cidr.jhmi.edu>. Any IC may request service	Genotyping, DNA banking, statistical genetics consultation, mouse genotyping. Review: CIDR Access Committee (Jerry Roberts, NHGRI)

Research Resource	*Location*	*Governance/Contact/Participants*	*Research Services/Review*
NIH Intramural Sequencing Center	Advanced Technology Center, Gaithersburg, MD	Lead IC: NHGRI, E. Green, director. Multi-Institute Access Review Committee: <http://www.nisc.nih.gov>. Participants: NHGRI, NCBI, NIDCD, NIAAA, NIDA, NHLBI, NIDDK, NICHD, NEI, NIAMS, NINDS, NIDCR, NIEHS, NIMH	Production-scale DNA sequencing, assimilation and analysis of sequence data, acquisition and development of new sequencing chemistry, instrumentation, sequence analysis software. Review: Users Committee
Microarray services	1. Multiple sites 2. Building 12A	1. NHGRI, NCI, NIA 2. CIT (P. Munson, J. Powell), with contributions from NINDS, CC, NHLBI, NIAID, NCI	1. Chips prepared by special arrangement. Review: ICs. 2. Analysis, database storage and retrieval, bioinformatics services for microarray data. Review: ICs
Protein Expression Lab	Building 6B, Room 1B130	Lead IC: NIAMS, P.Wingfield, chief <http://www.nih.gov/niams/about/irp/pelhome.htm. Participants: NHGRI, NCBI, NIDCD, NIAAA, NIDA, NHLBI, NIDDK, NICHD, NEI, NIAMS, NINDS, NIDCR, NIEHS, NIMH	Expression, purification, and structural characterization of HIV and HIV-related proteins via a variety of techniques; protein EXE software; supply HIV-1 protease. Review: IATAP, ICs
Biotechnology unit (pilot plant)	Building 6, Room B1–33	Lead IC: NIDDK, J. Shiloach, director <http://www.niddk.nih.gov/intram/people/jshiloac.htm>. Major client: NICHD Other recent users: NEI, NCI, NHLBI, NIDCR. Any IC may request service	Production and purification of biological material, especially scale-up protein production and purification. Review: BSC, ICs
Mass spectroscopy	Building 8A, Room B2A19–21; Building 10	Lead ICs: NIDDK, NHLBI, NIMH, NIAID, NINDS; <http://proteome.nih.gov/shared.html>. advisory group	QTOF–LCMS; high-resolution magnetic sector; MALDI, LC-ion trap. Review: ICs, BSC
Bioinformatics support	Building 38A, NCBI	Lead IC: NCBI. Any IC may request training	Extended training in bioinformatics for intramural investigators. Review: ICs
Synchrotrons: 1. Advanced photon source. 2. National synchrotron light source	1. Argonne National Lab 2. Brookhaven National Lab	DOE. Lead IC: NCI; major users: NIDDK, NIEHS, NIAID, NHLBI. 1. <http://www.aps.anl.gov> 2. <http://nslsweb.nsls.bnl.gov/nsls/Default.htm>	1. High-brilliance X-ray beams 2. Intense focused beamlines throughout the spectrum
Integrative Neural Immune Program	Multiple locations	NIMH, NINDS, NCI, NIAID, NIAMS, NIA Esther Sternberg, director	Lecture series, conferences, workshops, retreat; training that bridges neuroscience and immunology; cyberlab to oversee virtual cores
MULTI-INSTITUTE FACILITIES			
Warren Grant Magnuson Clinical Center	Building 10/ future Clinical Research Center	Board of Governors. John Gallin, director <http://www.cc.nih.gov/>. Access to the Clinical Center is available to all ICs	Research hospital that accommodates 300 inpatients and outpatients and provides comprehensive services and facilities in support of clinical research sponsored by the ICs. Review: Joint Commission on Accreditation of Healthcare Organizations, BSC. Advisory: CC Research Steering Committee, CC Board of Governors
Neuroscience Center	Site of Buildings 35 and 36	NINDS, NIMH, NEI, NIDA, NIAAA, NIA, NIDCR, NHGRI, and NICHD	Neuroscience research Review: BSCs, ICs
Vaccine Research Center	Building 40	NIAID, NCI, OAR. Gary Nabel, director <http://www.niaid.nih.gov/vrc/default.htm	Comprehensive HIV (and eventually other) vaccine research, development, and testing. Review: BSCs, ICs
Musculoskeletal Center	Navy Medical	NIAMS (P. Lipsky), NIA, NIDCR, NICHD	Musculoskeletal, cartilage, and orthopedics research. Review: BSC, ICs

Interinstitute Interest Group Directory

Web Access

Note: Although not all the sites are up to date, nearly all the Interest Groups have web sites that can be accessed through the NIH Home Page (<http://www.nih.gov/>) by clicking on "Scientific Resources," then "Special Interest Groups," and then the targeted group(s).

Major Interest Groups

Cell Biology Interest Group
Meeting time: Once every four months
Meeting place: Building 32, Library
Contact: Jennifer Lippincott-Schwartz
Phone: 402-1010; 402-1009
E-mail: <jlippin@helix.nih.gov>
ListServ: subscribe to CELBIO-L

Clinical Research Interest Group
Meeting time and place: sponsors CC Grand Rounds once every other month
Contact: Cliff Lane
Phone: 496-7196
E-mail: <clane@nih.gov>

Genetics Interest Group
Meeting time: Usually 2nd Tuesday, 3:30 pm; may sponsor several symposia a year
Meeting place: Building 49, Conference Room A and B; symposia sites would vary
Contact: Dan Kastner
Phone: 496-8364
E-mail: <kastnerd@exchange.nih.gov>
ListServ: subscribe to <GIG-L@list.nih.gov>

Immunology Interest Group
Meeting time: Each Wednesday (except summer), 4:15 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: Jon Yewdell
Phone: 402-4602
E-mail: <jyewdell@nih.gov>
ListServ: subscribe to IMMUNI-L by joining the interest group at its web site

Molecular Biology/Biochemistry Interest Group
Meeting time: Yearly to consider speakers
Meeting place: Building 8, Room 122
Contact: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>

Neuroscience Interest Group
Meeting time: alternate Fridays, 4:30 pm
Meeting place: Cloisters, Rathskeller
Contact 1: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@helix.nih.gov>
Contact 2: Betsy Murray
Phone: 496-5625, X-227
E-mail: <eam@ln.nimh.nih.gov>

Structural Biology Interest Group
Meeting time and place: Announced to members by e-mail and regular mail
Contact 1: Adrian Parsegian
Phone: 496-6561
E-mail: <aparsegi@helix.nih.gov>
Contact 2: Marius Clore
Phone: 496-0782
To register for e-mail announcements:
E-mail <kesselm@mail.nih.gov>

Other Interest Groups

AIDS Interest Group
Meeting time and place: Varies
Contact: Fulvia Veronese
Phone: 496-3677
E-mail: <veronesef@od.nih.gov>
ListServ: subscribe to AIDSINTG-L

Apoptosis Interest Group
Meeting time: 1st Monday, 4:00 pm
Meeting place: To be arranged
Contact 1: Colin Duckett
Phone: 594-1127
E-mail: <ducketc@helix.nih.gov>
Contact 2: Yves Pommier
Phone: 496-5944
E-mail: <yp4x@nih.gov>

Behavioral and Social Sciences Interest Group
Meeting time: Varies, in the fall and spring
Meeting place: See NIH Calendar of Events
Contact: Ronald Abeles
Phone: 496-7859
E-mail: <abeles@nih.gov>

