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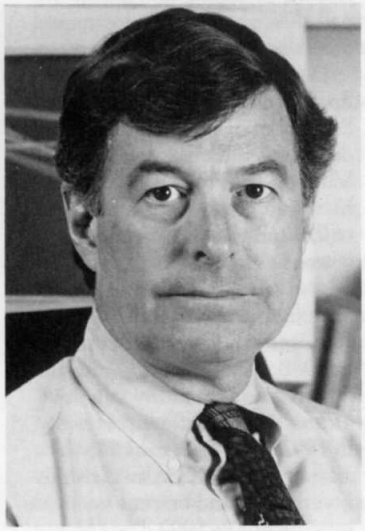
The Rockefeller University

news & notes

January 26, 1996 Volume 6, Number 15 — *The Rockefeller University*

President of blood center to discuss safety of blood supply



Courtesy of John Adamson

John Adamson served as president of the International Society for Experimental Hematology in 1992-93.

John W. Adamson, president of The New York Blood Center, will speak on "Maintaining the Safety of the Blood Supply—The New York Blood Center in the Age of AIDS" at the next Cohn Forum, Tues., Jan. 30.

"While John has conducted basic and clinical research on blood and blood products, he has also served on many public policy committees struggling with issues of supply and demand," said Alexander Bearn, chair of the forum selection committee. "He will talk to the forum about what health professionals are doing and can eventually do to make blood and blood products safer."

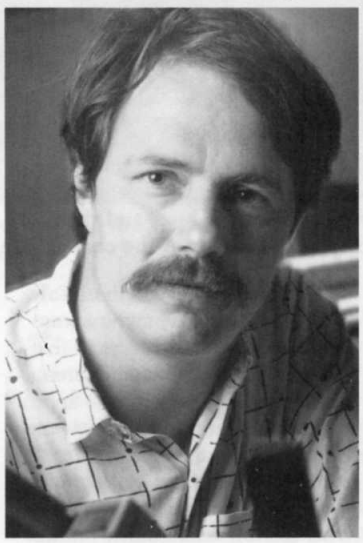
After earning his M.D. from the University of California, Los Angeles in 1962, Adamson trained in hematology and internal medicine at the University of Washington and the National Institutes of Health's Clinical Center in Maryland. He returned to the University of Washington as assistant professor in 1967, becoming professor in 1978. In 1989, he became president of the New York Blood Center and director of its Lindsley F. Kimball Research Institute.

Adamson serves as president of the American Society of Hematology and is a past member of its Advisory Board and past chairman of its committee on scientific affairs and transfusion medicine. He has served on a half-dozen NIH committees and as editor-in-chief of *Blood*. In 1988, the American Cancer Society designated him a clinical research professor and the American Association for the Advancement of Science elected him a fellow in 1991.

The talk will take place at 5:30 P.M. in Abby Aldrich Rockefeller Dining Room. Sherry will be served at 5:00 P.M. All are welcome.

At the Friday lecture

Molecular geneticist discusses hallmark of PAX developmental regulators



Claude Desplan studies molecular mechanisms of embryo development.

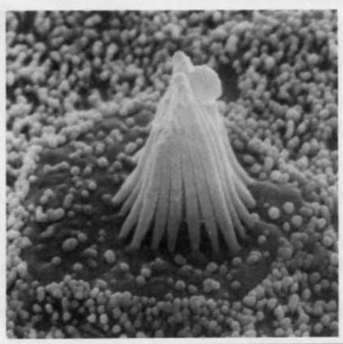
Associate Professor Claude Desplan, an associate investigator of the Howard Hughes Medical Institute (HHMI), discusses "Paired Domain and Homeodomain: A Synergy for Pax Developmental Functions" at the Friday lecture today (Jan. 26).

Desplan and his colleagues study the fruit fly *Drosophila* to investigate the molecular mechanisms underlying early development. Desplan focuses on homeoproteins, transcription factors that switch genes on or off, controlling segmentation of the body plan. These proteins are named after the 60 amino acid conserved DNA-binding region called the homeodomain.

One of the molecules the lab studies is the *Drosophila paired* gene, which encodes a protein that contains a homeodomain and a paired domain, another conserved DNA-binding motif that is the hallmark of the PAX class of developmental regulators. A combination of in vitro, crystallographic, and in vivo studies has resulted in the precise determination of the mechanisms of action of the Paired protein, which serves as a paradigm for PAX molecules. Recently, in conjunction with Professor John Kuriyan's laboratory, Desplan and his coworkers showed how two paired-class homeodomains bind cooperatively to DNA. Among the other insights Desplan's lab has made into the genetic mechanisms of early *Drosophila* development is the synergy between the morphogens Hunchback and Bicoid, which act together in the formation of the body's axis.

