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The Rockefeller University

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news&notes

MARCH 3, 2000 VOLUME 10, NUMBER 18 THE ROCKEFELLER UNIVERSITY

RU scientists featured at NYAS neuroscience lecture series

A New York Academy of Sciences spring lecture series focuses on the basic biology and clinical implications of the discovery that the adult brain is capable of producing new neurons. In a series of six talks, scientists responsible for breakthroughs in neuronal stem cell science will review the origins of the research, discuss current work and future directions and examine the clinical and ethical implications for this line of research. Scientists from Rockefeller make up about half of the program, a reflection of the university's prominence in neuroscience.

RU Professor Fernando Nottebohm presented the first lecture in the New York Academy of Sciences' spring lecture series on neuroscience. *Photo by Lisa Stillman.*

Dorothea L. Leonhardt Professor Fernando Nottebohm opened the series on Wed., Mar. 1. His topic was "Neuronal Replacement in the Adult Vertebrate Brain: Hope for a New Neurology." Many different kinds of brain cells, or neurons, are produced in adult fish, reptiles, birds and mammals, and these new neurons are added to many parts of the brain. This process—which for many years was thought to be impossible—has been intensely studied in the song system of songbirds.

Recent work (see story on page 3) by Assistant Professor Constance Scharff and Nottebohm, John Kirn from Wesleyan University and Jeffrey Macklis from Harvard shows that survival of the new neurons is encouraged by "vacancies" created by prior cell death. For reasons not understood, however, only some kinds of neurons are replaced; others are not, even if prior deaths create vacancies.

Nottebohm also described earlier work he did with Associate Professor Arturo Alvarez-Buylla on the manner of neuronal migration. "The challenge now," says Nottebohm, "is to discover the purpose of spontaneous neuronal replacement in adult brains and how to control this process for clinical purposes. The practical goal will be to rejuvenate circuits and repair broken ones." To do this, it will be important to learn how to replace any kind of neuron that may die. "Though fixing broken brains—and spinal cords—may still sound like something out of science fiction," he says, "the discovery that some kinds of neurons are normally produced and replaced in the adult brain opens the door for a whole new neurology."

Alvarez-Buylla will expand on Nottebohm's remarks in a talk on Wed., April 5, entitled "Identification and Regulation of Stem Cells for Adult Neurogenesis." The adult brain's germinal layers provide unique advantages for identifying cell types important for neurogenesis and studying how this process is regulated. His lecture will focus on the primary neuronal precursors in the adult brains of birds and mammals (see story on page 3).

After Nottebohm's lecture on March 1, Elizabeth Gould of Princeton University discussed "Neurogenesis in the Adult Mammalian Brain." Her work on neurogenesis began at Rockefeller in the laboratory of Alfred E. Mirsky Professor Bruce McEwen. Gould has gone on to show that neurogenesis occurs in adulthood in the hippocampus of infrahuman primates as well as rodents, and that it is inhibited by stress. Moreover, she has recently shown that a type of learning that involves the hippocampus leads to a prolongation of the survival of newly formed neurons in the dentate gyrus of the hippocampus.

The series will conclude on Wed., May 31, with a lecture by McEwen. He will discuss "Resilience and Vulnerability of the Adult Brain: From Serendipity to Clinical Relevance." The adult brain is capable of considerable adaptive plasticity in terms of its structure as well as its neurochemistry, McEwen notes. Besides neurogenesis in some brain regions, there is synaptic replacement and remodeling of dendrites in other regions of the brain as a result of experience and the actions of circulating hormones. "Collectively, this plastic-

see **Neuroscience lecture**, page 2

Friday lecture: Levine to discuss using DNA chips to study cancer

New technology using the DNA chip, which can analyze the activities of thousands of genes at a time, promises to speed up biomedical applications from the discovery of new drugs to the prediction of disease susceptibility. At the Friday lecture today (March 3), President Arnold J. Levine will discuss "The Regulation of Gene Expression in Cancer Cells Probed with DNA Oligonucleotide Chips."

President Arnold J. Levine will present today's Friday lecture. *Photo by Robert Reichert.*

DNA chips, or microchip arrays, are small glass wafers that resemble computer chips but are studded with bits of DNA instead of transistors. The chips work by detecting the levels of messenger RNAs in a preparation and pinpointing the changes between a tumor cell and its normal counterpart. Levine uses DNA chips to study the expression patterns of the tumor suppressor gene *p53*.

Discovered by Levine at Princeton University with colleague Daniel Linzer in 1979, *p53* is the gene with the single most common mutations in human cancer, appearing in about 60 percent of all cancers and in 80 percent of all colon cancers. Normal functioning *p53* is an important checkpoint that helps monitor cells for DNA damage, killing those that are mutated. For instance, after receiving a signal of cell damage, *p53* can be activated to function as a transcription factor. Binding to DNA sequences near certain downstream genes, *p53* can initiate transcription leading to cell-cycle arrest or cell suicide.

