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NEWS AND NOTES 2000, VOL.10, NO.21

The Rockefeller University

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The Rockefeller University 1901

news&notes

MARCH 31, 2000 VOLUME 10, NUMBER 21 THE ROCKEFELLER UNIVERSITY

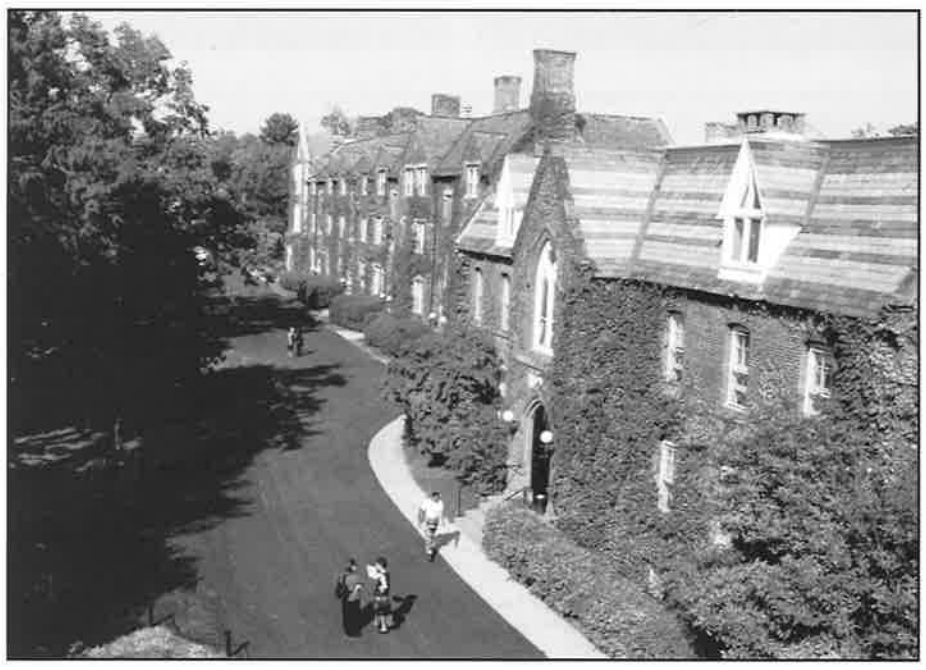
RU collaborates with Bard College to establish new science education program

Bard College and The Rockefeller University have established a collaborative program in science education, Rockefeller President Arnold J. Levine and Bard President Leon Botstein announced on Thurs., March 16.

The new Bard Rockefeller Program, which starts this year, brings together the strengths of each institution for the benefit of both. The program allows Rockefeller to build on its strong tradition in the arts and music by drawing undergraduates and liberal arts faculty to campus, who bring a different perspective to learning, teaching and research. At the same time, Bard College undergraduates will have the opportunity to study the sciences at one of the world's premier research universities while attending one of the nation's top liberal arts colleges.

Rockefeller President Arnold J. Levine says both institutions will benefit greatly from the arrangement. "The Bard Rockefeller Program will allow for extensive consultation between those with scientific and liberal arts backgrounds, enriching the perspectives of all involved," he says.

Rockefeller University graduate students and postdoctoral fellows also will have the opportunity to gain teaching experience at Bard. At the same time, some of Rockefeller's first-year graduate students will have the chance to take introductory computer science courses taught by the Bard faculty. "Bard students and faculty will interact with leading scientists, and Rockefeller will have the opportunity to expand and extend its outreach to small prestigious colleges," Levine says.



Bard College and Rockefeller University announced plans for a partnership in science education on Thurs., March 16. RU graduate students and postdoctoral fellows will get classroom teaching experience at Bard. Bard College (pictured above), is an independent, coeducational college of liberal arts and sciences. *Photo courtesy of Bard College.*

Bard College's President Botstein agrees, saying, "This unique arrangement between Bard College and The Rockefeller University demonstrates how contrasting institutions of distinction can collaborate to create new opportunities for their students and faculty. The creativity shown by The Rockefeller University and the program's advisory committee point to new paths for institutional cooperation and the development of enthusiasm for science among future college students."

Bard College is an independent coeducational college of the liberal arts and

see **Bard College**, page 2

Immunologist to join RU faculty

Alexander (Sasha) Tarakhovsky will join the RU faculty as associate professor and head of laboratory in fall 2000. *Photo courtesy of Alexander Tarakhovsky.*

The RU board of trustees approved the appointment of Alexander (Sasha) Tarakhovsky as associate professor and head of laboratory at its spring meeting, Wed., March 8. Tarakhovsky, an immunologist and currently an associate professor at the Institute for Genetics in Cologne, Germany, has accepted the appointment and will join the RU faculty in fall 2000.