"Claude began his study of how gene control plays a role in development of the fruit fly by doing the first determination that homeobox proteins actually bind to DNA," said Professor James E. Darnell, Jr., who introduces Desplan today. "Here, he and his students are now engaged in how

See ***Desplan****, page 2*



Courtesy of Jim Hudspeth

Public lecture series opens with talk on hormones, stress, and development

Felton Earls, professor at the Harvard School of Public Health (right) *and Mary Carlson* (center), *associate professor at the Harvard Medical School, gave the first of three public lectures on behavior and the brain sponsored by the Arthur Vining Davis Foundations. Organized by Professor Bruce McEwen* (left) *of RU and Professor Jack Barchas of Cornell University Medical College* (not shown), *the series next features a talk by McEwen Thurs., Feb. 22 on "Stress, Brain, and Behavior." The talk will take place at 6:00 P.M. in Caspary Auditorium.*

Lighting up the way to beauty and camaraderie

LeannaMiuccio

Bob Francis, director of Plant Operations, explains the proposed upgrade to lighting of the grounds near Caspary Dome and the Faculty and Students Club. The display is on view at the club.

Plant Operations is developing a landscape lighting plan for the grounds surrounding Caspary Dome and the Faculty and Students Club to add light for nighttime activities and aesthetic polish.

"Increased use of the gardens outside the Faculty and Students Club this past fall brought about requests for improvements in lighting, particularly for cookouts. That spurred us on," said Bob Francis, Plant Operations director. "Artful lighting complements our lovely buildings, statuary, and grounds. This is the first phase of what we hope will be a five-year effort to light up the landscape and show it at its best at all times."

Along with the landscape lighting design company Brandston and Partners, Francis is refining blueprints to install six types of lights to serve four purposes: dramatize the restored Caspary Dome, increase visibility on the pathways to the club, brighten the cookout area, and enhance the nighttime appearance of the garden's decorative features—reflecting pools, tall trees, and sculptures.

For comments and suggestions from the RU community, Francis posted a display of preliminary plans in the club in mid-December. This display will remain on view until mid-February, when he must finalize plans with the lighting company.

"Often when I visit the club, people express their opinions informally about the proposal. So far, about 15 people have said they liked the ideas," said Francis, and none has objected.

The artistic component of the proposal calls for reflecting lights over the pools. "Choosing soft lights that won't be perceived as any specific color is quite a trick," he noted. Also, spot lighting of sculptures will create an outdoor gallery effect, and fixtures in trees will cast light downward to counterfeit a dappled, moonlit look. Finally, the four fountains surrounding the dome will be restored and lighted.

The lights will draw power from the Caspary and Abby Aldrich Rockefeller buildings. Francis noted that in fact the project requires little raw power. New wiring, however, may need additional conduits. If so, workers will dig trenches when the project begins in the spring.

"More people are visiting the club, and more people reserved the barbecue pit last year, perhaps because we moved it from its previous location in the Berlin Garden. This place is on the move, scientifically and socially," said Francis.

Club adds McSorley's Ale

The Faculty and Students Club now has on tap McSorley's Ale, a New York brew with an Irish background. The ale replaces Weinhard's Red Lager. Draft Fuller's ESB is still served.

Desplan discusses developmental regulators at Friday lecture

(continued from page 1)

interactions between transcription factors, including homeobox proteins, produce developmental decisions."

Desplan, a graduate of the Ecole Normale Supérieure de Saint Cloud, received his doctoral degree from University of Paris VII in 1983. From 1984 to 1987 he was a postdoc at the University of California in San Francisco, where he worked with Pat O'Farrel on the function of homeodomain proteins during early development. He joined the Rockefeller faculty in 1988 as an assistant professor and head of laboratory. He was promoted to associate professor in 1992. He began his HHMI affiliation in 1988 as an assistant investigator and became associate investigator in 1992.

Desplan received postdoctoral support from the Fogarty International Center and the European Molecular Biology Organization. He was an André Meyer fellow during his first year at Rockefeller, and he has received awards from the Fondation pour la Recherche sur le Cancer and the Fondation Simone et Cino Del Duca.

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.