"The quest for identifying the downstream genes for *p53* is the next big

see **Friday lecture**, page 2

RU welcomes a new neighbor: Herbert Pardes to talk at next Cohn Forum

Herbert Pardes, the newly elected president and chief executive officer of New York-Presbyterian Hospital, will present the next Zanvil A. Cohn Forum on Health Affairs on Mon., March 6. His talk is entitled "Toward a Sound Policy on Academic Medicine and Medical Research."

Pardes brings a broad approach to the problems of health and mental health. Formerly the vice president for health sciences and dean of the faculty of medicine at Columbia University, a position he held for 10 years, he has an extensive background in psychiatry, academic medicine and government leadership in mental health. In his role at Columbia, he developed major changes in the education of physicians, enhanced the clinical and basic science research of health sciences and assumed a national role as an advocate for education, health reimbursement reform and support of biomedical research.

Herbert Pardes, new head of neighboring NYPH, will discuss the future of academic medicine. *Photo courtesy of Herbert Pardes.*

He has served as president of the American Psychiatric Association (APA) and chair of the APA's council on research, as well as chair of the Association of American Medical Colleges. In 1997, he was appointed by President Clinton to serve on the Advisory Commission of Consumer Protection and Quality in the Health Care Industry and was elected a member of the Institute of Medicine.

Pardes has an extensive record of national advocacy and interaction with government leadership. He has testified to Congress and Congressional committees extensively and has been called upon as a consultant to the National Institutes of Health. Through the 1980s, he was one of the primary leaders in developing alliances and facilitating the growth of citizen groups on mental illness; he has received awards from most of the major citizen organizations by virtue of his advocacy on behalf of patients and their families.

The Cohn Forum is a series of colloquia on issues in health and biomedicine. The lecture will be held in Abby Aldrich Rockefeller Dining Room at 5:30 p.m. and will be preceded by a wine and cheese reception at 5:00 p.m. All are welcome. Admission is free.

Prospective students visit RU campus

Prospective graduate students arrived on campus last night for two days of the RU experience. This week's open house and another next week allow students to learn more about the university, both its research and its ambiance.

President Arnold J. Levine and Professor Titia de Lange and Associate Professor Robert Darnell welcomed the students at a pre-dinner reception yesterday and spoke to them about the research being done at RU. Today the prospective students will visit labs, take part in a roundtable discussion lunch session with current students and attend a poster session describing RU research. Later they will attend Levine's Friday lecture. In the evening they will be treated to a party at Scholar's Residence.

According to Dean Fred Cross, the applicant pool this year was extremely competitive. "Outstanding students interested in graduate school are highly sought after by programs all over the country, but we're pleased that so many of these students were interested in visiting our program. We hope that when they meet with Rockefeller scientists (both faculty and students) and learn about their research, they will want to join us."

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Music news at Rock U:
Fresh Fruit brings a taste of austral summer to campus

The Feb. 18 Tri-institutional Noon Recital featured the pop sounds of Fruit. *Photo by Paul Schneck.*

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When the Australian pop band Fruit arrived at RU on a snowy Friday (Feb. 18) to play for the Tri-institutional Noon Recital, it was a first for both audience and performers. "We've never played a recital before," laughed singer Susie Keynes as she tuned up her electric guitar.

The Noon Recitals tend to feature classical music, so concert-goers who hadn't checked the program beforehand were surprised to see a Caspary stage set-up that looked more Rolling Stones than Rachmaninoff. After a couple of songs, however, the audience was clapping along to the band's "pop/funk/Latin/punk" sound. Some young people in attendance had never been to a Noon Recital before but planned to return. Many were impressed with the musicianship of Fruit, whose members play a variety of instruments and all have trained voices.

Best described as acoustic pop, Fruit's eclectic music incorporates funk, blues, rock and groove. The band seemed unused to an audience that remained seated, but, as one of the singers noted after the performance, "It was great to have people who were actually listening."

Archive center acquires the Fosdick papers

The Rockefeller Archive Center recently acquired 25 reels of microfilm of the papers of Raymond B. Fosdick, a trustee of the Rockefeller Institute for Medical Research from 1921 to 1936 and a longtime friend and advisor to John D. Rockefeller Jr. and president of the Rockefeller Foundation (1936-1948). Fosdick also authored a biography of John D. Rockefeller Jr. and histories of both the Rockefeller Foundation and the General Education Board. Fosdick (1883-1972) donated his papers to Princeton University in 1966.

Recently the Archive Center joined forces with Princeton's Seeley G. Mudd Library to preserve the collection on microfilm. Since the Fosdick papers at Princeton contain much correspondence with members of the Rockefeller family and about various Rockefeller endeavors and institutions, including the Rockefeller Institute, the Archive Center thought it fitting to join in an effort to preserve the collection in exchange for a copy of the film for researcher access at the Archive Center in Sleepy Hollow, N.Y.