BSSR Methodology and Measurement Interest Group
Meeting time: 1st or 2nd Tuesday, 8:30 am
Meeting place: Building 45, Room 3AS10
Contact: Jared Jobe
Phone: 435-0407
E-mail: <Jared_Jobe@nih.gov>

Bioethics Interest Group
Meeting time: 1st Monday (except 2nd Monday following holidays; usually does not meet during summer), 3:00 pm
Meeting place: Natcher, Room D, or Building 31, conference room; check yellow sheet or web site
Contact: Miriam Kelty
Phone: 496-9322
E-mail: <mk46u@nih.gov>
Sign up at <http://BIOETHICSinterestgroup@list.nih.gov/>

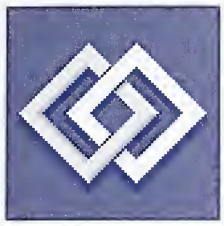
Biomedical Computing Interest Group
Meeting time: Alternate Fridays, 3:00 pm
Meeting place: Through August, Building 10, Room 9S235; varies after that
Contact: Jim DeLeo
Phone: 496-3848
E-mail: <jdeleo@nih.gov>
Contact 2: Susan Harris
Phone: 435-8721
ListServe: subscribe to BCIG-L

Biophysics Interest Group
Meeting time and place: Varies (often Building 10, Bunim Room
Contact: Peter Basser
Phone: 435-1949
E-mail: <pjbasser@helix.nih.gov>

Birth Defects and Teratology Interest Group
Meeting time: Quarterly seminars
Meeting place: Videoconference between Bethesda and Research Triangle Park, N.C.
Contact: Megan Adamson
Phone: 443-4354
E-mail: <madamson@willco.niaaa.nih.gov>

Breast Cancer Think Tank
Meeting time and place: Varies
Contact 1: Barbara Vonderhaar
Phone: 496-3625
E-mail: <bv10W@nih.gov>
Contact 2: JoAnne Zujewski
Phone: 402-0985

Calcium Interest Group
Meeting time: Usually Tuesday, 3:00 pm
Meeting place: Building 49, Room 1A50
Contact 1: Arthur Sherman
Phone: 496-4325
E-mail: <asherman@nih.gov>
Contact 2: Indu Ambudkar
Phone: 496-1478
ListServ: Subscribe to CALCIUM-L



Cancer CAM Research Interest Group
Meeting time and place: Varies
Contact: Jeffrey White
Phone: 435-7980
E-mail: <jeffreyw@mail.nih.gov>

Chemistry Interest Group
Meeting time: (Almost) monthly seminars
Meeting place: Varies
Contact 1: John Schwab
Phone: 594-5560
E-mail: <schwabj@nigms.nih.gov>
Contact 2: Kenneth Kirk
Phone: 496-2619

Chromatin and Chromosomes Interest Group
Meeting time: One Thursday a month, 11:00 am
Meeting place: Building 5, Room 211
Contact: David Clark
Phone: 496-6966
E-mail: <djclark@helix.nih.gov>

Clinical Immunology Interest Group
Meeting time: Monthly, last Wednesday, noon
Meeting place: Building 10, Room 9S235
Contact: Oral Alpan
Phone: 402-3447
E-mail: <oalpan@nih.gov>

Clinical Pharmacology Interest Group
Meeting time: 2-3 times a year in conjunction with special lectures in the NIH Principles of Clinical Pharmacology course, 6:30–7:30 pm
Meeting place: Building 10, Lipsett
Contact: Donna Shields
Phone: 435-6618
E-mail: <dshields@mail.cc.nih.gov>

Cognitive Neuroscience Consortium
Meeting time: Every two months, last Wednesday, 4:15 pm
Meeting place: Building 31, Room 6C10 (starts 9/26/01; extramural program directors' forum: last Friday every 3rd month, 3:00 pm, NSC Building, Conf. Rm. 2120, starts 8/31/01)
Contact: Emmeline Edwards
Phone: 496-9964
E-mail: <ee48r@nih.gov>

Cornea Interest Group
Meeting time: 1st Monday, 8:30 am
Meeting place: Building 6, Room 409
Contact 1: Joram Piatigorsky
Phone: 496-9467
E-mail: <joramp@intra.nei.nih.gov>
Contact 2: Janine Davis
E-mail: <davisj@intra.nei.nih.gov>

Cultural and Qualitative Research Interest Group
Meeting time: 2nd Tuesday, 9:15 am
Meeting place: EPN, room varies
Contact 1: Suzanne Heurtin-Roberts
Phone: 594-6655
E-mail: <sheurtin@mail.nih.gov>
Contact 2: Emeline Otey
Phone: 443-1636 or 3728

Cytokine Interest Group
Meeting time: three to four symposia/year
Meeting place: Varies; one symposium/year at NCI-Frederick
Contact 1: Howard Young
Phone: 1-301-846-5700
E-mail: <youngh@mail.ncifcrf.gov>
Contact 2: Warren Strober
E-mail: <ws9j@nih.gov>

Developmental Biology Interest Group
Meeting time and place: Varies
Contact 1: Tom Sargent
Phone: 496-0369
E-mail: <tsargent@nih.gov>
Contact 2: Peggy Zelenka
E-mail: <zelenkap@intra.nei.nih.gov>

DNA Repair Interest Group
Meeting time: 3rd Tuesday, 12:30 pm
Meeting/Videoconference: Natcher, Room H; GRC (Baltimore), Room 1E03; FCRDC, Building 549, Conf. Rm. A; NIEHS (Research Triangle Park, NC) Building 101, Room B200; SUNY, Stony Brook; Univ. of Texas, M.D. Anderson Cancer Center, Smithville, TX; Lawrence Livermore (CA) National Laboratory; Univ. of Michigan, Ann Arbor; Univ. of Kentucky, Lexington; Brookhaven National Laboratory, Upton, NY; Univ. of Pittsburgh
Contact 1: Kenneth Kraemer
Phone: 496-9033
E-mail: <kraemerk@nih.gov>
Contact 2: Vilhelm Bohr
E-mail: <vbohr@nih.gov>

Domestic Violence Research Interest Group
Meeting time and place: To be announced
Contact: John Umhau
Phone: 496-7515
E-mail: <umhau@nih.gov>

Drosophila Interest Group
Meeting time: 3rd Tuesday, 1:15 pm
Meeting place: Building 6B, Room 4B429
Contact 1: Sue Haynes
Phone: 295-9791
E-mail: <shaynes@usuhs.mil>
Contact 2: Jim Kennison
E-mail: <kennisoj@exchange.nih.gov>

Drug Discovery Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room
Contact: John N. Weinstein
Phone: 496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Economics Interest Group
Meeting time and place: Varies
Contact 1: James A. Schuttinga
Phone: 496-2229
E-mail: <js41z@nih.gov>
Contact 2: Agnes Rupp
E-mail: <ar24f@nih.gov>

Endocrinology Interest Group
Meeting time and place: Varies
Contact 1: George Chrousos
Phone: 496-5800
E-mail: <George_Chrousos@nih.gov>
Contact 2: Phil Gold
Phone: 496-1945

End of Life Research Interest Group
Meeting time: Typically Thursdays, 3:00 pm, on an as-needed basis
Meeting place: Natcher, room as available
Contact: Ann Knebel
Phone: 402-6796
E-mail: <aknebel@nih.gov>

Epidemiology and Clinical Trials Interest Group
Meeting time and place: Varies (subscribe to ListServ for notices)
Contact: Martina Vogel-Taylor
Phone: 496-6614
E-mail: <martinav@nih.gov>
ListServ: subscribe to Epidem-L at <listserv@list.nih.gov>