"The appointment of Sasha Tarakhovsky represents an important step in our recruitment process as we implement the five-year academic plan," says President Arnold J. Levine. "I want to commend the search committee, led by David Ho, for its extraordinary job in presenting such a strong field of candidates. I am also grateful to RU Trustee Chris Browne and to the Irene Diamond Fund for gifts to the RU Centennial campaign that helped fund the position."

Tarakhovsky is interested in understanding the mechanisms of the dynamic tuning of antigen receptor-mediated signaling in lymphocytes. Using a combination of methods, including conditional gene targeting and biochemical and cell biology analyses, he addresses the signaling mechanisms of immune cell development and responses to self- and non-self-antigens.

Born in Chernovtzy, USSR, Tarakhovsky received his medical degree from the Kiev Medical Institute in 1978. He then performed doctoral work at the Institute for Developmental Biology at the Academy of Science in the USSR and at the Institute for Oncology at the Academy of Science in the Ukraine, Kiev, where he received his doctorate in 1982. Tarakhovsky continued his work at the institute from 1982 to 1990. During these years he actively collaborated with F. Kisselev at the All-Union Cancer Research Center in Moscow and M. Saarma at the Institute for Molecular Genetics in Tallinn, Estonia. In 1990, Tarakhovsky received a two-year Alexander von Humboldt fellowship at the Institute for Genetics at the University of Cologne, where he joined the laboratory of Klaus Rajewsky. Following his fellowship, Tarakhovsky became group leader and, since 1996, has been an associate professor and head of the Laboratory for Lymphocyte Signaling at the Institute for Genetics.

Tarakhovsky belongs to the German Society for Immunology, is a member of the editorial board of the *European Journal of Immunology* and is a reviewer for several other journals, including *Nature* and *The Journal of Experimental Medicine*.

The position Tarakhovsky has accepted serves one of the goals of the university's five-year academic plan, which was formulated with the contributions of students, faculty members and members of the board of trustees and approved by the board of trustees in June 1999. The plan calls for adding new faculty in fields that are likely to produce important discoveries in the next 10 years. Immunology is one of the prime areas identified by the plan for recruitment.

Friday lecture: Neural mechanisms of visual perception

Nikos Logothetis, professor of neuroscience and director of the Max Planck Institute for Biological Cybernetics in Tuebingen, Germany, and an adjunct professor at the Salk Institute and Baylor College of Medicine, will present today's Friday lecture (March 31). His topic will be "Neural Mechanisms of Visual Perception."

Logothetis' lab studies the neural basis of visual awareness in monkeys, whose visual system is very similar to that of humans. The lab uses an elaborate experimental paradigm for training monkeys to report what they perceive when viewing conflicting images, such as optical illusions, and then evaluates the mechanisms of perception via electrophysiological and functional magnetic resonance imaging (fMRI).

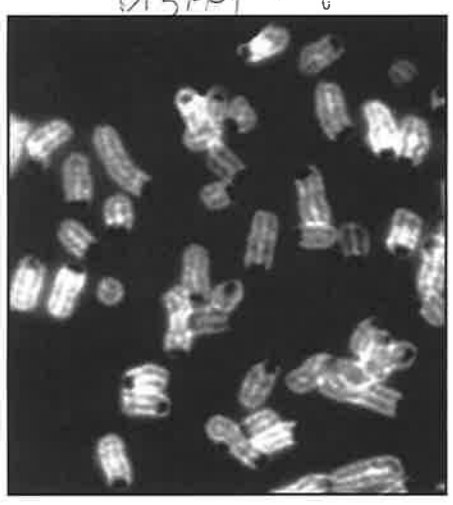
The lab's work indicates that only a fraction of the brain's neurons seem to be responsible for conscious visual perception. In addition, the work suggests that these neurons, which mediate the visual awareness of a stimulus interpretation, are distributed over the entire visual pathway, rather than residing in a single higher visual association area.

Logothetis received a diploma in mathematics from Kapodistria University and a diploma in biology from Aristotle University, both in Greece. He then received a doctorate in human neurobiology from Ludwig Maximillians University in Germany. He did postdoctoral work at the Massachusetts Institute of Technology, conducting psychophysical and electrophysiological work on the visual system of monkeys in the Department of Brain and Cognitive Sciences. Among the many honors and awards he has received are the DeBakey Award for Excellence in Science in 1996 and the Golden Brain Award of the Minerva Foundation in 1999.

The talk will begin at 3:45 p.m. in Caspary Auditorium and is preceded by a tea in Abby Aldrich Lounge. All are welcome.

Nikos Logothetis will present today's Friday lecture (March 31). *Photo courtesy of Nikos Logothetis.*

Brothers team to show that double-strand DNA repair is required for maintaining genomic stability



Brothers and collaborators: Andre Nussenzweig (at left), NIH researcher, and Michel Nussenzweig, RU professor and HHMI investigator, have found that the gene *Ku80* (center) acts as a caretaker, preventing chromosome pairs from rearranging. The above image shows chromosome aberrations in cells lacking *Ku80*. *Photos courtesy of Andre Nussenzweig (left) and NIH (center). Photo at right by Linne Ha.*

Most people at Rockefeller University are familiar with the institution's growing collaborations with the other two medical research centers surrounding the intersection of 68th St. and York Ave. and the advantages that come from pooling resources and expertise. But in the mid-'90s, cooperation on a more personal scale began between a Rockefeller University scientist and his neighboring brother.