Save the Date:
Thursday, June 8, 2000
RU's 42nd Convocation for Conferring Degrees
to be held in Caspary Auditorium

Potpourri

Theater tickets
Human Resources is offering a limited number of reduced price tickets for the following performances: Lauren Bacall and Rosemary Harris in Noel Coward's hit comedy, "Waiting in the Wings" on Fri., March 10, at 8 p.m.; tickets are $19.30 each. The Paul Taylor Dance Company at the Manhattan City Center on Sat., March 11, at 8 p.m.; tickets are $16.30 each. Christopher Walken and Faith Prince in the hit musical production of James Joyce's "The Dead" on Thurs., March 16, at 8 p.m.; tickets are $21.30 each. To reserve your tickets call Ron Kurtz, x8303.

92nd Street Y Lecture
The 92nd Street Y will present a panel discussion on the legacy of Marilyn Monroe in Caspary Auditorium on Tues., April 11. Panelists include authors Joyce Carol Oates and Dominick Dunne, columnist Liz Smith and film critic Molly Haskell. Tickets are $20 and can be purchased at the 92nd Street Y's box office or through Y charge at 996-1100. A number of free tickets will be available for RU students. Call x8072.

Abby Aldrich Dining Room
The Abby Aldrich Dining Room will be closed Wed., March 8, due to a meeting of the Board of Trustees. The dining room will open again Thurs., March 9.

Online calendar training session
Need to know how to post events on the RU online calendar? Individual training sessions will be held next Thurs., March 9, in A21 Smith Hall between 2 and 4 p.m. To schedule an appointment call Jennifer Goldschlag, x8073.

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Arnold J. Levine, President
Mariellen Gallagher, Vice President of Communications and Public Affairs
Joseph Bonner, Director of Communications
Lisa Stillman, Associate Director, Media Relations

Ann-Marie Blaber, Editor
Jim Stallard, Science Writer
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problem in the field," says Levine. "We use DNA chips—which have about 6,500 different sequences, or about 5 to 10 percent of the genome—to look for genes that are transcriptionally activated after *p53* is turned on."

Using a DNA chip, Levine's group identified 107 genes that *p53* positively regulates and 54 genes that *p53* negatively regulates. The researchers also studied the kinetics of transcription—which genes are turned on or off rapidly or slowly and how long they remain on after *p53* is activated.

"We found very heterogeneous kinetics," Levine says. "Some genes were turned on, then turned off; others were turned off and then turned on. Some genes were delayed 8 to 10 hours before being turned on."

The scientists then asked, "Is there a hierarchy in genes turned on if you regulate the level of p53 protein?" For example, would more genes be turned on if there were five times as much *p53* than if there were one-fifth? The answer is yes. According to Levine, some genes required very high levels of *p53* to be turned on; others needed very little.

"We think this could reflect differences in binding constants of the proteins to the DNA," says Levine. "Or it could reflect the stability of the message the genes receive from *p53*."

Levine and his colleagues also looked at what happens to the genes that *p53* regulates when DNA-damaging agents—ultraviolet light and gamma radiation—were introduced. Each of these agents damages DNA in different ways, and the genes that activate *p53* and the repair mechanisms are also different.

"We think different kinds of damage activate different signals for *p53* activity," Levine says.

The experiments were done in tissue culture cells, a very controlled type of study. Levine's group went on to look at a more complicated situation: colon cancers freshly isolated from patients. As a control, the scientists used adjacent normal colon tissue. This minimizes genetic variations because the tissue comes from the same patient, and it decreases physiological variations because it comes from identical adjacent tissue. The researchers looked for differences in gene expression patterns between the colon cancer tissues and the normal tissues.

"We think there might be differences in gene expression because of the nature of the mutations that drive colon cancer, which have been characterized by Bert Vogelstein and his colleagues," says Levine. "These mutations are found in genes that form pathways that activate transcription factors or in the transcription factors themselves."

"If you could take colon cancers at different stages, you might expect to see these progressive changes in transcription patterns due to mutations in certain genes," continues Levine, "and that is exactly what we saw."

Using a DNA chip, the researchers took 61 tumors and 21 normal adjacent tissues, lined them up for comparison and clustered all the tumors together and all the normal tissues together to show patterns of transcription for more than 2,000 genes. The patterns are "illuminating," says Levine, because they show sets of genes that are important for growth regulation. Furthermore, the researchers were able to show clustering in subtypes of colon cancer. For example, benign tumors called adenomas, which have a mutation only in a gene called APC, cluster and separate from the cancer and from the normal tissue.

