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The Rockefeller University

news&notes

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University community catches the World Wide Web wave

The World Wide Web may seem trendy, with Hollywood movies and insurance companies flashing home page addresses—those strings of characters that begin http://www—in their ads. But the Web, a subset of the Internet, is in fact a serious place, offering scientists mighty engines for finding and sending information all over the world. Thousands of institutions have joined the global electronic community with Web sites.

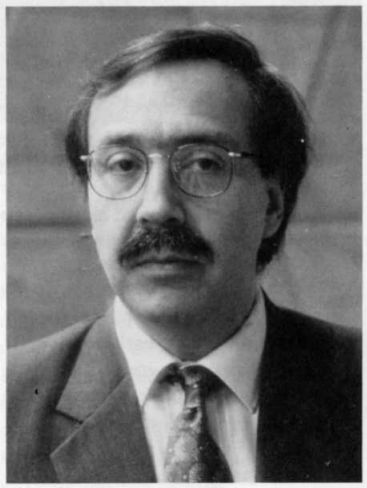
At Rockefeller, the Gotschlich-Fischetti lab was the first to place a database on the Web. "Our Lancefield collection of streptococcal strains was known only through traditional scientific publications. The Web makes the resource more accessible to all interested members of the scientific community," said John Robbins, research associate.

Computing Services's staff produce and maintain Rockefeller's Web server and home page, offering assistance to would-be and current Web users as well as digital space to departments and labs. Laboratory Safety placed its safety manual on the RU home page, Sponsored Programs Administration offers access to the annual funding guide, and the Office of Public Affairs posts the *Calendar of Events* and *News&Notes*. *Scientific and Educational Programs* will soon be up on the Web, and the library and Rockefeller Archive Center have Web sites.

While many scientists on campus use the RU home page's links to

See ***Scientific****, page 2*

Biophysicist lectures today on mica, microscopes, and macromolecules



Courtesy of Carlos Bustamante

Carlos Bustamante's main research interests are chromatin and chromosome structure and regulation of transcription.

Carlos Bustamante, professor at the University of Oregon and a Howard Hughes Medical Institute (HHMI) investigator, discusses "Imaging Protein DNA Complexes with the Scanning Force Microscope" at the Friday lecture today (Sept. 29).

Bustamante studies the structure and dynamics of biological macromolecules using the atomic force microscope and methods of single molecule manipulation. He and his colleagues recently developed a method to deposit macromolecules on atomically flat mica making it easier to view these nonconductive substances by force microscopy. Bustamante successfully applied the atomic force microscope to investigate several protein–nucleic acid complexes important in eukaryotic and prokaryotic transcription.

"Carlos is a pioneer in applying relatively new microscopic technologies to studies of biological macromolecules," said Assistant Professor Seth Darst, who hosts today's lecture.

Bustamante received a Ph.D. in biophysics from the University of California, Berkeley, in 1981. He then joined Lawrence Berkeley Laboratory for a one-year postdoctoral fellowship. In 1982, Bustamante moved to the University of New Mexico, where he joined the chemistry faculty as an assistant professor. He was promoted to associate professor in 1986 and to professor in 1989. He became professor in the Department of Chemistry and a member of the Institute of Molecular Biology at the University of Oregon in 1991. In 1994 he received his HHMI appointment.

Bustamante received a Searle Scholarship in 1984 and an Alfred P. Sloan Fellowship in 1985. In 1989, the state of New Mexico honored him as an Eminent Scholar. Bustamante is the author or co-author of 115 papers.

The lecture will be held at 3:45 P.M. in Caspary Auditorium and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Lounge. All are welcome.

Rockefeller's first Nobel laureate attracts film makers

In 1906, when Alexis Carrel joined the Rockefeller Institute for Medical Research, the gifted French surgeon had already pioneered techniques for joining severed blood vessels and transplanting organs. During his tenure here he contributed other important medical advances. This summer, more than 50 years after his death, Rockefeller's first Nobel Prize winner became the subject of two documentaries chronicling the history of organ transplants.

Don Holmes, an independent film maker who wrote and produced an education program for suture manufacturer U.S. Surgical, said, "Surgeons who know of Carrel's work hold him in high esteem for his innovations, but he is constantly being rediscovered."

A second team, London's Barraclough Carey Productions, included Carrel in a four-hour PBS–BBC history of transplant surgery, which is tentatively scheduled to air in the United States in April 1996.