Fluorescence Interest Group
Meeting time: Usually even Fridays, 4:00 pm; see website
Meeting place: Building 10, usually Room 5N264
Contact: Jay Knutson
Phone: 496-2557
E-mail: <jaysan@helix.nih.gov>
Contact 2: Dan Sackett
E-mail: <sackettd@mail.nih.gov>

Gene Therapy Interest Group
Meeting time: 2nd & 4th Thursday, 2:00 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: Fabio Candotti
Phone: 402-1833
E-mail: <fabio@nhgri.nih.gov>

Interinstitute Interest Group Directory

Genomics and Bioinformatics Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room
Contact: John N. Weinstein
Phone: 496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Glycobiology Interest Group
Meeting time and place: Varies
Contact: Diana Blithe
Phone: 435-6990.
E-mail: <blithed@nih.gov>
ListServ: Subscribe to GLYCO-L@LIST.NIH.GOV

GTP Binding Proteins Interest Group
Meeting time: Irregular
Meeting place: FAES Social & Academic Ctr.
Contact: R. Victor Rebois
Phone: 496-2007
E-mail: <rebois@box-r.nih.gov>

Hard Tissue Disorders Interest Group
Meeting time: Day varies, 9:30 am
Meeting place: Building 30, Room 117
Contact: Pamela Robey
Phone: 496-4563
E-mail: <probey@yoda.nidr.nih.gov>
Contact 2: Michael Collins
Phone: 496-4913

Head and Neck Cancer Interest Group
Meeting time: To be announced
Meeting place: Building 30, Room 117
Contact 1: Adrian Senderowicz
Phone: 594-5270
E-mail: <adrian.senderowicz@nih.gov>
Contact 2: Wendy Weinberg
Phone: 301-827-0709
E-mail: <weinberg@cber.fda.gov>

History of Biomedical Research Interest Group
Meeting time: Second Tuesday, 3:30 pm
Meeting place: Varies; check web site
Contact 1: NIH History Office
Phone: 496-6610
Contact 2: Victoria Harden
E-mail: <hardenv@od31tml.od.nih.gov>

Image Processing Interest Group
Meeting time: 3rd Thursday, 11:00 am
Meeting place: Building 10, Room B1N256
Contact 1: Benes Trus
Phone: 496-2250
E-mail: <trus@helix.nih.gov>
Contact 2: Matt McAuliffe
Phone: 594-2432

Imaging Ligand Development Consortium
Meeting time and place: To be announced (every 3 months; steering committee meetings will be held every 2 months in the Neuroscience Center)
Contact: Linda Brady
Phone: 443-5288
E-mail: <LB@helix.nih.gov>

Integrative Neuroscience Interest Group
Meeting time: Alternate Thursdays, 4:00 pm
Meeting Place: Building 49, Room 1A51
Contact: Betsy Murray
Phone: 496-5625, X-227
E-mail: <eam@ln.nimh.nih.gov>

In Vivo NMR Interest Group
Meeting time: Varies
Meeting place: Building 10, Room B1N256
Contact: Jeff Duyn
Phone: 594-7305
E-mail: <jhd@helix.nih.gov>

Java Interest Group
Meeting time and place: See <http://jig.nih.gov> for upcoming events and talks
Contact: Jai Evans
Phone: 594-2900
E-mail: <evansj@helix.nih.gov>

Knowledge Management Interest Group
Meeting time: 4th Wednesday, 2:30 PM (changes will be noted on NIH Calendar and KMIG website)
Meeting place: Wolff Conference Room, Building 10, Room 11S235
Contact 1: Geoffrey Marsh
Phone: 301-594-9683
E-mail: <geoff@mail.nih.gov>
Contact 2: Robert Lomax
E-mail: <lomaxr@mail.nih.gov>

Lambda Lunch (Bacterial and Phage Genetics)
Meeting time: Each Thursday, 11:00 am
Meeting place: Building 36, Room 1B13
Contact: Susan Gottesman
Phone: 496-3524
E-mail: <susang@helix.nih.gov>
Anonymous FTP site:FTP.CU.NIH.-GOV
directory "LAMBDA_LUNCH"

Light Microscopy Interest Group
Meeting time: Monthly, Tuesday, noon
Meeting place: Building 10, Room 4B51
Contact: James McNally
Phone: 402-0209
E-mail: <mcnally@exchange.nih.gov>

Lymphoma and Leukemia Interest Group
Meeting time: Varies
Meeting place: Building 10, Room 12S235a
Contact: Michael Bishop
Phone: 435-2764
E-mail: <mbishop@mail.nih.gov.>
ListServ: LLig-1

Mass Spectrometry Interest Group
Meeting time: 1st & 3rd Thursday, 10:30 am
Meeting place: Building 10, Room 7C101
Contact: Lewis Pannell
Phone: 402-2196
E-mail: <L_Pannell@nih.gov>

Membrane Microdomains Interest Group
Meeting time: 1st Tuesday, 12:00 noon
Meeting place: Building 10, Room 9C209
Contact: Teresa Jones
Phone: 496-8711
E-mail: <tlzj@helix.nih.gov>

Microarray Users Group
Meeting time and place: Varies
Contact: Katherine Peterson
Phone: 402-6537
E-mail: <petersonk@intra.nei.nih.gov>

Mitochondria Interest Group
Meeting time: 1st Monday, 3:00 pm
Meeting/Videoconference: Natcher, Room H; NIEHS, Research Triangle Park, NC; GRC, Baltimore; UC Davis; Univ. of Maryland, Baltimore
Contact: Steve Zullo
Phone: 435-3576
E-mail: <zullo@helix.nih.gov>

Molecular Modeling Interest Group
Meeting time: See <http://mmignet.nih.gov>
Meeting place: Building 12A, conf. rooms
Contact: Peter Steinbach
Phone: 496-1100
E-mail: <steinbac@helix.nih.gov>

Molecular Recognition and Quantitative Interaction Interest Group
Meeting time: 1st Wednesday, 5:30 pm
Meeting place: Building 6A, Room 4A05
Contact: Robert Crouch
Phone: 496-4082
E-mail: <robert_crouch@nih.gov>

Motility Interest Group
Meeting time: 1st Monday, 4:00 p.m.
Meeting place: Building 10, Bunim Room (9S235)
Contact: Jim Sellers
Phone: 496-6887

Mouse Club
Meeting time: 1st Tuesday, 4:00 pm
Meeting place: Building 31, Room 2A52, or Building 6A, Room 405
Contact: Heiner Westphal
Phone: 402-0545
E-mail: <hw@helix.nih.gov>

Mycobacterial Interest Group
Meeting time: Alternate Mondays, 10:30 am
Meeting place: Building 29, Room 121, or Twinbrook II, 2nd-floor conference room
Contact 1: Clifton Barry
Phone: 435-7509
E-mail: <clifton_barry@.nih.gov>
Contact 2: Mike Brennan
Phone: 496-9559

Nerve-Muscle Interest Group
Meeting time: Alternate Wednesdays, 9:00 am
Meeting place: Building 36, Room 1B07
Contact 1: Matt Daniels
Phone: 496-2898
E-mail: <mdaniels@codon.nih.gov>

Neural-Immune Interactions Interest Group
Meeting time: Alternate Mondays, 2:00 pm
Meeting place: Building 10, Conference Room 4N230
Contact: Socorro Vigil-Scott
Phone: 496-9255
E-mail: <vigilscs@intra.nimh.nih.gov>

Neurobiology Interest Group
Meeting time: alternate Fridays, 4:30 pm
Meeting place: Cloisters, Rathskeller
Contact: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@helix.nih.gov>
ListServ: <http://intra.ninds.nih.gov/nig/>