"The key is the nature of the cluster analysis," says Levine. "'Which two tissues have the same pattern of gene expression?' is one way to ask the question. And when you do that one at a time, two at a time and so on, you find all the cancers clustering, all the adenomas clustering, etc."

Thus, according to Levine, the DNA chip demonstrates that there are different patterns of gene expression in cancer cells. The patterns can be useful, he says, for understanding heterogeneity between tumors—for example, why some tumors respond to chemotherapy and others do not.

"Some of that heterogeneity will lead to prognostic uses in treating cancer," he says.

The lecture will be held at 3:45 p.m. in Caspary Auditorium and preceded by a tea in Abby Aldrich Lounge. All are welcome.

Neuroscience lecture, from page 1

ity confers a degree of resilience upon the adult brain in the face of its vulnerability to damage by stress, insults and the ravages of neurodegenerative disorders," he says. "The resilience of the brain, initially gained by serendipity and regarded as a scientific curiosity, is relevant to interpreting new data on structural changes in the adult human brain in depressive illness, post-traumatic stress disorder, schizophrenia and aging, as well as to understanding the potentially protective effects of estrogens on the aging brain."

All lectures take place at the New York Academy of Sciences, 2 East 63rd Street, New York, N.Y. They are free and open to the public. For more information, call 838-0230, x410.

RU welcomes new catering manager

Kathrina Deignan (left), Food Service director, welcomes new catering manager Naezen Dukes (right) and bids a fond farewell to Mary Menzer (center), departing catering manager. Menzer, who has organized RU food events for the past two years, leaves RU to head up the catering at the Guggenheim Museum. Dukes, who arrived at RU on Mon., Feb. 28, will quickly fill her shoes. For information about the catering services available or to place an order, call Dukes at x7890. *Photo by Ann-Marie Blaber.*

disfet

Life after death: Selectively killing neurons in the brain can lead to the birth of new ones

Ever since 1983, when Professor Fernando Nottebohm and his then-graduate student Steve Goldman discovered that new neurons are spontaneously generated in the brains of birds, one question continued to puzzle the burgeoning field of adult neurogenesis. What caused some kinds of cells to be replaced and others not? In the Feb. 24 issue of *Neuron,* scientists in the Nottebohm lab, along with Jeffrey Macklis at Harvard University's Children's Hospital and John Kirn at Wesleyan University, have found an explanation for the difference in the cell types. Even more intriguing, the new finding raises the possibility that induced neuronal replacement can restore a learned behavior.

"These findings are so appealing to me because they combine some basic insights into the regulation of neuronal addition into the fully mature brain with a glimpse at whether neuron addition is really the long-suspected source of song plasticity," says RU Assistant Professor Constance Scharff, who initiated these studies and is the lead author on the paper.

The RU scientists wondered why some neurons in the bird brain are continuously replaced during adulthood, while their neighbors are not. Could it be that death triggers the birth of new cells, and therefore only the type of cell that dies gets replaced? What would happen, they wondered, if they killed the other type of cell, the type that normally doesn't die? Would this cell type then also be replaced?

To answer these questions, the lab selectively killed certain neuron populations in one of the areas responsible for song production in adult zebra finches. (Using a laser technique that was pioneered by Macklis, they were able to kill only those neurons that had previously been retrogradely labeled. Thus the elimination of cells was much more specific than what had been possible in the past.)

The researchers killed both types of cells and found that death does indeed stimulate the replacement, but only in those neuron types that are replaced normally. The neurons that don't "turn over" naturally didn't get replaced. This is the first direct demonstration that death can in fact cause replacement, but that this process is cell-specific.

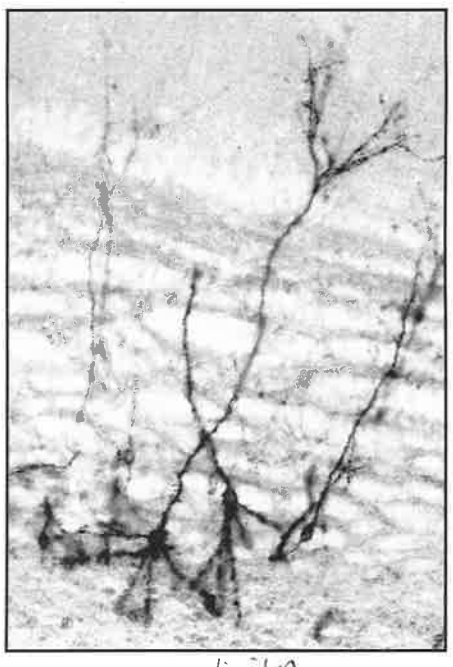
"What's even more fascinating," says Scharff, "were the effects on the birds' behavior." In intact zebra finches, the two targeted neuron populations are known to have different jobs: those that continuously turn over are part of the pathway that allows the bird to sing. The other neurons, those that do not normally die and also do not normally get replaced, are part of a pathway that allows the bird to learn his song during development.