Professor Michel Nussenzweig, head of the Laboratory of Molecular Immunology and a Howard Hughes Medical Institute investigator, teamed with his younger brother, Andre, who was across York Avenue in Sloan-Kettering's Department of Medical Physics and Radiation Oncology, to investigate the role of a gene called *Ku80*.

The brothers produced a knockout mouse that lacked the *Ku80* gene. In their first paper, published in the journal *Nature* in 1996, the researchers reported that *Ku80* is involved in cell growth and in the recombination of DNA segments to produce antibodies.

That was four years ago. Andre is no longer across the street; he currently heads a laboratory in the Experimental Immunology Branch at the National Cancer Institute, which investigates how cells monitor and repair DNA damage. Michel remains at Rockefeller, where his lab uses the tools of molecular biology to investigate the development and function of the cells in the immune system.

Nonetheless, the Nussenzweigs have found that their areas of expertise intersect at *Ku80*, and the gene continues to yield important insights. In yesterday's issue of *Nature*, a team of researchers led by Andre reported that *Ku80* acts as a "caretaker" that prevents chromosome segments from rearranging. Michel Nussenzweig and Eric Meffre, a postdoctoral associate in the Laboratory of Molecular Immunology, were co-authors on the paper.

"We've learned that chromosomes are constantly breaking and being repaired by non-homologous end joining" says Andre Nussenzweig. "Genes in this pathway are critical for maintaining the integrity of the genome, and if the genes aren't working properly, it can lead to cancer down the road."

A number of genes in mammals have been linked to cancer because tumors are more likely to develop if the genes are mutated. In recent years, biologists have classified these "cancer-susceptibility genes" into two groups: "gatekeepers," which act as brakes on uncontrolled cell growth and division, and "caretakers," which keep the body's DNA from breaking or rearranging into the wrong sequence. The most significant gatekeeper gene identified so far is *p53*, which was co-discovered by Rockefeller President Arnold J. Levine in 1979.

Ku80 already was known to play an important role in repairing "double-strand breaks" in DNA produced during V(D)J recombination in lymphocytes. But it was not known until now that *Ku80* and non-homologous end joining have a caretaker role in preserving the stability of the genome. The research reported in *Nature* shows that the cells of mice with a mutated *Ku80* gene display a marked increase of chromosome breakage and jumbled sequence.

Despite these chromosomal instabilities, mice engineered to lack *Ku80* develop cancer only slightly earlier than do normal mice, evidence that absence of *Ku80* does not cause tumors directly. Instead, deficiency in *Ku80* indirectly leads to tumors because it produces genetic changes that result in increased mutation of other genes.

At first thought, it might seem inevitable that the Nussenzweigs would be involved in medical science. As the boys grew up in Greenwich Village, both parents were involved in medical research, and other close relatives—cousins, uncles—were physicists and mathematicians. Their father, Victor, currently is a professor of pathology at NYU Medical Center, and their mother, Ruth, is chair of the Department of Medical and Molecular Parasitology at NYU Medical School.

But Michel Nussenzweig says he and his brother were not pushed into scientific research when they were young. "I wanted to be a surgeon," he says. "Andre wanted to be a basketball player." Indeed, Andre's path into biology was indirect. He earned a Ph.D. in physics from Yale University and then was a research fellow at the Ecole Normale Superieure in France. It wasn't until he finished his fellowship that he became interested in biology and went to Sloan-Kettering. Eventually, the brothers' interests converged at *Ku80*. Michel stresses that in the *Ku80* work, Andre is doing the major research and Michel is just contributing his expertise in immunology.

Potpourri

Recent talks

On Tues., March 21, Michele Hiltzik, archivist at the Rockefeller Archive Center, spoke at the Colonial Williamsburg Garden History Club meeting in Williamsburg, Penna. The topic of her talk was: "Before Williamsburg: John D. Rockefeller Jr. and his work at Versailles, Fontainebleau, Rheims Cathedral and The Cloisters."

Before John D. Rockefeller Jr. was involved in the restorations at Williamsburg, he aided the restorations of the palaces at Versailles and Fontainebleau and Rheims Cathedral (after World War I). He was also involved in the creation of the Metropolitan Museum of Art's Cloisters at Fort Tryon Park. An understanding of Rockefeller's vision of historic restoration in these projects is important to understand his involvement in Colonial Williamsburg, says Hiltzik.

Run or walk to help fight cancer

This year's Revlon Run/Walk for Women is on Sat., May 6. The annual 5K run/walk raises funds to aid research of cancers that affect women. For more information, or to join the RU run/walk team, call Jennifer Goldschlag, x8073.