Neuroinformatics Interest Group
Meeting time: 2nd Tuesday, 12:00 noon
Meeting place: Building 49, Conference Room 1A/B
Contact 1: Rochelle Small
Phone: 594-9898
E-mail: <rochelle_small@nih.gov>
Contact 2: Yuan Liu
Phone: 496-3108

Pain Interest Group
Meeting time: Varies
Meeting place: Usually Building 49, Room 1B07
Contact: M. A. Ruda
Phone: 402-4980
E-mail: <maruda@dir.nidcr.nih.gov>

PET Interest Group
Meeting time: Each Friday, 2:00 pm
Meeting place: Building 10, Room 1C520
Contact: Peter Herscovitch
Phone: 402-4297
E-mail: <herscovitch@nih.gov>

Phage-Tech Interest Group
Meeting time and place: Varies
Contact 1: Steve Zullo
Phone: 435-3576
E-mail: <zullo@helix.nih.gov>
Contact 2: Carl Merril
Phone: 435-3583

Pigment Cell Research Interest Group
Meeting time: 3rd Monday, 3:00 pm
Meeting place: Building 49, 1st-floor Conference Room
Contact 1: Bill Pavan
Phone: 496-7584
E-mail: <bpavan@nhgri.nih.gov>
Contact 2: Vincent Hearing
Phone: 496-1564

Polyunsaturated Lipid Function Interest Group
Meeting time: Usually 1st Wednesday of each month (journal club; resuming in September), 1:00 pm
Meeting place: Flow Bldg. Conference Room, Rockville, 12501 Washington Ave.
Contact: Norman Salem
Phone: 443-2393
E-mail: <nsalem@niaaa.nih.gov>

Prostate Cancer Interest Group
Meeting time: Each Tuesday, 4:00 pm
Meeting place: Building 10, Room 2S235
Contact: Kathleen Simon
Phone: 496-6353
E-mail: <simonk@mail.nih.gov>

Protein Trafficking Interest Group
Meeting time: 2nd Tuesday, 3:30 pm
Meeting place: Building 10, Room 9S235
Contact 1: Harris Bernstein
Phone: 402-4770
E-mail: <harris_bernstein@nih.gov>
Contact 2: Peng Loh
Phone: 496-3239

Proteome Interest Group
Meeting time and place: To be announced, check website: <http://proteome.nih.gov>
Contact: Donita Garland
Phone: 496-6999
E-mail: <dgarland@helix.nih.gov>

Reactive Oxygen Species Interest Group
Meeting time and place: Monthly seminars held in conjunction with Oxygen Club of the Greater Washington Area (info via NIH Calendar and members' e-mail; also via Leslie McKinney <lmckinney@usuhs.mil>
Contact: Mike Chiueh
Phone: 301-402-2892
E-mail: <chiueh@helix.nih.gov>

RNA Club
Meeting time: 1st Tuesday (except August), 4:00 pm
Meeting place: Building 41, Room C509
Contact 1: Carl Baker
Phone: 496-2078
E-mail: <ccb@nih.gov>
Contact 2: Susan Haynes
E-mail: <shaynes@usuhs.mil>

Science Writing Interest Group
Meeting time and place: To be announced
Contact: Edward McSweegan
Phone: 402-8370
E-mail <emcsweegan@niaid.nih.gov>

Signal Transduction Interest Group
Meeting time: Alternate Fridays, 4:30 pm
Meeting place: 5 Research Court, Room 2A08
Contact 1: John Northup
Phone: 496-9167
E-mail: <drjohn@codon.nih.gov>
Contact 2: James Battey
Phone: 402-0900

Stem Cell Interest Group
Meeting time and place: TBA; check website
Contact 1: Peter Gasper
Phone: 1-410-558-8260
E-mail: <gasperpe@grc.nia.nih.gov>
Contact 2: Kevin Becker
E-mail: <beckerk@grc.nia.nih.gov>

Synaptic and Developmental Plasticity Interest Group
Meeting time: Wednesday, 12:00 noon
Meeting place: Building 49, Room 1A50
Contact: Bai Lu
Phone: 435-2970
E-mail: <lub@codon.nih.gov>

Interinstitute Interest Group Directory

Therapeutic Oligonucleotides Interest Group
Meeting time: Last Thursday, 4:00 pm
Meeting place: Building 10, Room 2C116
Contact : Yoon Cho-Chung,
Phone: 496-4020
E-mail: <chochung@helix.nih.gov>

Transcription Factors Interest Group
Meeting time: 1st Thursday (except July-Sept.), 1:30 pm
Meeting place: Building 49, Conference Room B
Contact 1: Stoney Simons
Phone: 496-6796
E-mail: <steroids@helix.nih.gov>
Contact 2: Uli Siebenlist
Phone 496-8917
ListServ: subscribe to TFACTORS

Tumor Angiogenesis & Invasion Working Group
Meeting time and place: Posted at web site
Contact 1: William Figg
Phone: 402-3622
E-mail: <wdfigg@helix.nih.gov>
Contact 2: Steven Libutti
Phone: 496-5049

Veterinary Interest Group
Meeting time: 3rd Thursday, 12:00 noon
Meeting place: Varies
Contact: Kay Jordan
Phone: 402-4547
E-mail: <ekj@helix.nih.gov>

Viral Hepatitis Interest Group
Meeting time: One Monday a month, 3:30 pm
Meeting place: Building 10, 9S235 (Bunim)
Contact: T. Jake Liang
Phone: 496-1721
E-mail: <jliang@nih.gov>

Virology Interest Group
Meeting time: Mini-symposia 1-2 times/year
Meeting place: to be announced
Contact 1: Klaus Strebel
Phone: 496-3132
E-mail: <kstrebel@nih.gov>
Contact 2: John Patton
E-mail: <jpatton@niaid.nih.gov>
ListServ: Contact <CBuckler@nih.gov>

Washington Area Yeast Club
Meeting time: 2nd Wednesday, 5:15 pm
Meeting place: Building 6A, Room 4A05
Contact 1: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>
Contact 2: Alan Hinnebusch
Phone: 496-4480
E-mail: <ahinnebusch@nih.gov>

Women's Reproductive Health Interest Group
Meeting time and place: Every 4 months at times decided by the group.
Contact: Phyllis Leppert
Phone: 496-6515
E-mail: <LeppertP@nih.gov>

WorldWideWeb Interest Group
Meeting time: 2nd Tuesday, 2:30 pm
Meeting place: Building 10, Lipsett
Contact 1: Sandy Desautels
Phone: 402-6553
E-mail: <sandy_desautels@nih.gov>
Contact 2: Dale Graham
E-mail: <degraham@helix.nih.gov>

Xenopus/Zebrafish Interest Group
Meeting time: Last Monday (except summer), 3:30 pm
Meeting place: Building 6B, Room 429
Contact 1: Brant Weinstein
Phone: 435-5760
E-mail: <bw96w@nih.gov>
Contact 2: Ajay Chitnis
E-mail: <chitnisa@mail.nih.gov>

X-ray Crystallography Interest Group
Meeting time: Quarterly, announced by e-mail, 2:00 pm
Meeting place: Building 5, Room 127
Contact: Xinhua Ji
Phone: (301) 846-5035
E-mail: <jix@ncifcrf.gov>

Addenda

Considering starting a new Interest Group? Contact* Celia Hooper *(fax: 301-402-4303; e-mail: <hooperc@od.nih.gov>.

Need to correct your group's listing? Contact CIT's web publishing group: <publish@cit.nih.gov>.

Iran pollner

Joint Mission: *NICHD's Josh Zimmerberg (left) and Baruch Blumberg, director of the NASA Astrobiolology Institute, on Earth at NIH in April*

Lift-Off!