When the team killed the neurons in the "song production" pathway, some birds started singing very garbled and abnormal songs, as expected. It was proof that those particular neurons are vital for normal song production. What was surprising, however, was the remarkable recovery that followed: some zebra finches sang songs that were identical to their original song three months after the laser treatment, which happened also to be the time when many more newly generated neurons were seen in their brains. This correlation suggests that the recovery of the behavior and the brain repair go hand in hand. "If this is in fact so," says Scharff, "it remains to be seen what kind of information, including molecular cues, contacts with neighbors, access to memory and auditory experience is needed to prepare a new neuron for a new job."

Professor Fernando Nottebohm and Assistant Professor Constance Scharff have shown for the first time that neuron death can cause neuron replacement.

The search for the source: RU scientists identify neural stem cells in the adult brain

The discovery that new neurons continue to be formed in certain regions of the adult brain in vertebrates, including humans, is considered one of the most important advances of the last two decades. How this unexpected regenerative capacity is maintained has been the focus of intense research. The laboratory of Associate Professor Arturo Alvarez-Buylla recently added surprising contributions to this area of neuroscience.



New nerve cells, above, derive from the division of astrocytes.
Image courtesy of Arturo Alvarez-Buylla.

Other parts of the body that retain regenerative capacity in adult life (such as the digestive tract, skin or blood) were known to retain cells of unique powers known as stem cells. Stem cells are important because they not only renew themselves to maintain a pool of precursors throughout life, but also generate the differentiated cells responsible for adult tissue function. In the case of the brain, it was thought that stem cells were consumed during development. However, if new neurons are formed in the adult brain, as scientists now know, somewhere in the nervous system there must be progenitors or stem cells. Alvarez-Buylla's laboratory has shown that the source of new neurons is different from what scientists had expected, and they also have identified neuronal precursors that have the ability to move around in the adult brain.

Earlier work from the Alvarez-Buylla laboratory revealed a large germinal layer in the adult mammalian brain that produces thousands of new neurons every day. Called the subventricular zone (SVZ), this region lies next to the walls of the brain ventricles (the large cavities filled with cerebrospinal fluid in the cerebral hemispheres). Young neurons created in the SVZ migrate along each other in chains to other parts of the brain. The fully mature brain contains a complex and extensive network of pathways for chain migration.

When the RU lab, in collaboration with Jose Manuel Garcia-Verdugo of the University of Valencia in Spain, looked closely at the SVZ, they found that chains of migrating neuroblasts were ensheathed by slowly proliferating glial cells called astrocytes. Next to the chains were clusters of highly proliferative immature precursors they called Type C cells. But which cells really gave rise to the new neurons? It was suspected that Type C cells might be the true source of new neurons, but the Alvarez-Buylla lab wanted direct evidence for the origin of the new neurons.

To find out which cells were the real precursors, they used various approaches. In work published in *Cell* and *Proceedings of the National Academy of Sciences* last year, Fiona Doetsch, a graduate fellow in the Alvarez-Buylla laboratory, developed methods to eliminate actively dividing cells from the SVZ, which resulted in the complete elimination of Type C cells and young neurons. Remarkably, the SVZ network rapidly regenerated. After 10 days, the migratory network was back in business moving large numbers of newly formed young neurons.

"This is a dramatic phenomenon, the only example in the adult mammalian brain of full functional regeneration," says Alvarez-Buylla. "As in other regenerative tissues like the blood or skin, this regeneration suggested the presence and activation of stem cells."

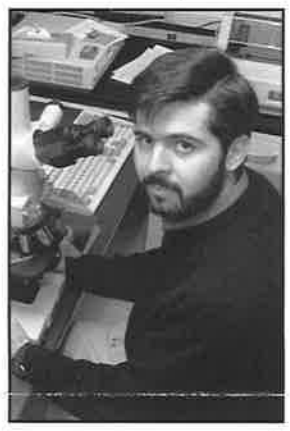
Doetsch and her colleagues noticed that only SVZ astrocytes and neighboring ependymal cells, which can be identified by their structure and long cilia (hair-like structures on the outside of the cell), were left after the elimination of actively dividing cells. Ependymal cells were never seen to divide, but during the early stages of regeneration, astrocytes divided and gave rise to Type C cells, which in turn gave rise to the young neurons.

"This was surprising because astrocytes are considered highly specialized cells that were thought not to procreate in this manner, much less be able to mother young neurons," says Alvarez-Buylla. Was this normal behavior of SVZ astrocytes, or was it a product of the experimental killing of the dividing cells?

Using genetically modified mice whose SVZ astrocytes could be selectively tagged, the Alvarez-Buylla laboratory demonstrated that, in normal mice, astrocytes also give rise to new neurons. The work went on to show that SVZ astrocytes also give rise to self-renewing stem cells in the culture dish. The results confirmed that new neurons that formed in the adult brain, in both the normal and the regenerating brain, originate from the division of resident astrocytes.