AwardsCorner

★ In its November-December 1999 issue, *American Scientist* named Professor Emeritus Abraham Pais' 1986 book *Inward Bound* to its "100 or so Books that shaped a Century of Science." According to the journal, "some books trace a single theme, like Pais' volume about the journey of physicists toward finer and finer scales in the analysis of matter until in the mid-1980s the realm of quarks inside the nuclear particles was reached."

★ On Sun., March 26, Susan Richer, RU Hospital administrative manager, advanced to Fellow status in the American College of Healthcare Executives (ACHE) at the organization's 66th annual Convocation ceremony during the College's Annual Congress on Healthcare Management. Fellow status is the highest level of professional achievement in the College. To attain Fellow status, affiliates must demonstrate their education, experience and leadership in the healthcare field over a period of several years, and they must pass comprehensive written and oral examinations, as well as complete a significant project related to healthcare management.

Bard College, from page 1

sciences dedicated to promoting a rigorous education through innovative programs and high academic standards. The college, located north of New York City, offers undergraduate degrees in the arts, languages and literature, social studies, and natural sciences and mathematics, as well as graduate degrees in the arts, environmental studies and curatorial studies, and graduate and postgraduate degrees in the history of the decorative arts.

As part of the arrangement, Rockefeller will offer a course to Bard students relating to scientific inquiry and its impact on society. The first course, offered for the fall 2000 semester, will be a seminar entitled "Bacteria, Viruses and Cancer: Perspectives on Human Disease," taught by President Levine, incoming Dean Sidney Strickland, Assistant Professor Terry Gaasterland, and Betsy Hanson of the Office of Public Affairs, who is writing the university's Centennial photo history book. Fifteen first- and second-year Bard undergraduates will travel once a week to Rockefeller University for the three-hour seminar and dinner.

Bard students will have places reserved for them in Rockefeller's Summer Undergraduate Research Fellows (SURF) program, in which college students work in Rockefeller research labs and are provided room and board on the Rockefeller campus, along with a summer stipend.

Bard's Institute for Writing and Thinking will work with Rockefeller's Precollege Science Outreach Programs to offer further opportunities for secondary school students and teachers. This collaboration also will play a role in the development of the science component of Bard's planned Master of Arts in Teaching (MAT) program. Bard faculty will support Rockefeller's recruitment of graduate students by facilitating contacts with teachers and students from Bard's consortium of liberal arts colleges.

Gaasterland will join Bard's committee of outside advisors to provide advice on Bard's science initiative, including the recruitment of faculty in the area of computational biology.

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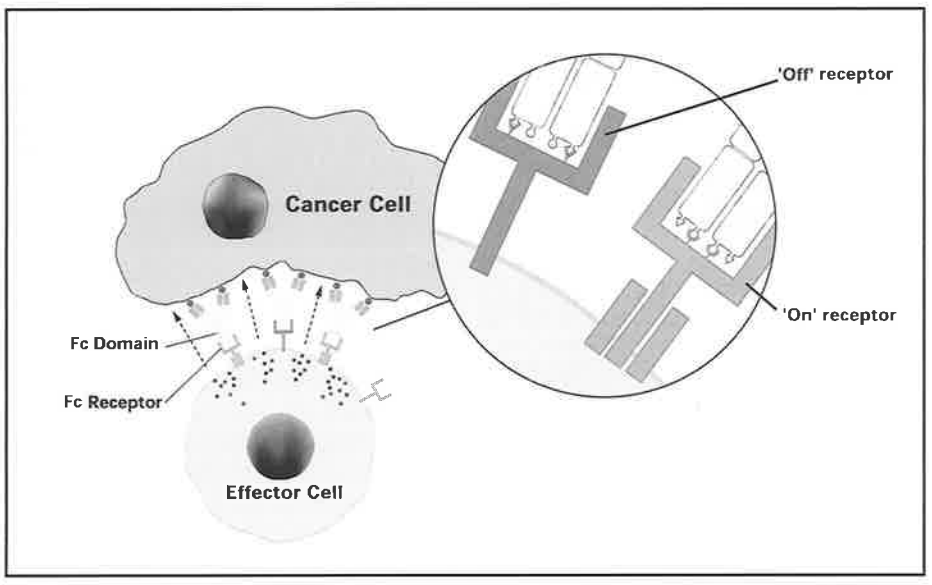
Ravetch lab finds unexpected mechanism by which anti-tumor antibodies mediate their in vivo response against tumors



Ravetch's lab discovered that anti-tumor antibodies like Herceptin and Rituxan use a segment called the Fc domain to engage receptors on the surface of effector cells in the immune system. The receptors act in pairs—one serving as an "on" switch to start an immune response, and one acting as an "off" switch to keep the response in check. Each kind of receptor binds to a specific piece of the antibody. Mice genetically engineered to lack their "on" receptors showed no response to an experimental antibody, while mice genetically altered to lack the "off" receptor experienced a very powerful—and beneficial—immune reaction. The researchers think they can design drugs that will engage the "on" receptors without engaging the "off" receptors. *Diagram by Ravi Rajakumar.*

by Jim Stallard

The immune system in vertebrates is an ingenious mix of precision and power. It must be highly specific to recognize foreign particles without mistakenly attacking the body's own cells, while being able to mount a swift, strong response to overwhelm any threat that it detects. This capacity to be both subtle and overt hinges, in part, on the body's antibodies, Y-shaped proteins that seek out antigens and then provoke the immune cells into action.