Both producers turned to Professor Emeritus Merrill W. Chase for insight into Carrel's life and personality. Chase, who celebrated his 90th birthday this month, is the only living person who knew Carrel and his work.

"Carrel's influence on medicine was twofold," said Chase. "Most importantly, he was the first to successfully and repeatedly suture blood vessels, making organ transplants possible. Second, he developed techniques to grow cells of warm-blooded animals in vivo."

Born in 1873 in Lyons, France, at 20 Carrel began working as a surgeon. He received his medical degree from the University of Lyons in 1899. When French President Marie François Carnot bled to death after an assassin's

See ***Chase****, page 2*

The Rockefeller University Archives

Two film makers are featuring in documentaries Alexis Carrel, Rockefeller investigator, Nobel laureate, and self-proclaimed mystic, shown here in 1918 demonstrating a new method for treating infected wounds. Developed with Henry Dakin in the preantibiotic era, the procedure aided soldiers injured in the battles of World War I as they fought in the hospital against wound infection.

Chase interviewed for two documentaries on Alexis Carrel

(continued from page 1)

bullet severed a major artery, Carrel became interested in devising a method to join separated blood vessels. He studied embroidery, and using superfine needles, silk thread, and miniature clamps, Carrel developed a surgical technique to reunite blood vessels without clotting before he reached 30.

Carrel left France in 1904 and joined the physiology department at the University of Chicago, where he perfected his surgical techniques and conducted his first experiments in organ transplantation. In 1906, Carrel came to the Rockefeller Institute as a fellow. During his early years here, Carrel further perfected his surgical techniques, transplanting not only blood vessels but organs from one animal to another.

In 1912, Carrel received the Nobel Prize in physiology or medicine—the first awarded to a scientist at a U.S. institution—for his work on suturing blood vessels and transplanting organs.

During World War I he served as a major in the Medical Corps of the French army. Before the age of antibiotics began with the discoveries by Rockefeller's René J. Dubos, Carrel and Henry Dakin developed a disinfectant that greatly reduced the incidence of gangrene, which saved many lives. He received the French Legion of Honor for his war service.

Carrel returned to the institute in 1919, directing his attention to problems associated with organ transplants. He cultivated living tissue in the laboratory, successively transferring tissue taken from the heart of a chick embryo to fresh nutrient media. While some scientists claim that this strain of connective tissue stayed alive for 34 years, outliving Carrel, others dispute the accomplishment. In the 1930s he cultivated entire organs in the laboratory, assisted by a device called a perfusion pump, invented by American aviator Charles Lindbergh. His cultivated thyroids synthesized hormones. These experiments foreshadowed the heart–lung machine and other vascular surgical techniques. Carrel retired in 1939 as member emeritus and returned in 1940 to Paris, where he died four years later.

Chase remembered Carrel as an aloof figure. "He would perform surgery in the morning," said Chase "after which he would arrive at the very end of the lunch hour, wearing a freshly laundered white surgeon's cap and coat. He was seen only by those who lingered long at lunch or arrived late."

Leif Carlsson

Professor Emeritus Merrill Chase (*center*) and Tony Stark (*right*), producer of the PBS–BBC history of organ transplants, wait as the cameraman prepares to record the interview.

Employee Health Office to conduct free prostate cancer screening

With new techniques available for early detection of prostate cancer, the American Cancer Society recommends screening for all men age 50 and older, who are most at risk. Rockefeller's Employee Health Office is conducting a free two-component screening for the disease in October and November.

Annually, physicians diagnose 200,000 American men with prostate cancer, which causes 38,000 deaths per year. The disease's earliest stages are largely silent.

Participants in the screening will be asked to give a blood specimen in October to determine levels of prostate specific antigen. In November, an American Cancer Society urologist will conduct physical exams of the prostate in the Hospital Outpatient Clinic. These exams greatly improve chances of early detection.

"We strongly recommend that men who want the most well-informed assessment of their health status participate in both aspects of the screening protocol," said Mary Brust, supervisor of the Employee Health Office.

To arrange a screening, call Aurea Tuason or Brust, x8414.

Scientific workers of the world unite

(continued from page 1)

popular bio- and chemservers, others set up and maintain sites for electronic visitors to their labs.