When the shuttle Atlantis was launched from the Kennedy Space Center February 7, 2001—an hour after sunset and under a full moon—it generated what seemed like a megaton of explosive light and sound and an equal amount of awe in Joshua Zimmerberg, chief of the NICHD Laboratory of Cellular and Molecular Biophysics and director of the NASA/NIH Center for Three-Dimensional Tissue Culture.

Zimmerberg was among the scientists who watched from the ground as the shuttle zoomed into space carrying a 16-ton microgravity laboratory to be installed at the international space station for the purpose of scientific research, including the study of how cells—especially immune cells—respond under conditions of microgravity.

This space laboratory is one of a growing number of collaborations between NASA, its Astrobiology Institute (NAI; see *The NIH Catalyst*, "Astrobiology and the Search for Origins," May–June 2000, page 1), and NIH.

A video of the launch electrified participants at the first joint NAI-NIH symposium, which was held here earlier this spring and featured such topics as pathogenesis in modeled microgravity, molecular perspectives on the extremes of life, human oral biofilms, microbial mats, and the origins of stars and planets.

Zimmerberg is in the throes of creating an Astrobiology Interest Group and can be reached at 6-6571 or **<joshz@helix.nih.gov>**.

Microarray Mainstream
continued from page 1

increase in the sophistication and expectations of the users of this technology. We develop software for doing image analysis and preliminary statistics for P53-labeled arrays and for fluorescence-labeled glass microarray." The technology, he says, is "quite complicated, has limitations, and will require real work to apply to [complex] problems."

Earlier this year, before then-NCI clinical director Ed Liu left NIH to head the National Genomic Institute in Singapore, he presented an expression-array sampler of recent laboratory findings in the IRP and their relevance to human diseases. Among them were the identification of molecular pathways involved in breast cancer development and the means to distinguish low- and high-grade ovarian cancers.

Joanne Peter

Microarrayers: *Ed Liu (left), former NCI clinical director, and Lisa Gangi*

One Project

For Lisa Gangi—an NCI investigator with roots in Liu's lab who recently moved out to the microarray research facility at NCI's Laboratory of Molecular Technology in Frederick—microarrays are a "tool to look at thousands of genes at once, a snapshot of all gene expression at a given time."

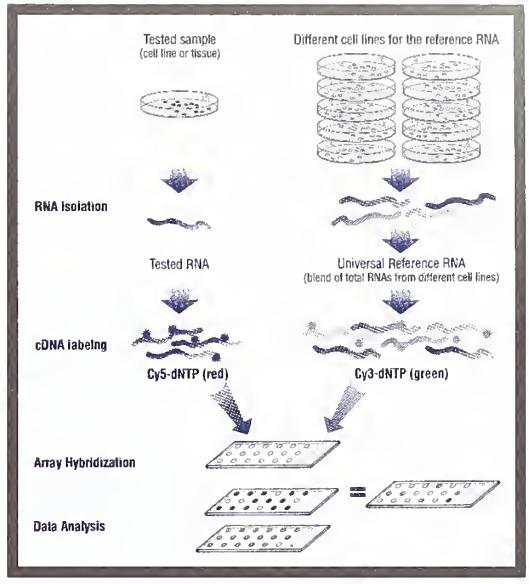
Gangi has been using that tool to track normal gene expression in mouse breast development and the upregulation of proteins that accompanies pregnancy, lactation, and involution. Her findings in the mouse now inform her examinations of patients' breast tumors. Specifically, she and her group are searching for correlations in the gene expression patterns of the DNA repair pathway seen in the mouse.

Gangi typically views 5,000 to 7,000 genes on any given glass slide and uses two-color probes to distinguish tumor from normal tissue in both mouse and human mammary samples. She has documented a ten-fold increase in the expression of DNA repair pathway genes during involution compared with during lactation; she is now focusing on the identification of novel genes that are upregulated in the apoptosis pathway during involution.

She and her team have observed a decrease in survival factors—also known as anti-apoptosis genes, such as *bcl-2*, *bcl-3*, and *ICH/IS*—and a concomitant increase in pro-apoptotic genes, such as *bcl-x*, *bax*, and the matrix metalloprotease genes during the first 24 hours of involution. At late time points, there is a marked increase in the expression of adhesion molecule genes and other cytoskeletal genes required for cellular remodeling.

This upregulation of repair genes suggests that normal mammary KU 70/80 and ATM, which are involved in the repair of DNA double-strand breaks, are involved in both mammary gland involution and breast cancer development.

"It's interesting," Gangi says, "that many human breast tumors appear to have aberrant levels of DNA repair genes. . . . We hope to elucidate whether the increase in the levels of these proteins is a normal consequence of cellular apoptosis and remodeling and whether there is a connection in DNA repair to downstream events leading to tumorigenesis." ■



Microarrays (or DNA chips) provide a rapid and simultaneous screening of many thousands of genes, displaying which genes are expressed at that given stage in the development of a cell. mRNA is isolated from cells at different stages of development, converted to cDNA (using reverse transcriptase), and labeled with fluorescent deoxynucleotides. The fluorescent cDNA can then be used as probes, each hybridizing to complementary sequences on the microarray chips. These chips are essentially glass slides coated with poly-L lysine and contain immobilized PCR-amplified cDNA fragments. The time and details of gene expression provide insight into a cell's role at a particular phase of cellular development. The patterns of gene expression are characterized for their relevance to disease. Additionally, software developed by NIH's CIT aids in detection of subtle differences of gene expression.

Calls for Abstracts

The Second Meeting to Discuss **Current Topics and Strategies in Urologic Oncology**, sponsored by NCI's Urologic Oncology Program and the Society of Urologic Oncology, will be held December 1–2, 2001, in the Natcher Conference Center. The meeting will focus on prostate, kidney, and bladder cancer.

Residents, fellows-in-training, and attending staff (1–5 years from completion of training) are invited to submit abstracts (on any research topic in urologic oncology) for the poster session. **Abstracts are due September 15**.

For info, contact Linda Gaskill, Matthews Media Group, at 301-348-1628 or e-mail: <**linda.gaskell@matthewsgroup.com**>. Register online at

<**http://www.matthewsgroup.com/urologiconcology**>.

The Society for Biological Therapy will hold its annual meeting November 9–11, 2001, at the Natcher Conference Center. Organized by NCI, Bayer Pharmaceuticals, and Beth Israel Deaconess Medical Center, it features sessions on cytokines, angiogenesis, gene therapy, vaccine/dendritic cells, antibodies, pharmacogenomics/discovery, and new agents in development.

Abstracts are due August 17. Six abstracts by students, postdoctoral fellows, or junior faculty (instructor or assistant professor) with three or fewer years on staff will be selected for presentation; one of these will be chosen to receive the 2001 Presidential Award and a check for $1,000. Program information, registration, and abstract guidelines and submission form are available at the society's website:

<**http://www.socbiother.com**>. ■

Recently Tenured

Josephine Egan *received her M.B., B.Ch. (M.D.) in 1979 from the National University of Ireland, Galway. After fellowships in clinical pharmacology (at Baylor College of Medicine in Houston) and endocrinology (the University of Virginia Health Sciences Center, Charlottesville), she joined the NIA in 1990, where she is now chief of the Diabetes Section, Laboratory of Clinical Investigation.*

Josephine Egan

My research focuses on insulin secretion. This means that anything that perturbs insulin secretion is fair game for study—from the most basic level to clinical investigation.

Because type 2 diabetes is the commonest form of diabetes in the elderly, and I work in the NIA, I am especially interested in that disease. But why insulin secretion?