Antibody molecules comprise two main segments: a variable region, which is highly specific in order to recognize any foreign shape—such as a pathogen—it may encounter; and the Fc domain, which couples the antibody to a cellular response, in turn dependent upon certain white blood cells, called effector cells. Much of what is known about antibody structure and effector cells was discovered in Rockefeller University laboratories. Gerald Edelman helped determine the structure of antibodies, an accomplishment for which he shared the 1972 Nobel prize for medicine or physiology. The laboratory of the late Zanvil Cohn defined the role of a critical effector cell, the macrophage, in translating the specificity of antibodies into potent cellular responses.

Understanding antibody structure eventually led to ways of bio-engineering antibodies to fight disease. In the 1970s, scientists began creating monoclonal antibodies in mice and tried to use them to attack tumors in humans. Results from this approach were limited, often complicated by the incompatibility of mouse antibodies in humans. In recent years, a significant breakthrough finally occurred, proving that monoclonal antibodies could be developed and modified to be effective anti-tumor therapeutics. In 1997, Rituxan, a lymphoma-fighting monoclonal antibody modified to make it more human in sequence and produced by the biotechnology company Genentech, Inc., became the first monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of cancer. The following year, the FDA approved Genentech's Herceptin as the first monoclonal antibody to treat breast cancer.

The conventional method for trying to develop anti-tumor antibodies like these has involved focusing on contact between the variable region and the tumor cell. A successful monoclonal antibody should be specific for tumor cells, sparing normal tissue, yet potent in its capacity to eliminate the tumor cell once recognized. Scientists assumed monoclonal antibodies' key to success was attaching to the tumor cell and disrupting essential functions that allow the tumor to grow and divide. Researchers based this notion on studies in cell culture, and it has guided their approach to developing new therapies. For example, the Herceptin antibodies were identified based on their ability to inhibit the growth of breast tumor cells in culture by blocking molecules called HER2 receptors that stud the surface of cancer cells. About 20 to 30 percent of breast cancer cases are associated with a mutation in the HER2 gene, which is thought to stimulate cancer cell growth.

Surprising discovery

The assumption, it turns out, was not the whole story. Rockefeller researchers in the Leonard Wagner Laboratory of Molecular Genetics and Immunology, working with material provided by Genentech, have made a surprising discovery about the mechanism by which Herceptin and Rituxan fight tumors. The lab, led by Theresa and Eugene M. Lang Professor Jeffrey Ravetch, found that antibodies like Herceptin and Rituxan require the coupling of the antibody to effector cells through the interaction of their Fc regions and cognate receptors (Fc receptors) on effector cells. Using a mouse model of human breast cancer, the investigators found that the antibodies' effectiveness actually was determined not so much by their interaction with tumor cells but by their engagement of Fc receptors on the surface of immune cells that are induced into action. If the antibodies do not engage these Fc receptors, or the mice are genetically modified to lack those receptors, the immune response will not be triggered, and the tumor will continue to grow.

The finding, reported in the April issue of *Nature Medicine*, has immediate implications for increasing the potency of an entire class of cancer drugs now on the market and for developing more effective anti-tumor antibodies in the future.

"This should have a significant impact on immunotherapy for cancer," says Ravetch, the paper's senior author. "There are more than 20 other antibodies now being developed that are in various stages of clinical trials, and this finding shows a way to make them much more effective."

The researchers found that the receptors on the surface of the effector cells connect to Herceptin and Rituxan in pairs. One of these receptors acts as an "on" switch to initiate an immune response, while the other acts as an "off" switch to hold the immune system in check and prevent it from attacking the body. When an antibody encounters a tumor cell and engages an effector cell through its Fc portion, it's really interacting with these receptor pairs.

Ravetch and his colleagues found that the Fc receptor system operates by maintaining a delicate balance between these pairs, the "on" and "off" switches of the immune response. The balance may be skewed, for example, during an immune response to an invading pathogen or a tumor cell, but in the resting state, the conflicting forces largely check one another so that overall response is minimal.

"This should have a significant impact on immunotherapy for cancer," says Ravetch. "There are more than 20 other antibodies now being developed that are in various stages of clinical trials, and this finding shows a way to make them much more effective."

As effective as Herceptin and Rituxan are, the researchers found that removing or disabling the "off" switch could make an antibody many times more potent than before. Ravetch says the technology to do this is within reach.