In work recently published in *The Journal of Neuroscience,* the Alvarez-Buylla laboratory has identified the primary precursors of the new neurons in adult canaries. These cells also have many of the characteristics of glial cells.

"The picture that begins to emerge suggests that neural stem cells are closely related to the glial lineage, a notion that goes against the current dogma," says Alvarez-Buylla. "The anticipation was that the stem cells were going to correspond to immature-looking cells, with no other function but procreation. Not so. The progenitors seem to have a job too, that of astrocytes. Our findings raise the possibility that other astrocytes within the adult brain may also act, or could be induced to act, as neuronal stem cells, a possibility with powerful implications for brain repair. Before that, there is much biology to be learned: in particular we want to understand the signals within the SVZ that make astrocytes behave in this manner."



Associate Professor Arturo Alvarez-Buylla's lab discovered that the source of new neurons in the brain is different from what scientists had expected.
Photo by Robert Reichert.

Knowing what the precursor cells were, however, didn't necessarily suggest an obvious medical application. Other researchers previously tried to introduce new neurons into damaged brains, but the grafted primary neuronal precursors stayed where they were inserted, unable to move into regions where new neurons may have been needed. It was believed that the environment of the adult brain, unlike that of the embryo, lacked the signals and scaffolding to support migration of grafted young neurons.

Studies that graduate fellow Hynek Wichterle pioneered in the Alvarez-Buylla lab have overturned this idea. In work published in *Nature Neuroscience,* Wichterle and colleagues tested the migratory potential of neuronal precursors from several different brain regions, using both in vitro and in vivo techniques. They found that cells in different germinal regions have remarkably different migratory potential. Most importantly, this work was able to identify a particular population of neuronal precursors that indeed can move very efficiently through the dense matrix of adult mammalian brain tissue. After moving for several millimeters, these cells integrate seamlessly to become fully mature nerve cells and part of adult brain circuits.

By changing the paradigm of how we think about the origins of nerve cells and their behavior in the adult brain, these findings suggest other neurobiological and medical areas of study. Thus the next decade is likely to be as surprising as the last one.

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http://www.rockefeller.edu/rucal

THE ROCKEFELLER UNIVERSITY—*Please post*

FRIDAY, MARCH 3

10:30 a.m. **Genotypic Analysis of *M. tuberculosis*: Implications for Antibiotic Resistance, Epidemiology, and Virulence.** David Alland, Montefiore Medical Center, Bronx, N.Y. New York TB Club Seminar. **110B Nurses Residence.** *Contact Claudia Manca, 327-8103.*

12:00 p.m. **Regulation of T Cell Activation through CD28/CTLA-4 Receptors.** Ellen Chuang, Assistant Professor of Medicine, Division of Hematology-Oncology, WMCCU. Immunology Seminar. **117 Whitney, WMCCU, 1300 York Ave.**

12:00 p.m. **Wiring Up the Brain: Molecular Mechanisms of Growth Cone Guidance.** Corey S. Goodman, Investigator, HHMI; Professor, Neurobiology and Genetics; Director, Neuroscience Institute, UC Berkeley. Cellular Biochemistry and Biophysics Seminar. **116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.**

MONDAY, MARCH 6

12:00 p.m. **Visualization of HIV in Living Cells: HIV Core Particles Travel on Microtubules to Reach the Nucleus during Infection.** Thomas Hope, Salk Institute for Biological Studies. CFAR Seminar. **Sixth Floor Conference Room, ADARC, 455 First Ave.**

4:00 p.m. **Challenges in High Resolution Solids NMR of Uniformly Labeled Macromolecules at Ultra High Fields.** Kurt Zilm, Professor, Dept. of Chemistry, Yale U. NMR Structural Biology Seminar. **301 Weiss.** *Contact Milton Werner, 327-7221.*

4:30 p.m. **Metabotropic Glutamate Receptor Signalling: From Test Tube to Mouse.** Robert Duvoisin, Associate Professor of Ophthalmology and Cell Biology, WMCCU. PBMM Research Seminar. **Weill Auditorium, WMCCU, 1300 York Ave.** *Coffee at 4:15 p.m.*

5:30 p.m. **Toward a Sound Policy on Academic Medicine and Medical Research.** Herbert Pardes, President and CEO, NYPH. Zanvil A. Cohn Forum on Health Affairs. **Abby Dining Room.** *Sherry at 5:00 p.m. in the Abby Lounge.*

TUESDAY, MARCH 7

3:00 p.m. **α-Kinases: A New Class of Protein Kinases with a Novel Type of Catalytic Domain and Multiple Functions.** Alexey Ryazanov, Dept. of Pharmacology, UMDNJ-New Jersey Medical School. Cellular Biochemistry and Biophysics Seminar. **101 Rockefeller Research Laboratories, MSKCC, 430 E. 67th St.**