Work in many parts of the world has established beyond doubt that type 2 diabetes is caused by reduced insulin action (insulin resistance) and faulty insulin secretion. In the 1980s and 1990s, there was an explosion in the understanding of how insulin actually activates its receptor, what intracellular processes became activated consequently, and how glucose transport occurs. When it was shown that insulin-mediated glucose transport is decreased in type 2 diabetes, insulin resistance became accepted as the dominant defect of type 2 diabetes. This assumption was regrettable because it is only part of the story.

Obesity, which is the commonest cause of decreased insulin-mediated glucose uptake, is present in 85 percent of type 2 diabetic subjects. But only a minority of obese subjects develop diabetes. This incongruity told us that something besides insulin resistance is needed to cause diabetes. Most obese subjects do not develop diabetes because they become hyperinsulinemic relative to their nonobese counterparts and so can compensate for the insulin resistance. When insulin secretion problems intervene, blood glucose rises and diabetes occurs.

Some of the derangements in insulin secretion in type 2 diabetes have been revealed in clinical studies. They are: 1) absent first-phase insulin secretion (insulin secreted from β-cells in the first few minutes after acute blood glucose elevation), 2) very weak, if any, insulin secretion in response to rising blood glucose—most obvious when glucose is given intravenously, 3) severely diminished 24-hour integrated insulin secretion, and 4) a flattening in the usual pulsatile manner in which insulin is secreted.

In our section, we have used rodent models and human physiology studies to elucidate what lies behind those derangements. We know that insulin secretory capacity depends on both function and mass of β-cells and that β-cells are heterogenous in their response to stimuli. Increasing glucose results in increasing recruitment of secretory β-cells. First-phase insulin secretion comes from a subpopulation of β-cells; in type 2 diabetes this subpopulation is silent.

β-cells that lack glucose competency—the ability to sense changes in blood glucose so that insulin secretion can be adjusted—will not become secretory. We are now gradually peeling back the layers of factors involved in glucose competency, and much of our research has focused on two specific gut peptides, GIP and GLP-1.

Both of these factors are released from the gut in response to food and act on specific receptors on the β-cells to render the β-cells glucose-competent. Activation of their receptors leads to increases in cAMP concentrations, a primary glucose-competency factor. GIP is secreted as soon as food enters the duodenum. We have seen that in type 2 diabetes the β-cells are resistant to GIP, and plasma GIP concentrations rise. No amount of exogenous GIP will induce the receptors to respond. We plan to elucidate the cause of the downregulation of the GIP receptors.

GLP-1 is secreted from the ileum, again after eating, but later than GIP. Its effects are also somewhat downregulated in type 2 diabetes, but, when given in pharmacological doses, it can restore first-phase insulin secretion, increase maximum insulin secretion, and improve pulsatile insulin secretion. Therefore, we have undertaken long-term studies with GLP-1 in treating type 2 diabetic patients. We are developing analogs of GLP-1 to overcome some of the drawbacks—due to its very short half-life of only a few minutes—inherent in using GLP-1 as a pharmacological agent.

We are also exploring the control of the second component required for insulin secretion—sufficient β-cell mass. In type 1 diabetes, as long as 30–50 percent of residual β-cell mass remains, hyperglycemia does not occur. Transplantation experiments have taught us that enough islets must be transplanted in order to restore euglycemia. The capacity of β-cells to synthesize insulin must also be preserved. Infiltrative diseases, such as hemochromatosis and perhaps amyloidosis, can diminish insulin synthesis.

Questions we have been focusing on in this area are: What happens to β-cell mass with age? What regulates the mass? Can the mass be manipulated by pharmacological means? Where do new β-cells come from? Are there endocrine progenitor cells in adult pancreas that can be manipulated? We have shown that GLP-1 also is involved in regulating total β-cell mass and function in rodents. Function is regulated via increasing insulin mRNA and insulin synthesis. We plan to ascertain whether this is so in humans.

Clinically, we are beginning to use data from the Baltimore Longitudinal Study of Aging (BLSA) to examine hormone activities in the natural history of type 2 diabetes. Within our BLSA population are people who have gone from a nondiabetic state to glucose intolerance to frank diabetes. We are asking when GIP concentrations begin to rise—is it at the point of glucose intolerance or only with frank diabetes? What happens to GLP-1 during the progression? We hope to answer these questions—to pinpoint the time in the progression to diabetes when insulin and gut derangements actually lead to diabetes—and thereby elucidate the cause of insulin deficiency.

Nicholas Restifo *received his M.D. degree in 1987 from New York University. He was a research fellow at the Memorial Sloan-Kettering Cancer Center in New York before coming to NIH. He is now a principal investigator in the Surgery Branch, NCI.*

fran pollner

Nicholas Restifo

The focus of our efforts is to develop new immunotherapies for cancer. Our approach is to create new animal models to study the basic immunology of the tumor-host interaction and to develop and test new treatments.

Animal models form the foundation of our current understanding of immunology in general and tumor immunology in particular; preclinical animal data form the core of almost any new therapy. But while animal models are very good for working out mechanistic questions, they are much less predictive of therapeutic benefit in humans. Put another way, animal models are useful to

describe what *can* happen in patients, but they are unreliable at predicting what *does* happen.

The focus of our mouse work is on the development of anticancer vaccines—vaccines designed to treat, rather than prevent, disease. We have accomplished this experimentally by identifying the mouse homologs of human tumor-associated antigens. We have created and tested recombinant and synthetic anticancer vaccines based on these antigens, examples of which are recombinant viruses, "naked" DNA immunogens, proteins, and peptides.

One of the most interesting and difficult models we work with is based on the B16 mouse melanoma. This tumor was initially discovered as a spontaneously occurring mouse melanoma and is now grown in culture and passaged in syngenic mice. It turns out that B16 expresses all of the homologs of the human melanocyte differentiation antigens that function as tumor antigens.

To elucidate important immunological and therapeutic questions, we use mice that are transgenic for human MHC molecules (such as HLA-A2 and HLA-DR4). We also use knockout mice lacking the antigens we are targeting. This enables us to assess the roles for immunological tolerance to these antigens. Most recently, we have created mice that are transgenic for T-cell receptors, enabling us to study tumor-specific T cells in a variety of activation states.

We are currently using our newly created mouse models to explore an immune strategy in which T lymphocytes are expanded outside the body and "adoptively" transferred to treat patients with cancer. Efforts to date at adoptive immunotherapy have focused on giving killer T lymphocytes or CD8+ T cells. We will soon add CD4+ T cells, which may help killer cells grow, survive, and localize to the tumor site after adoptive transfer.

We also plan to use what some term gene therapy to modify the functions or survival of transferred T cells. The insertion into T cells of genes encoding anti-apoptotic proteins or the gene encoding growth factor interleukin-2 is one possible approach. Alternatively, new reactivities could be conferred on T lymphocytes by inserting genes encoding T-cell receptors specific for tumor-associated antigens.

The immune system can eradicate tumor cells; our goal now is to induce the immune destruction of cancer more consistently. We plan a multipronged approach to the development of new immune-based treatments for patients whose cancers are not currently treatable with traditional chemotherapy, radiation, and surgery.

Jeffery Struewing *received his M.D. from Indiana University School of Medicine in Indianapolis in 1985 and his M.S. in preventive medicine from the University of Maryland at Baltimore School of Medicine in 1988. He joined the NCI's Genetic Epidemiology Branch in 1991 and is now a senior investigator in the Laboratory of Population Genetics.*

fran pollner

Jeffery Struewing

My research has focused on genetic aspects of breast and ovarian cancer. I have attempted to bridge the gap between epidemiologic studies in humans and more basic molecular and biochemical characterizations of genetic variation.