Switching directions

"This finding changes how we'll approach antibody development," Ravetch says. "The assumption guiding anti-tumor therapy has been that there are specific molecules needed for tumor-cell growth, and if you want to stop the tumor, you definitely have to target those molecules. Now we're learning that how the antibody binds to the tumor cell may be less important than its interaction with Fc receptors on effector cells. It shifts our focus to the other end of the antibody."

In the *Nature Medicine* study, the researchers found that blocking the "off" switch in mice unleashes the immune system's full power. First, they gave an experimental antibody to mice with lung tumors and reduced the tumors by a factor of three to five. In mice that were altered to lack the "on"-switch receptors in their effector cells, the antibody had no effect on the tumors at all. But when the researchers removed the "off" switch from the mouse, the same antibody was actually 100 times more potent. A similar experiment performed with Herceptin showed that a comparable level of amplification was achieved when the "off" switch was disabled, suggesting that the mechanism may be general to many antibodies.

The researchers believe the effect will hold true with human tumors and human antibodies. "We think there will be some exceptions to the rule, but the majority of antibodies we've looked at so far actually work this way," Ravetch says. "They all seem to converge on a common mechanism of action, which is this harnessing of the immune system. The crucial target for drugs may be simpler than we believed."

The applications, while powerful, should also be safe because of the specificity of the drugs for their tumor targets. Modifying the drug or the effector cell to make it more potent should not cause the immune system to rage out of control because the enhanced response is specifically targeted to tumor cells and not to innocent cells in the patient's body.

Ravetch points out that benefits from the discovery should come quickly because there is no mystery about where they first should be applied. It is possible to tailor the clinical antibodies by modifying certain amino acids in the Fc domain that minimize engagement to the inhibitory Fc receptors on effector cells. "Rather than starting from scratch and having to wait as long as 10 years before therapies are available, pharmaceutical researchers can modify drugs already well along in the development pipeline," he says. "This may represent the next wave of truly effective drugs for cancer."

Ravetch's co-authors are Terri L. Towers, an RU postdoctoral fellow, Raphael A. Clynes, a former M.D.-Ph.D student at Rockefeller (now assistant professor of medicine and microbiology at Columbia University) and Leonard G. Presta of Genentech. Funding for the research was provided in part by grants from the National Institutes of Health and the Cancer Research Institute and by Genentech.

in his file

Professor Jeffrey Ravetch's lab has found that the efficacy of some cancer drugs, such as Herceptin and Rituxan, is determined more by how they interact with effector cells rather than by how they bind to tumor cells, as was previously assumed. This finding switches the scientific direction of cancer-fighting immunotherapy.
Photo by Robert Reichert.

calendarofevents

MARCH 31 | 16 APRIL

http://www.rockefeller.edu/rucal

THE ROCKEFELLER UNIVERSITY—*Please post*

FRIDAY, MARCH 31
12:00 p.m. **NF-κB/Rel: Cellular Decision between Growth and Death.** Hsiou-Chi Liou, Assistant Professor of Medicine, WMCCU. Immunology Seminar. **117 Whitney, WMCCU, 1300 York Ave.** *Contact Michele Lavarde, 746-6452.*

MONDAY, APRIL 3
11:00 a.m. **Transgenesis and Metamorphic Neural Development in *Xenopus laevis*.** Nicholas Marsh-Armstrong, Dept. of Embryology, Carnegie Institution of Washington. Developmental Biology Seminar. **301 Weiss.** *Contact Bobbie Larraga, 327-7240. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

1:30 p.m. **Presentation of Simian Immunodeficiency Virus by Dendritic Cells: Immune Activation versus Virus Replication.** Melissa Pope, Assistant Professor, RU. Immunology Seminar. **B-307, WMCCU, 1300 York Ave.**

4:30 p.m. **Regulation of Prolonged Changes in Neuronal Excitability.** Leonard K. Kaczmarek, Professor of Pharmacology and Physiology, Yale U. School of Medicine. PBMM Research Seminar. **Weill Auditorium, WMCCU, 1300 York Ave.** *Coffee at 4:15 p.m.*

TUESDAY, APRIL 4
1:00 p.m. **GeneSpring—An Integrated Analysis and Visualization Environment for Gene Expression, including Analysis of Function and Pathways.** Silicon Genetics. Starr Center for Human Genetics Seminar. **301 Weiss.** *Contact Lynn Petukhova, 327-7181. Equipment demo will follow talk.Open to RU community and guests.*

2:00 p.m. **The Regulation of the p53 Network.** Moshe Oren, Dean, Faculty of Biology, Dept. of Molecular Cell Biology The Weizmann Institute of Science. **305 Weiss.** *Open to RU/WMCCU/NYPH/MSKCC community and guests.*

4:00 p.m. **Figuring Out Transcription Factor Networks.** Dennis Shasha, Professor, Courant Institute, NYU. Center for Studies in Physics and Biology Seminar. **B Level Conference Room, Smith Hall Annex.** *Tea at 3:30 p.m. Contact Martin Zapotocky, 327-8835.*