"If people want their own pages on private servers, we provide pointers to their sites on our home page," said Francis C. Lees, director of Information and Computing Services. "Some universities allow home pages for each member of their campus, but we don't, mostly because our staff is fully dedicated to existing support duties."

Professor Brian Chait is one of the scientists on campus who run Web sites. In collaboration with mass spectroscopists at New York University, Chait's lab operates a data resource that includes links to such databases as protein mass spectra and amino acid structures, masses, and properties. People browsing his Web site can download articles published by lab members. The Atick lab also offers downloadable articles, along with digital movies related to the lab's research and other information.

"We are making the Web an integral part of our dissemination efforts," said Jesse Ausubel, director of the Program for the Human Environment, which posts published research and a description of the program's mission on their Web page.

Assistant Professor Andrej Sali also describes his lab's research on his Web site and allows electronic visitors interested in protein modeling to download copies of its MODELLER program. The Cowburn laboratory maintains two home pages on optical and magnetic spectroscopies, one available only to RU investigators and one viewable by off-campus browsers.

Anyone with a networked computer can access the Web. RU's home page address, or URL (uniform resource locator), is http://www.rockefeller.edu/. Computing Services recommends using Netscape's browser. Contact the consultant, x8940. Anthony Popowicz, Stuart Cohnen, and Mark Kowitz serve as webmasters, and Lisa Dobruskin, Alla Minkova, Chris Pepper, Phil Sphicas, Amy Steingart, and Al Tucker contribute.

Call them webmasters, spinmeisters, or applications cognoscenti, Stuart Cohnen (*left*), Anthony Popowicz (*center*), and Mark Kowitz of RU's Computing Services spin together the necessary software for setting up sites on the World Wide Web.

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Rockefeller scientist studies genetic complexities of diabetes

by Susan Blum

Diabetes, the disease whose hallmark is high blood sugar, afflicts more than 14 million Americans, and about 650,000 new cases are diagnosed annually. The human and economic costs of the disease run high: complications include blindness, atherosclerosis, kidney failure, heart attacks, and strokes, and expenditures to treat it top $85 billion annually.

The disease, which affects the way food is metabolized, has two main types. Insulin-dependent diabetes mellitus (IDDM), an autoimmune disease, occurs when the pancreas' beta cells are destroyed and cannot produce insulin, the hormone that promotes cells' absorption of glucose and other nutrients. Non-insulin-dependent diabetes mellitus (NIDDM) results from insulin's ineffective secretion or action. NIDDM is by far the more common disease type, accounting for about 90 percent of all cases.

Diet, exercise, and drug therapy can usually control NIDDM if caught early enough, but often the condition is not diagnosed until considerable damage is done. Predictive tests would therefore be a boon, for "if we could identify risk factors before the disease's onset, we could alert people to their susceptibility and perhaps prevent complications," said Assistant Professor Markus Stoffel, who joined the Rockefeller faculty last January.

Genes are some of the most important risk factors in NIDDM, which is highly heritable—though environment also plays a role. Stoffel is searching for NIDDM genes, not only to devise better predictive measures, but also to derive a better understanding of how the disease develops.

Gene-hunting poses complexities

The search for NIDDM genes is a good example of just how complex gene hunting can be. To find DNA markers that point toward a gene whose mutations can spell trouble, researchers must be able to trace obvious profiles of disease and clear patterns of inheritance in many generations within a family. But NIDDM complicates that task in several ways. First, most forms of the disease are polygenic, meaning that more than one gene is involved in each person's case. Second, those genes have variable penetrance—that is, they can cause different degrees of disease in different people. Third, the disease usually does not manifest itself until middle age, so that patients' parents may already be deceased, and their children may still be healthy, when genetic tests might first be performed. All these factors can hinder the construction of family pedigrees that help home in on disease-causing genes.

But one rare form of NIDDM makes gene hunting simpler. Maturity-onset diabetes of the young (MODY)—also known as early-onset NIDDM—makes its presence known when people are in their 20s or even younger. Moreover, MODY is a monogenic disease with high penetrance: only one gene is needed to cause the disease, and if the mutation occurs, disease will inevitably develop.

Although MODY results from just one mutated gene, that gene is not always the same. So far, family studies have identified regions on three human chromosomes—7, 12, and 20—that harbor MODY susceptibility genes. Two of the genes remain undiscovered, but Stoffel nabbed the quarry on chromosome 7 in 1992, while he was a postdoc in the lab of the University of Chicago's Graham Bell, a pioneer in diabetes research. The gene codes for glucokinase (GCK), an enzyme produced in the pancreas' insulin-secreting beta cells.