Proceeds from sale of conference center will support research

Real-estate entrepreneur Donald Trump purchased Seven Springs, the university's 200-acre property in Mount Kisco, N.Y. in late December. Rockefeller will share the proceeds, $7.5 million, with Yale University, a former owner of the estate. The RU share, when added to a pre-existing separate endowment fund for the property, will cumulate to about $10 million and will then constitute a new unrestricted endowment to support research.

Seven Springs was the home of the late Eugene I. Meyer, Jr., who owned *The Washington Post* newspaper. In 1970, his widow donated the estate, which includes two mansions, orchards, and a marble swimming pool, to Yale. The Eugene and Agnes Meyer Foundation ran the estate for Yale as a conference center and gave the property to RU in 1984.

When Trump signed the contract to buy the estate in August 1995, his reported intention was to convert the estate into a small golf club.

© Skyview 1976

Seven Springs was completed in 1919 as a summer home for the publisher of *The Washington Post*, Eugene Meyer.

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To analyze hearing

Neuroscientist draws on biology, engineering, and thermodynamics

by Kay Locitzer

Philosophers dither about whether the tree that falls in a forest makes a sound if nobody hears it, but to neuroscientist Jim Hudspeth, the answer is simply, "Yes, it does. Just as lightning occurs when your eyes are closed. The problem is the semantics of the word *sound*. Sound means both the physical change in air pressure, which clearly exists when the tree falls, and the sensory perception of that change."

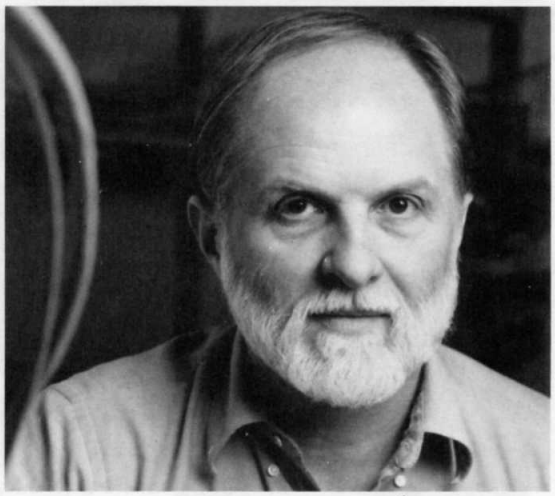
If it seems a fine hair to split, well, that is Hudspeth's expertise: splitting, or rather, slicing up the tiny hair cells of the ear to understand auditory perception—on the cellular not the philosophical level. Since his graduate student days in the Harvard lab of Torsten Wiesel and David Hubel, Hudspeth has studied how the ear converts the physical movement of air into electrical impulses understood as sound by the brain. A Howard Hughes Medical Institute investigator who joined the RU faculty in August 1995, he is the university's first F.M. Kirby Professor.

In labs in the Rockefeller Research Building (RRB) and Smith Hall, Hudspeth and 17 associates conduct experiments on hearing encompassing basic questions and techniques in areas as diverse as immunology, biophysics, and developmental biology. Hudspeth also is set on understanding why human hearing loss occurs and what might be done to prevent or rectify it.

The Cinderella sense

Indeed, the pathophysiology of hearing compelled him to tackle the subject back in the Harvard neurobiology lab, which was dedicated to vision. Scientists then so neglected hearing that its nickname was the "Cinderella sense," a moniker that proved prophetic given today's widespread interest. Scientists knew only the locations and roles of structures such as the stirrup, hammer, and anvil bones, the cochlea, and the neural pathway from the ear to the brain. The means by which the cochlea translates sound vibrations into neural code was hidden in a proverbial black box.

For more than two decades, Hudspeth has advanced understanding of the cochlea's crucial organelle—the hair cell, a neuron-like receptor that lines the ear in all vertebrates. A human cochlea contains some 16,000 cylindrical hair cells, each topped with a tuft of 50 to 100 whiskers, or stereocilia. The whiskers list inward, forming a cone, and the stereocilia are short on one side, taller on the other, forming a slope.



Jim Hudspeth joined the Rockefeller faculty in August 1995.

Hudspeth and David Corey, then a graduate student, found in an early experiment that this slope figures in sound reception. When they pushed a glass probe against the short side of the hair bundle—simulating air pressure—the receptor burst into electrochemical action. Only pushing on the tuft's tall side results in this activity, which conveys information to the neurons below the cell, which in turn synthesize messages for the cerebral cortex.

A unique gate

Hudspeth and Corey noticed that the electrochemical current flowed into the cell at its upper end. The team hypothesized that the channels allowing ions in were located there. They also noticed that stimuli boot hair cells into action within a few millionths of a second—in general, human ears hear 1,000 times faster than eyes see—and they reasoned that all known methods by which cells electrochemically open their channels were far too slow to account for such a rapid response.