4:00 p.m. **Signaling Pathways in PUFA-modulation of Colorectal Cancer.** Sergio A. Lamprecht, Professor of Biochemistry, Strang Cancer Research Laboratory. CNRU Research Lecture. **117 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** *Contact Linda M. Cotte, 639-8352.*

WEDNESDAY, APRIL 5
11:00 a.m. **S6 Kinase: A Regulator of Cell Size.** George Thomas Jr., Senior Scientist-Group Leader, Friedrich Miescher Institut, Basel, Switzerland. Pels Family Center for Biochemistry and Structural Biology Seminar. **301 Weiss.** *Contact Angus Nairn, 327-8871. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

6:00 p.m. **Identification and Regulation of Stem Cells for Adult Neurogenesis.** Arturo Alvarez-Buylla, Associate Professor, RU. **The Birth and Death of Neurons, from Stem Cells to Functional Circuits.** Ronald McKay, NIH. Neuronal Stem Cells, Breakthrough Research Seminar. **New York Academy of Sciences, 2 East 63rd Street.** *Contact Henry Moss, 838-0230x410. Presented by the Neuroscience Section of the New York Academy of Sciences, the Neuroscience Therapeutics Section of Parke-Davis Pharmaceuticals and the New York Section of the Society for Neuroscience.*

6:30 p.m. **Genetic Control of Physiological and DNA Damage-induced Apoptosis in the *C. elegans* Germ Line.** Michael Hengartner, Cold Spring Harbor Laboratory. **OPA-1, a Novel Schwann Cell Factor Involved in Neuronal Survival and Regeneration.** David Weinstein, Albert Einstein College of Medicine. Cell Death Society Meeting. **301 Weiss.** *Pizza at 6:00 p.m. RSVP to Ray Birge, 327-7412, with number of people attending. All are welcome.*

THURSDAY, APRIL 6
12:00 p.m. **Gonadotropin Signaling in the Male.** William F. Crowley, Director, Reproductive Endocrine Sciences Center, Massachusetts General Hospital, Harvard Medical School. Endocrinology and Reproductive Biology Seminar. **301 Weiss.**

12:00 p.m. **Insights into Potential Functions of Orphan Metalloprotease-disintegrins (ADAMs).** Carl P. Blobel, Associate Professor, Cellular Biochemistry and Biophysics Program, MSKCC. Biochemistry Lecture. **E-115 WMCCU, 1300 York Ave.**

3:00 p.m. **Maternal Care, Gene Expression and the Development of the Emotional Brain.** Michael Meaney, Professor of Neuroscience and Psychiatry, McGill U. Systems Neuroscience Seminar. **305 Weiss.** *Open to RU/WMCCU/NYPH/MSKCC community and guests.*

4:00 p.m. **Designing Engineered Vaccines for HIV and Hepatitis C Virus.** Jay A. Berzofsky, Chief, Molecular Immunogenetics and Vaccine Research Section, Metabolism Branch, NCI, NIH. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** *Contact Rosanna Martinez, 570-3357.*

FRIDAY, APRIL 7
9:00 a.m.–5:00 p.m. **Molecular Pathways to Cancer.** Judith Campisi, Lawrence Berkeley National Laboratory. Andrew J. Dannenberg, WMCCU; Napoleone Ferrara, Genentech; David Foster, Hunter College; Sumayah Jamal, NYU Medical Center; Christoph Lengauer, The Johns Hopkins Oncology Center; John Kuriyan, RU and HHMI; Chris Marshall, Institute of Cancer Research, London. Symposium. **714 West Bldg., Hunter College, 68th St. at Lexington Ave.** *Poster Session: The New York World of Cancer Research. Admission is free. No registration. For further information, http://biology.hunter.cuny.edu/symposium2000/.*

10:30 a.m. **Promoter Recognition and Gene Expression in Mycobacteria.** Sabine Ehrt, Cornell U. New York TB Club Seminar. **110B Nurses Residence.** *Contact Claudia Manca, 327-8103.*

12:00 p.m. **IκB Kinases and Innate Immunity.** Tom Maniatis, Professor, Dept. of Molecular and Cellular Biology, Harvard University. Molecular Biology Seminar. **116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** *Refreshments at 11:45 a.m.*

MONDAY, APRIL 10
11:00 a.m. **β-3 Integrin Receptors: From Molecular Insights to Improved Therapies.** Barry Coller, Murray M. Rosenberg Professor of Medicine, Chairman of The Samuel Bronfman Dept. of Medicine, Director and Chief of Medicine, Mount Sinai School of Medicine. Clinical Seminar. **301 Weiss.** *Refreshments will be served. Contact Bobbie Larraga, 327-7240. Open to RU community and guests.*

12:00 p.m. **Modeling Structured Treatment Interruption and Immunotherapy in the SIV251 Macaque Model.** Genoveffa Franchini, NCI, NIH. CFAR Seminar. **Sixth Floor Conference Room, ADARC, 455 First Ave.**