Researchers finger a likely suspect . . .

Stoffel identified the GCK gene through a type of candidate gene approach that draws on knowledge of physiology to pursue likely suspects. Scientists had proposed that GCK is a glucose sensor in pancreatic beta-cells, setting the threshold at which insulin is secreted in response to blood sugar. So when collaborators from the CEPH Institute in Paris found a linkage between GCK gene markers and MODY, Stoffel became determined to clone and characterize the human GCK gene. Collaborating with the French scientists, he identified the gene, determined its normal sequence, and ascertained that it was mutated in about 50 percent of cases in the French families studied. Biochemical and clinical studies confirmed the enzyme's role in regulating insulin secretion in response to blood sugar.

"This was something we were all waiting for—a true genetic defect in NIDDM. It showed that the genetics work," Stoffel said.

Encouraged by these results, he tried candidate gene approaches on a number of genes. Among them was a candidate for a type of cell-surface channel—an ATP-sensitive potassium channel—whose action helps control the beta cell's secretion of insulin. Using the DNA sequences of related channels already discovered in other tissues, he and co-workers fished out a likely looking gene expressed in the pancreas. As they reported in the May 1995 issue of *Diabetes*, the gene turns out not to be linked to MODY in any of the populations they have examined. But the researchers have found that the gene's expression declines by more than 30 percent in the beta cells of a strain of diabetic rodents. They are currently creating a knockout mouse without the gene to learn more about the role the channel might play in the development or maintenance of the diabetic state. (In an interesting twist, the gene—also expressed in the brain—has recently been reported to be involved in a neurologic defect in mice.)

Markus Stoffel seeks genes that increase the risk of developing diabetes mellitus.

Meanwhile, Stoffel and his colleagues are using another approach to search for a MODY gene, dubbed MODY1, located on a region of the long arm of chromosome 20. This strategy, known as positional cloning, hunts for genes with unknown functions. Stoffel has recently completed a physical map showing that about 6 million base pairs of DNA lie in the region of interest. That's a long stretch of DNA, and various gene mapping and cloning projects have already identified eight genes within it. But the MODY1 gene is not among them, and Stoffel seeks to find it by identifying other genes in the region, determining if they are expressed in beta cells, and analyzing those that prove promising. At the same time, he aims to narrow down the area through which he must search by finding new DNA markers and collecting more family pedigrees for potential linkage to the MODY 1 gene's locus.

. . . but in science, expect the unexpected

He expects to be surprised by his findings. "We've already studied a large number of very good candidate genes, and so far only GCK has been shown to be involved in MODY. Therefore MODY1 may point us to a very novel and important pathway we haven't been aware of before," he said.

Identifying the MODY1 gene may yield medical as well as intellectual bounty, for diabetes' course is especially severe in people whose mutated gene lies on chromosome 20. "These patients develop diabetic complications at a much higher rate than those with the glucokinase mutations," said Stoffel. Once the gene is identified and its action understood, better treatments, and more effective risk-prevention strategies, may be possible for this form of diabetes.

As Stoffel and his colleagues continue their gene hunt with DNA maps and markers in hand, they are also seeking to enlarge the base of their studies with information garnered from diabetic individuals living as close as New York and as far away as the Micronesian island of Kosrae. In New York, Stoffel is recruiting diabetic subjects for research at the Rockefeller University Hospital, where genetic insights can be tested and confirmed in the clinical setting. In Kosrae, where the population is highly susceptible to diabetes, obesity, hypertension, and heart disease, studies of over 2,500 adults initiated by Rockefeller Professors Jan Breslow and Jeff Friedman will soon provide Stoffel with a wealth of new data that may disclose genetic linkages pointing to hitherto-unknown genes involved in diabetes. "Isolated island populations have been useful for genetic studies since Darwin's pioneering work," said Stoffel. "Today, with more modern techniques, we have the tools to study the genetics of complex diseases, such as diabetes, in these populations."

Sculptor of nearby artwork finds inspiration in atomic arcs, dance

Atomic particles sprint in wild arcs when scientists smash them, and their spirals—along with loop-the-loop roller coasters and a diagram of a Fred Astaire choreography—inspired Alice Aycock's enormous steel sculpture, *The Roundabout*, recently installed atop the 60th St. Pavilion.