Hudspeth and Corey postulated that stereocilia sported an entirely new type of mechanical gate to the channel—an elastic spring. In 1984, researchers in England, having developed a new technique for preserving cells, discovered delicate filaments on the stereocilia, connecting them within a bundle like telephone wires swooping from pole to pole. This form was consistent with the spring function.

How does the filament work? In response to a sound vibration, the hair bundle bends, like grass in a breeze. The taut filament on a taller stereocilium pulls open the channel gate on its shorter neighbor, initiating ion flow. When the cell rebounds, the gate slams shut.

"The filaments have since been seen in every species examined. They are quite a universal feature, which strengthens the argument that they are intimately involved in gating," said Hudspeth.

He and his colleagues have studied the filament's point of origin, called the insertion plaque. Their work indicates that a motor protein, a type of myosin, moves the plaque up and down on the cell, controlling the filament's tension on the gate. The motor protein may also be responsible for auditory adaptation: in the face of ongoing stimulation, myosin will reset the plaque's position, releasing the filament and thereby allowing the gate to close and the cell to stop responding.

Nature, the engineer

In predicting the elastic string, Hudspeth sought a *biological strain gauge*, as he termed it. He often analyzes neuroscientific questions in mechanical terms and defines organelles in the parlance of an electrical engineer: hair cells are *transducers*, their membranes are *capacitors*. Changing electrical potentials in the saline solution surrounding the tip of a stereocilia pointed to a *current sink*.

To Hudspeth, nature is the ultimate engineer. "The broader way of construing hearing is in terms of thermodynamics, which considers energy transfer. Each of our senses should be as sensitive as it can possibly be. If some other creature can see or hear you before you see or hear it, it is very likely to pounce on you. And if your prey can see or hear you before you reach it, you'll starve and die. So evolution has pushed the system down to the physically optimal form, and thermodynamics describes the physical optimum."

This appreciation of things mechanical extends to the equipment and circumstances that enable him to conduct his science. Hudspeth is conversant with the myriad sources of noise—vibrational and electromagnetic—that can ruin experiments. Manhattan granite, he noted, insulates his Smith Hall labs from the FDR Drive traffic. Being on the lower floors of the RRB and Smith shields his labs from the Manhattan air full of pesky television, radio, and cellular phone wavelengths.

And copper paint coats several of his rooms. "The copper reflects electrical energy. The old way was to encase labs in galvanized steel, but the copper paint Robert Schill [of RU's Planning and Construction staff] found was better and cheaper," Hudspeth said, adding, "The copper looks so nice we didn't paint."

Unexplained phenomena

Hudspeth is currently pursuing two major quests in his Rockefeller labs. The first is the physiological system behind the phenomenon called cochlear amplification, and the second is cell development. The ear, explained Hudspeth, "outperforms its apparent specifications. It is not a passive recipient of sound but amplifies it a hundredfold. Just consider the analog—light goes into your eye, and the photoreceptors begin to glow and emit their own light, which is picked up by other photoreceptors. That would be extraordinary."

The hair bundle responds to a stimulus that has only enough energy to displace it by 0.3 billionths of a meter. This corresponds to wind displacing the tip of the Eiffel Tower by an inch.

Aside from intellectual curiosity in such a mechanism, Hudspeth's interest stems from the fact that hearing loss begins when cochlear amplification ceases. And amplification ceases when hair cells are damaged, a clue that the mechanism resides somewhere in these receptors. Hudspeth is eyeing the stereocilia.

Probe a hair bundle, he's noticed, and after it bows, it kicks back and oscillates. "This is the sort of thing one would look for. One needs a system in which even the smallest sound waves are enhanced, supplemented with vibrations of the same frequency but of a larger amplitude," he said. His lab is working with pharmacological reagents to try to shut down proteins that may cause the oscillation.

The second major project in the Hudspeth lab focuses on an outstanding problem in cell biology: What organizes the development of a cell? "Because of its precise and elaborate structure, the hair cell is a good place to ask what molecules choreograph development and how they do it," Hudspeth said.

However complex the process may prove, Hudspeth is sure that it will also have a basic simplicity and mechanical virtue, because nature does not squander energy.

In winter winds, lab members rescue kitten from Plaza homestead

With a butterfly net and cat food laced with mild tranquilizer, members of the McEwen lab captured a lone kitten who had holed up for weeks last month under the southern staircase between Sophie Fricke Hall and the Plaza patio.