In doing so, I have progressed from family-based studies of genes with large effects, such as *BRCA1* and *BRCA2*, to more population-based studies of the genetic and environmental determinants of cancer susceptibility.

I began work in this area by recruiting breast and ovarian cancer families for clinical and epidemiologic study in NCI's Genetic Epidemiology Branch. Our studies helped localize the genes to chromosomal locations, and other groups finally isolated single genes, *BRCA1* and *BRCA2*, that, when mutated, lead to a predisposition to cancer, with the observed dramatic pedigrees.

After obtaining training in molecular genetics, my laboratory studies in breast and ovarian cancer began in 1994 with the analysis of 24 NCI families, 10 of which were found to have *BRCA1* mutations. Most of these families had different *BRCA1* mutations, but three —all Ashkenazi Jewish—shared the same mutation, designated 185delAG.

In collaboration with Larry Brody of NHGRI, this observation led to our finding that approximately 1 percent of stored DNA samples from Ashkenazi Jews contained the *BRCA1* 185delAG mutation. For several years, *BRCA1* and *BRCA2* were studied almost exclusively in high-risk families, in which a very high risk of breast cancer (penetrance) was estimated—85 percent or more by age 70 and nearly 100 percent lifetime. In other words, *BRCA1* appeared to be a nearly fully penetrant, autosomal dominant disease gene.

Studies in less restricted populations, however, have shown the situation to be much more complex. Our finding of the 185delAG mutation at a high frequency in Ashkenazi Jews was a prelude to more population-based, genetic epidemiologic studies of this gene. It also gave rise to the possibility of almost immediate commercial testing in this population, despite the fact that it was unknown whether cancer risk estimates from the high-risk families applied to carriers identified from a broader population base.

We therefore quickly designed and implemented a study of the prevalence and penetrance of the 185delAG mutation in the Washington Ashkenazi Jewish population. In more than 5,000 volunteers, we demonstrated a combined 1.2 percent carrier frequency for the 185delAG and 5382insC *BRCA1* mutations and a 1.2 percent carrier frequency for 6174delT, the founder mutation of *BRCA2* (this gene and mutation were identified after the initiation of the study).

More importantly, using the newly developed kin-cohort method, we estimated that the risk of breast cancer among mutation carriers was 56 percent (40 percent to 73 percent for the 95 percent confidence interval) by age 70—a high risk, but one well below most previous estimates.

Subsequent estimates of penetrance have generally been even lower than our estimate, supporting the idea that the average risks of cancer among *BRCA1/2* mutation carriers are much lower than initial estimates from high-risk families.

This discovery opens the door to studies aimed at identifying environmental and genetic factors that modify cancer risk in *BRCA1/2* mutation carriers and in the majority of women who do not carry these mutations. This will be a main focus of my future work.

Which genetic loci are likely to be related to cancer susceptibility? The precise biochemical basis for cancer predisposition in *BRCA1/2* mutation carriers is unknown, but the protein products of both genes are likely to be involved in DNA double-strand break repair. Variations in genes involved in all aspects of DNA damage recognition and repair, therefore, make ideal candidates as breast cancer susceptibility factors.

We are planning comprehensive analyses of all single nucleotide polymorphisms in DNA repair genes using matrix-assisted laser desorption/ionization–time of flight assays.

Recently Tenured

Irving W. Wainer *received his Ph.D. from Cornell University in Ithaca, N.Y., in 1970 and did postdoctoral work at the Institute of Molecular Biology, University of Oregon, Eugene, and Thomas Jefferson University Medical School in Philadelphia. He held positions at the FDA, St. Jude Children's Research Hospital (Memphis), and McGill (Montreal) and Georgetown (Washington) universities before joining NIA in May 2001 as chief of the Bioanalytical and Drug Discovery Unit.*

The research programs in my laboratory include clinical pharmacology and the development of online high-throughput screens for new drug discovery. Our clinical work is primarily focused on how disease state can alter drug metabolism.

We have identified several discordances between genotype and expressed phenotype in patients with advanced cancer and AIDS. For example, patients with advanced cancer or AIDs who also have extensive or fast genotypes for cytochrome P450 2C19 and *N*-acetyltransferase-2 have displayed poor and slow phenotypes, respectively.

Irving Wainer

Because these observations were associated with advanced disease, we have initiated studies in patients with terminal syndromes such as cancer cachexia, or wasting. In particular, we have developed a direct measure of a "proteolysis-inducing factor" (PIF) associated with cachexia. PIF is measured in spot urines using capillary electrophoresis (CE). The presence of PIF in urine has been correlated with clinical status and with PIF in tumor biopsies. We have also correlated the presence of PIF in urine with treatment response and clinical relapse. This fall, we will begin a longitudinal study on PIF as a disease marker.

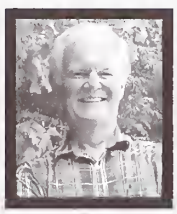
Based on these results, we have initiated a study using CE coupled with mass spectrometry and matrix-assisted laser desorption/ionization–time of flight spectrometry to quantify PIF in tissues and to examine the effect of cachexia on pre- and post-translational expression of hepatic enzymes and transporters. We will also use laser capture microdissection and CE with mass spectrometry or laser-induced fluorescence to study these effects in single cells.

In a second line of work, we have developed liquid chromatographic stationary phases containing immobilized receptors, enzymes, and transporters as an online flow system for new drug discovery and characterization of drug candidates.

These columns can range in size from standard liquid chromatography columns to microcolumns and can be used to screen complex chemical mixtures, characterize single compounds, and screen phage libraries. The columns can be used with known targets—for example, nicotinic, GABA, NMDA, and estrogen receptors; P-glycoprotein and other ABC transporters; and cytochrome P450 and other enzymes. They can also be used with orphan receptors and other expressed proteins, and they can be placed online with mass spectrometers or other instruments that detect structure or activity, providing real-time data that cannot be obtained using standard microtitration plates. ■

FAES: A Rush to Immunology (and Much More)

There's never an empty space in John Finerty's course. Since its introduction in 1985, when the the AIDS epidemic was creeping into the public mind and challenging the scientific community, students have rushed to fill Immunology 403, "Basic Principles of Immunology and Hypersensitivity." The demand is so great for this graduate level course that two sections are offered in the fall semester of the FAES (Foundation for Advanced Education in the Sciences) Graduate School at NIH. A one-year advanced immunology course—Immunology 521—is also on deck this fall and has been fully subscribed since its inception as well.



John Finerty, chief of the NCI cellular immunology section, is involved not only in graduate education but also mentors high school students and elementary school teachers.

The success of these two courses can be credited to Finerty, who is chair of the FAES Department of Microbiology and Immunology, and to the NIH immunologists who volunteer to lecture on their rapidly evolving field. Immunology 403 is one of the FAES' "M" courses—approved for continuing medical education credits; it covers such topics as natural immunity, the genetics of and molecular mechanisms in specific immune responses, cellular cooperation, immunodeficiency disease, hypersensitivity, and autoimmunity.

Each year, about 2,000 to 3,000 students enroll in what are now about 200 FAES courses. These offerings sweep the introductory-to-advanced spectrum and keep pace with unfolding topics such as bioinformatics and biomedical ethics law. And the FAES Language Department is the place where new visiting fellows will find courses to help in honing English communication skills. While most classes are conducted in the evenings without laboratory, the BioTrac courses include lecture and laboratory components and are taught during the day.