The art completes the 12,000 square-foot river-front plaza, an amenity negotiated between Rockefeller, New York Hospital, the Hospital for Special Surgery, and community civic groups in exchange for air rights over the FDR Drive. To celebrate, representatives of the organizations gathered Thurs., Sept. 14 on the 38th floor of Scholars Residence, which overlooks the pavilion.

"I spend a lot of time looking at all different kinds of schematics. I find diagrams and movement fascinating," said Aycock, who did not construct the artwork herself but contracted it out to a company that fabricates bridges and chemical tanks. Between the time she first conceived the idea for the roof sculpture and the reception this month, three years elapsed. "Arranging the practical things takes the most time," she said.

Leif Carlsson

Heads up to view the recently installed steel roof sculpture above the 60th St. Pavilion.

Aycock found particular motivation for *The Roundabout* in the Pavilion's location. In her artist's statement, she wrote, "The site is surrounded by movement, both natural and man-made; movement through the air, on the water, over bridges, and across highways. . . . The pavilion should be an event itself."

Among the American museums that have collected and exhibited Aycock's work are the Metropolitan Museum of Art, the Museum of Modern Art, and the Whitney Museum of American Art.

Potpourri

Tri-Institutional Noon Recital

The New York Metamorphoses Orchestra performs works by Frank Martin, Gustav Mahler, and Johannes Brahms today (Sept. 29) at noon in Caspary. Guest artists will join the 22-person ensemble. Admission is free. All are welcome.

Business travel

American Express now provides travel services to the RU community, replacing the Thomas Cook Group. Reservations for university purposes can be made by calling 800-451-4145 or fax, 201-896-4792. For personal travel, calling 800-356-8540. For more information, contact David Lyons, x8292.

Weekly Research Seminars

Dates are still available to invite speakers for the Weekly Research Seminar, which meets Wednesdays at 11:00 A.M. Submit your proposals as soon as possible to Claude Desplan, x7965, fax x8370, box 151, or e-mail desplan.

Pool and beer

Anyone interested in competing in a pool tournament may sign up in the Faculty and Students Club. Also, Weinhard's Pale Lager replaces Elk Mountain Ale Draft on tap.

Free drafting tables

The Instrument Shop is giving away two used drafting tables. Contact John Doherty, x8590.

Jeopardy!

Ray Fastiggi, associate director of finance at the RU Press, appeared on the syndicated game show *Jeopardy!* yesterday (Sept. 28). Fastiggi came in second to the week's champion.

Music Room

Practice time is available in the Music Room on the first floor of Caspary. The room, equipped with a Steinway grand piano, music stands, and chairs, may be reserved for one hour during the day or evening. Because the voice carries through the building, singing is not permitted during office hours. Contact Sandi Walsh, x8072 or e-mail walsh, to sign up.

Arrivals

Visiting Associate Professor: Naoki Isu, Wilson lab.
Senior Research Associate: Ann Sostman, Cranefield-Gadsby lab.
Research Associates: Michael Boschmann, Hirsch-Leibel lab; Janet Cyr, Hudspeth lab; Naomi Morrissette, Aderem lab.
Postdoctoral Associates: Kim Caldwell, DiNardo lab; Christian Chabbert, Hudspeth lab; Juliette Desdouits-Magnen, Kathrin Kirsch, and Suzana Petancesca, Greengard lab; Satoshi Ishimaru, Hanafusa lab; Hal Lewis, Burley lab; Toshifumi Tomoda, Hatten lab; David Underhill, Aderem lab; Liang Xu, Heintz lab; Melody Yaman and Weiguo Ye, Steinman lab; Olga Yurieva, Kuriyan lab.
Postdoctoral Fellows: Stephen Alves and Christina Bjenning, McEwen lab; Roland Beckmann, Blobel lab; Qiong Cheng, Tuomanen lab; Todd Coven, Carter lab; Yoshiko Fukushima, Hideki Hasegawa, and Kazuyoshi Ishii, Hall lab; Andrew Hodtsev, Choi lab; Makoto Kimura, Roeder lab; Benedikt Kost and Baudouin Michelet, Chua lab; Antonio Parraga, Burley lab; Mark Sapp, Steinman lab; Stefan Schlussman, Kreek lab; Giovanni Stefani, Greengard lab; Douglas Strathdee, Gaul lab; Christian Vaisse, Stoffel lab.
Guest Investigators: Hayes Dansky and Jim Vitarius, Breslow lab; Paul G. Feinstein,Mombaerts lab; Salome Gomes, Steinman lab; David Green, Hanafusa lab; Yoshiaki Itoh, J. Cohen lab; Steven Kane, Gilbert lab; Hung-Teh Kao, Greengard lab; Stefan Oelman, de Lange lab; Dietmar Schmucker, Gaul lab; Keisuke Shiba, Wilson lab; Atsushi Takamiyagi, Sassa lab; David M. Weiner, R. Darnell lab.
Adjunct Faculty: Robert J. Donovan, Agosta lab; Toshiharu Suzuki, Greengard lab.