4:00 p.m. **Cell Culture Models for Organsite Cancer Prevention.** Nitin Telang, Senior Scientist and Head, Julian H. Robertson Jr. Chemoprevention Research Lab, Strang Cancer Prevention Center. CNRU Research Lecture. **117 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.**

4:00 p.m. **Nitric Oxide Signaling: Pathways Of Neuronal Survival and Death.** Ted Dawson, Associate Professor of Neurology and Neuroscience, Johns Hopkins U. School of Medicine. Progress in Neuroscience Seminar. **Weill Auditorium, WMCCU, 1300 York Ave.** *Tea at 3:45 p.m.*

4:00 p.m. **Statistical Structure of Spike Trains of Visual Cortical Neurons.** Jonathan Victor, Professor, WMCCU. 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.*

WEDNESDAY, MARCH 8

10:30 a.m. **Biostatistics Course.** Biostatistics Course. **128 Hospital.** *Contact Knut Wittkowski, 327-7175.Open to RU/WMCCU/NYPH/MSKCC community.*

11:00 a.m. **Studying Drug Abuse in *Drosophila*.** Ulrike Heberlein, Associate Professor, Dept. of Anatomy, UC San Francisco. Seminar. **305 Weiss.** *Contact Ulrich Unnerstall, 327-8677. Open to RU/WMCCU/NYPH/MSKCC community.*

12:00 p.m. **HIV-Specific CTL and Protection against Infection with HIV.** Douglas Nixon, Assistant Professor, RU; Staff Scientist, ADARC. Seminars in Clinical Research. **110B Nurses Residence.**

3:45 p.m. **Asymmetry and Cell Fate.** Richard Losick, Maria Moore Cabot Professor of Biology, Dept. of Molecular and Cellular Biology, Harvard U. Seminar. **Auditorium, Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** *Tea at 3:15 p.m.*

6:30 p.m. **Key Role for avb5 Integrin in Phagocytosis by Retinal Pigment Epithelial Cells.** Silvia C. Finnemann, WMCCU. **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 will be served at 6:00 p.m. Please RSVP to Ray Birge at 327-7412.*

THURSDAY, MARCH 9

12:00 p.m. **Cdc42: More Surprises & Questions.** Richard A. Cerione, Molecular Medicine, Veterinary Medical Center, Cornell U., Ithaca. Biochemistry Lecture. **E-115 WMCCU, 1300 York Ave.**

12:00 p.m. **Developmental Regulation by Nuclear Orphan Receptor Coup-Tf.** Sophia Y. Tsai, Professor, Dept. of Molecular and Cell Biology, Baylor College of Medicine. Endocrinology and Reproductive Biology Seminar. **301 Weiss.**

4:00 p.m. **Integrin Signaling.** Filippo G. Giancotti, Associate Member and Lab Head, Cell Biochemistry and Biophysics Program, MSKCC. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** *Tea at 3:45 p.m.*

4:00 p.m. **Interactions of Dietary Nutrients and Environmental Toxins: Lead Poisoning as a Model.** John D. Bogden, Professor, Dept. of Preventive Medicine and Community Health, UMDNJ-New Jersey Medical School. CNRU Special Nutrition Lecture. **D-417 WMCCU, 1300 York Ave.**

4:00 p.m. **Thermodynamics of the Origin of Life.** Philip W. Anderson, Professor, Princeton U. Center for Studies in Physics and Biology Seminar. **B Level Conference Room, Smith Hall Annex.** *Contact Martin Zapotocky, 327-8835.*

FRIDAY, MARCH 10

12:00 p.m. **NK Receptors for HLA Class I Molecules.** Bo Dupont, Professor, Immunology Program, Member, MSKCC. Immunology Seminar. **117 Whitney WMCCU, 1300 York Ave.**

12:00 p.m. **The EGF-CFC Gene Family and Axis Formation in the Mouse Embryo.** Michael Shen, Assistant Professor, UMDNJ–New Jersey Medical School; Resident Member, Center for Advanced Biotechnology and Medicine. Molecular Biology Seminar. **116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** *Refreshments at 11:45 a.m.*

7:00 p.m. **Psoriasis Support Group.** Patricia Gilleaudeau, Research Nurse, RU. Psoriasis Support Group Meeting. **110B Nurses Residence.** *Contact Patricia Gilleaudeau, 327-8333.*

MONDAY, MARCH 13

10:00 a.m. **Membranolytic Active Peptides—Forms and Functions.** James P. Tam, Professor of Microbiology and Immunology and of Biochemistry, Vanderbilt U. Seminar. **302 Weiss.** *Contact Nam-Hai Chua, 327-8126. Open to RU community.*