"We tried six times to catch her. She would accept food, then run away," said administrative assistant Anne Conners, who adopted the kitten and took her home, but added that the lab has designated her as an official mascot.

In early December, several people glimpsed the fluffy grey orphan resting on a nest of leaves adjacent to the heating vent below the staircase. How she got there no one knows, but rumors circulate of a stray calico who lives on campus and had a litter. Karen Bulloch, visiting assistant professor in the McEwen lab, began to feed the kitten, and lab members attempted to rescue her.

As a December snowstorm approached, they feared for the kitten's survival and sought advice from Michael Hayre, director of the Laboratory Animal Research Center. He suggested spiking cat food with tranquilizer, then catching the kitten in a butterfly net.

Courtesy of Anne Conners

Administrative assistant Anne Conners (*left*) adopted a kitten she caught on campus with other members of the McEwen lab, which has made the kitten, named Rockyj, its mascot. *Right*: Rockyj expresses her thanks to the lab head.

"About four of us trooped out there. It was snowing hard and the wind was whipping across the Plaza," recalled Conners. "We gave her the food with the tranquilizer, but it didn't take effect right away. She ate, she licked the can, she started batting it back and forth, and this went on for half an hour.

"Finally, we were freezing, so we approached her, and like a flash of lightning she ran under the steps. I lay down and started pounding on the steps on one side and waving the butterfly net. Liisa Galea [postdoctoral fellow] stood on the other side and caught her with her bare hands, which was an act of bravery. Even Michael said he wouldn't have picked her up with his bare hands. The kitten was shaking, she was so scared."

Hayre gave the kitten shots, dusted her for fleas, guessed her age to be three months, and supplied a crate in which Conners carried her Christmas present home. The kitten promptly hid in her apartment for three days.

"I still don't know where she was, but now she's Miss Congeniality," said Conners. "She'll lick your ears." When Conners recently went away on a five-day vacation, McEwen took care of her. "He's in love with her. We all are. She rules the lab," she said.

The kitten's name? Rockyj—after one of RU's Computing Services servers. Conners said, "We wanted her to have a Rockefeller name. We were going to name her Sophie Fricke, but that's too delicate. She is such a scrappy fighter, really a survivor."

Potpourri

Friday film

Ride the High Country (USA, 1962), directed by Sam Peckinpah, will be shown today (Jan. 26) at 8:00 P.M. in Caspary Auditorium. Two aging gunfighters, portrayed by Randolph Scott and Joel McCrea, reunite to deliver a gold shipment across the Sierras. Admission is free.

Clinical Research Seminar

H. Leon Bradlow, director of the Laboratory of Biochemical Endocrinology and professor of biochemistry in surgery and pediatric endocrinology at Cornell Medical School, discusses "Dietary Modulation of Estradiol Metabolism: A Novel Approach to Breast Cancer Chemoprevention" at the Clinical Research Seminar Wed., Jan. 31 at noon in Nurses Residence 110B.

Children's School applications

The RU Children's School and Infant-Toddler Center are accepting applications for the academic year beginning September 1996 for children from 3 months to 5 years old. Priority for members of the university community ends Wed., Jan. 31. For further information contact Marjorie Goldsmith, x8580.

MassMutual

MassMutual's Life & Health Benefits Management division was recently acquired by WellPoint Health Networks, Inc. Despite the change in ownership, plan and claims procedures will remain the same. MassMutual assures that Rockefeller employees and their dependents will not be inconvenienced. Please call the Personnel Office, x8300, with any questions.

Jack Mitchell

The Brentano String Quartet, winner of the 1995 Walter W. Namburg Chamber Music Award, performs works by Beethoven and Charles Wuorinen at the Tri-Institutional Noon recital today (Jan. 26). The concert, to be held at noon in Caspary Auditorium, is free. All are welcome.

History play

The Abigail Adams Smith Museum, 417 East 61st Street, presents *Fare for All*, an interactive historical play in which audience members may participate. The play, performed by *Drama*MUSE Associates, reflects the period 1826 to 1833, when the museum site functioned as the Mount Vernon Hotel. Appropriate for children ages 8 and older, the play will be held Sundays at 2:00 P.M. on Feb. 4, Mar. 24, Apr. 28, and May 19. Admission is $3 per person and includes a tour of the museum.

Calendar of Events

Entries for the *Calendar of Events* can now be made from the World Wide Web through an on-line form located at http://www.rockefeller. edu/rucal/ru-entry.html/. For further information contact Joseph Bonner, e-mail bonnerj.