Computing Services Workshops

The workshop schedule for the next four weeks is:

Introduction to the Macintosh:
Tues., Oct. 3, 10:00 A.M. to noon;
Word for the Macintosh: Part I:
Tues., Oct. 10, 10:00 A.M. to noon;
Word for the Macintosh, Part II:
Tues., Oct. 17, 10:00 A.M. to noon;
UNIX for Sequencers, Part I:
Tues., Oct. 24, 10:00 A.M. to noon;
UNIX for Sequencers, Part II:
Tues., Oct. 31, 10:00 A.M. to noon;
WordPerfect for Windows, Part I:
Thurs., Oct. 26, 10:00 A.M. to noon;
WordPerfect for Windows, Part II:
Thurs., Nov. 12, 10:00 A.M. to noon.

Call x7768 to register.

Departures

Associate Professor: Richard Galbraith, Sassa lab.
Assistant Professors: Mark Evans, Khuri lab; Naomi Fukugawa, Hirsch-Leibel lab.
Visiting Assistant Professors: Mary Gail Mercurio, Sassa lab.
Senior Research Associates: Pamela Moore, Lederberg lab.
Research Associates: Pawel Kurzepa, Khuri lab; Yoshiaki Ohkuma, Roeder lab; Michelangelo Rossetto, Knight lab.
Postdoctoral Associates: Rupa Bandyopadhyay, Desplan lab; Heike Endemann, Zinder-Model lab; Shawn Erickson, Manning lab; John Gubbay, Heintz lab; John Hanish, de Lange lab; Hanh Huynh, Steinman lab; Hitoshi Ikegami, Wilson lab; Pavol Kois, Konarska lab; Christine Neyt, Alvarez-Buylla lab; Pilar Nosti, Breslow lab; Jeffrey Price, Young lab; Catherine Priest, Pfaff lab; Christoph Schumacher, Hanafusa lab.
Postdoctoral Fellows: David Albeck and Miles Orchinik, McEwen lab; Amitabha Chakrabarti, Cheng-Ming Chiang, Jeff Dejong, Alexander Hoffman, and Shwu-Yuan Wu, Roeder lab; Dawei Dong, Atick lab; Luc Faucheux, Libchaber lab; Stephan Feller, Hanafusa lab; Hiromasa Imaishi, Chua lab; Ping Liang, Hirsch-Leibel lab; Wei-Ming Leu, Chua lab; Lyle Najita, Konarska lab; Andrew Plump, Breslow lab; Harumi Shirakawa, Hall lab; Mark Weber, Cranefield-Gadsby lab; Florina Zaitseva, Tuomanen lab; Chunyi Zhang, Pfaff lab.
Guest Investigators: Nicholas Bouche, Xiang Ling Cao, Mathilde Fagard, and Rong-Xiang Fang, Chua lab; Ivan Cohen, Libchaber lab; Toshio Isohara, Greengard lab; Yoshiaki Itoh, J. Cohen lab; Meena Jhanwar-Uniyal, Pfaff lab; Erin Kershaw, Hirsch-Leibel lab; Yan Lavrosky, Kappas lab; Michiko Minami, Blobel lab; Faina Riftina, McEwen lab; Antonio Soares and Adam Stracher, Tomasz lab.
Adjunct Faculty: Armin Bender, Henry W. Murray, William Rom, Kendall Smith, and Jane M. Tramontana, Steinman lab; Jeremy Bernstein, Khuri lab; Dennis Hruby, Gotschlich-Fischetti lab; Eseng Lai and Christian V. Schindler, J. Darnell lab; Margaret Perkins, Müller lab; Jay Schulkin, McEwen lab.