12:00 p.m. **Presentation of Simian Immunodeficiency Virus by Dendritic Cells: Immune Activation Versus Virus Replication.** Melissa Pope, Assistant Professor, RU. CFAR Seminar. **Sixth Floor Conference Room, ADARC, 455 First Ave.**

TUESDAY, MARCH 14

11:00 a.m. **Unnatural Substrate-based Cellular Engineering and Evolution: Applications to Cancer and Glycosylation Disorders.** Kevin Yarema, Assistant Specialist, Dept. of Chemistry, UC Berkeley. Pels Family Center for Biochemistry and Structural Biology Seminar. **305 Weiss.** *Contact Bobbie Larraga, 327-7240. Open to RU/WMCCU/NYPH/MSKCC community.*

11:00 a.m. **Using Zebrafish to Explore the Genetic Basis of Vertebrate Neural Development and Behavior.** Su Guo, Dept. of Neuroscience, Genentech Inc. Developmental Biology Seminar. **301 Weiss.** *Contact Bobbie Larraga, 327-7240. Open to RU/WMCCU/NYPH/MSKCC community.*

4:00 p.m. **Biomimetic Carpentry of Self-assembling Functional Protein Nanostructures.** Edward Goldberg, Professor, Tufts U. 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.*

WEDNESDAY, MARCH 15

12:00 p.m. **Autoimmunity—Molecular Impressionism.** Antony Rosen, Johns Hopkins U. Seminars in Clinical Research. **110B Nurses Residence.**

3:00 p.m. **TGF-β/SMAD Signaling.** Joan Massague, Professor, MSKCC. Student-Sponsored Seminar. **301 Weiss.** *Refreshments at 4:00 p.m. in the Weiss 17th Floor. Open to RU community.*

5:00 p.m. **Mammalian Cloning, a Progress Report.** Jose Cibelli, Vice-President Research, Advanced Cell Technologies. Seminar. **301 Weiss.** *Contact Peter Mombaerts, 327-7300.*

THURSDAY, MARCH 16

11:00 a.m. **Control of Cell Division and Growth in the Developing Drosophila Wing.** Laura A. Johnston, Division of Basic Sciences, Fred Hutchinson Cancer Research Center. Developmental Biology Seminar. **301 Weiss.** *Contact Bobbie Larraga, 327-7240. Open to RU/WMCCU/NYPH/MSKCC community.*

12:00 p.m. **Does Estrogen Make the Man?** Charles E. Roselli, Associate Professor, Dept. of Physiology and Pharmacology, Oregon Health Sciences U., Portland. Endocrinology and Reproductive Biology Seminar. **Weiss 17th NE DR.**

2:00 p.m. **Structural Basis for Histone Acetylation by the GCN5 and P/CAF Transcriptional Coactivators.** Ronen Marmorstein, Associate Professor, The Wistar Institute, U. of Penna. Pels Family Center for Biochemistry and Structural Biology Seminar. **301 Weiss.** *Contact Bobbie Larraga, 327-7240. Open to RU/WMCCU/NYPH/MSKCC community and guests.*

3:00 p.m. **Neuroimaging of Frontal Lobe Function.** John Duncan, Research Staff, Attention Group, MRC Brain and Cognition Unit, Cambridge, UK. Systems Neuroscience Seminar. **305 Weiss.**

5:00 p.m. **The Legacy of Dolly: Biomedical and Research Applications of Nuclear Transfer.** Alan Colman, Director of Research, PPL Therapeutics. Seminar. **302 Weiss.** *Contact Peter Mombaerts, 327-7300.*

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 3

The Regulation of Gene Expression in Cancer Cells Probed with DNA Oligonucleotide Chips. Arnold Levine, President, RU.

FRIDAY, MARCH 10

Potassium Channels. Rod MacKinnon, Professor, RU; Investigator, HHMI.

MONDAY, MARCH 13

***Thesis Presentation*: A Close Look at the Strong Coupling Constant.** Christina Mesropian, Graduate Fellow, RU.

TUESDAY, MARCH 14

***Thesis Presentation*: Learning to See: Experience and Attention in Primary Visual Cortex.** Roy Crist, Graduate Fellow, RU.

The Arts and Other Events

THURSDAY, MARCH 9

8:00 p.m. **Rockefeller University Film Series.** *Public Enemy* (1931). Directed by William Wellman. **Caspary Auditorium.** *Open to RU/WMCCU/NYPH/MSKCC community and guests.*

FRIDAY, MARCH 10

12:00 p.m. **Tri-Institutional Noon Recitals.** Matt Haimovitz, cello. Performing Cello Suites of Johann Sebastian Bach. **Caspary Auditorium.** *Contact John Gerlach, 327-7776.Open to RU/WMCCU/NYPH/MSKCC community and guests.*

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