12:30 p.m. **The Regulation of the p53 Protein.** Arnold J. Levine, President, RU. Immunology Lecture. **Second Floor Conference Room, HSS, 535 East 70th St.**

TUESDAY, APRIL 11
4:00 p.m. **Doxycycline Induction of Photoreceptor-specific Genes in Transgenic Mice.** Dean Bok, Professor of Neurobiology and Dolly Green Professor of Ophthalmology, UCLA. Progress in Neuroscience Seminar. **Weill Auditorium, WMCCU, 1300 York Ave.** *Tea at 3:45 p.m.*

WEDNESDAY, APRIL 12
12:00 p.m. **Seminars in Clinical Research.** M. Alan Permutt, Washington University. Seminars in Clinical Research. **110B Nurses Residence.**

1:00 p.m. **Animal Welfare—Reason, Regulations and the 3 R's.** Brian Corning, Director of LARC, RU. Seminar. **302 Weiss.** *Refreshments will be served. Contact Joanne De Stefano, 327-7012. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

3:00 p.m. **John Merck Scholars Program 10th Anniversary Celebration.** Linda Buck, Harvard Medical School; Allison Doupe, UC San Francisco; Ali Hemmati-Brivanlou, RU; Earl Miller, MIT; Timothy Tully, Cold Spring Harbor Laboratory. **301 Weiss.** *Contact Nancy Stockford, 617-723-2932. Afternoon Symposium. Moderated by Rockefeller President Emeritus Torsten Wiesel. Refreshments will be served at 3:00 p.m.*

4:00 p.m. **The Miraculous Development of The Scientific Method: A Historical Overview.** Frederick Seitz, President Emeritus, RU. Lecture. **110B Nurses Residence.** *Contact Florence Arwade, 327-8423.Open to RU/WMCCU/NYPH/MSKCC community and guests.*

THURSDAY, APRIL 13
3:00 p.m. **Timing, Temporal Coupling and Response Selection.** Richard Ivry, Professor of Psychology, UC Berkeley. Systems Neuroscience Seminar. **305 Weiss.** *Open to RU/WMCCU/NYPH/MSKCC community and guests.*

4:00 p.m. **Effect of Fibrinogen and FDP's on Fibroblast Gene Expression.** Mitchell A. Olman, Associate Professor of Medicine and Pathology, U. of Alabama at Birmingham. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** *Tea will be served.*

The Arts and Other Events

FRIDAY, MARCH 31
12:00 p.m. **Tri-Institutional Noon Recitals.** Fitzwilliam String Quartet. Performing quartets of Purcell, Haydn, Shostakovich and Glazunov. **Caspary Auditorium.** *Contact John Gerlach, 327-7776. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

THE ROCKEFELLER UNIVERSITY Friday Lectures & Thesis Presentations

These events are held in Caspary Auditorium at 3:45 p.m. Tea is served in Abby Aldrich Rockefeller Lounge at 3:15 p.m. All are welcome.

FRIDAY, MARCH 31
Neural mechanisms of visual perception. Nikos Logothetis, Professor of Neuroscience, Director, Max Planck Institute for Biological Cybernetics Tübingen, Germany.

WEDNESDAY, APRIL 5
***Thesis Presentation*: Toward Immunophenomics: The Unbiased Characterization of Antibody Recognition.** Bradley Messmer, Graduate Fellow, RU.

FRIDAY, APRIL 7
On the Evolution of Transcriptional (and Other Regulatory) Systems. Mark Ptashne, Ludwig Professor of Molecular Biology, MSKCC.

MONDAY, APRIL 10
***Thesis Presentation*: Gene Expression during Song and Sleep: Studies on Brain Representation.** Sidarta Ribeiro, Graduate Fellow, RU.

TUESDAY, APRIL 11
***Thesis Presentation*: Modulation of Dendritic Cells and T Cells through Nef and the Implications for SIV Replications.** Davorka Messmer, Graduate Fellow, RU.

FRIDAY, APRIL 14
***First Annual Richard M. Furlaud Lecture*: Structural Biology of Eukaryotic Gene Expression.** Stephen Burley, Professor, RU; Investigator, HHMI.

THURSDAY, APRIL 6
8:00 p.m. **Rockefeller University Film Series.** *Fragrance of the Wild Flowers.* **Caspary Auditorium.** *Open to RU/WMCCU/NYPH/MSKCC community and guests*

FRIDAY, APRIL 7
12:00 p.m. **Tri-Institutional Noon Recitals.** Valerian Ruminiski, bass, and William Hicks, piano. Performing arias from operas and oratorios, and songs. **Caspary Auditorium.** *Contact John Gerlach, 327-7776. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

THURSDAY, APRIL 13
8:00 p.m. **Rockefeller University Film Series.** *Fast, Cheap and Out of Control* (1997). Directed by Errol Morris. **Caspary Auditorium.** *Open to RU/WMCCU/NYPH/MSKCC community and guests.*

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