FAES department chairs are always on the lookout for new instructors and updated course offerings. Those interested in organizing a specific course should contact the appropriate FAES chair or Connie Noguchi, dean of the Graduate School (301-496-1163 or <**cnoguchi@helix.nih.gov**>). A database of postdoctoral fellows interested in teaching is maintained in a Teaching Opportunities for Postdocs online database in cooperation with the NIH Fellows Committee.

The 2001–2002 course catalog is at the FAES Office (Building 60, Suite 230) and the FAES Bookstore (Building 10, Room B1-L-101). The last day for mail registration for fall 2001 is **August 31**. Walk-in registration will be accepted **September 5 to 11** (weekdays 10 a.m.–4 p.m., with added hours from 5–7 p.m. on September 11). Classes begin **September 24**. The catalog is also available online at the FAES website: <**www.FAES.org**>. For additional information, contact the FAES Office at 301-496-7976. ■

Meant To Be Mentors

Class Acts: *(left) Constance Tom Noguchi, chief of the Molecular Cell Biology Section, Laboratory of Chemical Biology, NIDDK, and dean of the FAES Graduate School, and Joan P. Schwartz, chief of the Neurotrophic Factors Section, NINDS, and assistant director of the Office of Intramural Research, were accorded Awards for Excellence in Mentoring by the Association for Women in Science, Bethesda chapter.*

American Philosophical Society Elects:

***Anthony Fauci**, director, NIAID, and chief of the Laboratory of Immunoregulation*

***Marshall Nirenberg**, chief of the Laboratory of Biochemical Genetics, NHLBI*

Nicole Le Douarin

French developmental biologist Nicole Le Douarin has been chosen as an NIH Fogarty Scholar and will deliver a lecture on "Relationships of the Neural Ectoderm to the Notocord and the Cephalic Neural Crest during Central Nervous System Development" at the Lipsett Auditorium, noon to 1 p.m., **Thursday, July 26**.

Le Douarin's eminent scientific positions—she is director of the Institute of Embryology of the CNRS, professor of the Collège de France, and Secrétaire Perpétuelle de l'Académie des Sciences—prevent her from spending an extended period of time in the United States. Instead, she is planning a series of shorter visits, the first of which is from July 23 to August 17, 2001. Hosted by Heiner Westphal (LMGD/NICHD, Bldg. 6B, Rm. 413), she plans to interact with several NIH laboratories involved in developmental biology.

Among her contributions to this field are the use of a unique structure of the quail interphase nucleus in a cell-marking technique to follow cell migrations and morphogenetic movements in the avian embryo, the discovery of totipotent neural crest stem cells, and the demonstration that behavioral traits, such as song, can be transferred from donor to recipient by transplantation of brain tissue.

Contacts with Le Douarin will be arranged by Carol Duffy, phone: 301-402-0545. ■

From the Bedside To CC Grand Rounds

A procession of "great teachers" of clinical medicine will grace the Clinical Center Grand Rounds roster once a month from September to June, thanks to a joint program arranged by the NIH/FAES Continuing Medical Education Committee and the Office of Education.

Topics chosen for this first annual series on Contemporary Clinical Medicine were based on the results of an NIH-wide survey of physician learning needs. Speakers were selected based on their clinical expertise and teaching abilities.

The Great Teachers Series aims to bring up-to-date information on important clinical topics to both clinical practitioners and research physicians on the NIH campus. The viewpoint will be from the bedside with emphasis on the practical. Some novel teaching techniques, including audience participation, are anticipated.

The series will be held on the second Wednesday of each month at noon in the Lipsett amphitheater. Each program will also be available in the NIH archives. For more information, contact OE's Sylvia Scherr or Ione Lagasse at 301-435-8012. ■

Contemporary Clinical Medicine—Great Teachers

Date	Speaker	Institution	Topic
September 12, 2001	Eugene Braunwald	Harvard	Ischemic heart disease
October 10, 2001	Jay Mohr	Columbia	Stroke (includes exam of a patient)
November 14, 2001	Richard Wenzel	Medical College of Virginia	Hospital-acquired infection
December 12, 2001	Norman Kaplan	Texas Southwestern	Hypertension
January 9, 2002	Sam Katz	Duke	Immunization
February 13, 2002	Bob Kreisberg	U. South Alabama	Diabetes
March 13, 2002	John Bartlett	Hopkins	HIV
April 10, 2002	Irwin Braverman	Yale	Skin signs of systemic disease
May 8, 2002	Anthony Miller	Heidelberg	Cancer screening
June 12, 2002	Faith Fitzgerald	UC Davis	Cases

Standing on Ceremony

Ruth Kirschstein, NIH acting director, and Michael Gottesman, deputy director for intramural research (bottom row, 3rd and 4th from left) honored this year's Ph.D. graduates: (from left to right, with mentor and institute in parentheses): Teri Manolio (Alexander Wilson, NHLBI), Dongmei Yang (Peace Cheng, NIA), David Hattery (Amir Gandjbakhche, NICHD), Rachel Poltilove (Simeon Taylor, NIDDK), David Kaufman (Jeff Struewing, NCI), Ruth Kirschstein, NIH acting director, Mohammad Khoshnevisan (Scott Diehl, NIDCR), Michael Gottesman, deputy director for intramural research, Sohail Chaudhry (Kevin Garner, NCI), Tara Garvey (Jeffrey Cohen, NIAID), Mirza Baig (Henry McFarland, NINDS), Aparna Mohan (Martha Linet, NCI), Tara Vogt (Regina Ziegler, NCI), Aviva Jacobs (Simeon Taylor, NIDDK), Frank Addivinola (Marshall Nirenberg, NHLBI), Michelle Rudek (William Figg, NCI). Not pictured: Carole Carter (Edison Liu, NCI), Shubhashini Chandrasekaran (Edison Liu, NCI), Anand Chokkalingam (Ann Hsing, NCI), Yunsheng He (Louis Staudt, NCI), Stephen Martin, Jr. (Dale Sandler, NIEHS), Alex McCampbell (Kenneth Fischbeck, NINDS), Lance Miller (Edison Liu, NCI), Ann Scher (Karin Nelson, NINDS), Ming Zheng (Peace Cheng, NIA).

Formalizing what has been a long-time activity at NIH—providing research training for Ph.D. candidates, an activity that is expanding under the auspices of the NIH Office of Graduate Program Partnerships—NIH held its first Certificate Award Ceremony May 9 for 23 graduating doctoral students who had been training in NIH labs. They received their Ph.D.s from 10 different partner universities: George Washington University, Washington, D.C.; Howard University, Washington, D.C.; University of Maryland, at College Park and Baltimore; the Johns Hopkins School of Public Health, Baltimore; Virginia Commonwealth University, Richmond; University of North Carolina, Chapel Hill; University of Michigan, Ann Arbor; University of Pennsylvania, Philadelphia; and Yale University, New Haven, Conn. ■

Call for Catalytic Reactions

In this issue, we are asking for your reactions in four areas: shared resources, the design of science buildings, special interest groups, and *Catalyst* content.

Send your responses on these topics or your comments on other intramural research concerns to us via e-mail: <catalyst@nih.gov>; fax:402-4303; or mail: Building 2, Room 2W23.

In Future Issues...

- New Directors
- Eugenics: Cold Spring Harbor Revisited
- OE's 10th

1) Do you have any ideas for shared resources currently not available at NIH?

2) Are there any elements of design of science buildings that you feel would improve the research environment at NIH?

3) In how many NIH Interest Groups do you participate? What are their strengths and weaknesses?

4) What features of the *Catalyst* do you most appreciate? What issues would you like to see covered?

The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 2, Room 2W23, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; fax: (301) 402-4303; e-mail: <catalyst@nih.gov>

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