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The Rockefeller University

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# news & notes

November 10, 1995 Volume 6, Number 9

The Rockefeller University

## The landscape in fall and winter



Campus horticulturist Sarah O'Leary (left) and volunteer Peter Giles plant bulbs in the garden between Flexner and Caspary halls. This fall, grounds workers are bedding some 10,600 spring-blooming bulbs—crocuses, daffodils, snowdrops, tulips, and more.

Flowers are at their busiest in spring and summer, blooming, pollinating, and strutting their stuff, but in the fall, the workload of the groundskeeper mushrooms.

"Fall is the time we fortify the soil, prune, and plant," explained Lulu Leibel, consultant to the Grounds Department, part of Plant Operations, which has been out and about in full force during the past few weeks.

Soil preservation is chief among the fall tasks.

"The soil needs constant replenishment," said Sarah O'Leary, cam-

pus horticulturist. "In beds not covered by ivy, we work mulch into the soil and create a three-inch layer on the surface. If we didn't use the mulch, the soil would get compacted, which would prevent water from penetrating. It would just run off. The mulch also keeps weeds down and helps soil preserve what moisture it has."

For the mulch project, grounds workers applied more than 200 square yards of "Sweet Peat." The Mary Lasker Gardens on the east side of the Abby Aldrich Rockefeller Lounge alone required 25 square yards.

The Rockefeller gardens are susceptible to drought because the soil is porous and does not hold much water. The Grounds Department began its current soil management program about a year and a half ago. Even so, weather extremes dating back almost three years—droughts in the 1993 and 1995 summers and severe cold and ice in the winter of 1994—may have damaged the landscape.

"We still don't know how hard the drought hit our plantings and grass. We will know more in the spring," Leibel commented. "The New York City water regulations allowed watering of shrubs and trees because plants are important to the quality of life. We also watered the lawn, not to care for the grass, but to get water to the roots of the trees."

In addition to maintaining soil, groundskeepers also tend to the special needs of RU's plants, shrubs, and trees. As Leibel explained, the campus has a mature landscape.

See *Grounds*, page 2

## Stein memorial lecture focuses on molecular protein recognition

The William H. Stein Memorial Lecture today (Nov. 10) features James Wells, staff scientist at Genentech, Inc., who will discuss "Probing and Designing Hormone-Receptor Interactions."

Wells's research focuses on probing and designing molecular recognition properties in proteins, especially with regard to enzyme catalysis and protein-protein interactions. Work in his laboratory aims to provide a rule-based approach to protein engineering and to develop technologies that facilitate protein design. In 1983, he and his colleagues cloned and expressed subtilisin, a serine-class protease and the first bacterial protease gene cloned. Wells also studies the structure and function of human growth hormone (hGH). His group developed expression systems that produced for the first time large amounts of the extracellular domain of the hGH receptor, which led to the solution of the hGH-receptor complex.

"Jim has made fundamental contributions to our understanding of protein function," said Professor Stephen Burley, who introduces Wells today. "More recently, he has played an important role in unraveling how protein hormones are recognized by their receptors."

Wells received a Ph.D. from Washington University in 1979. He joined Genentech in 1982 and became staff scientist in 1989. He also holds an appointment with the

University of California at San Francisco as an adjunct associate professor.

Wells, a Damon M. Runyon-Walter Winchell fellow, received the 1990 Pfizer Award from the American Chemical Society and the 1992 Alumni Achievement Award from Washington University. He serves on the editorial boards of several journals, including *Protein Engineering*, *Proteins: Structure, Function, and Genetics*, *Chemistry and Biology*, and *Protein Folding and Design*. He is a member of the executive council of the Protein Society, a member of the board of the UCLA/Keystone symposia, and senior mentor and coordinator of the Genentech postdoctoral program.

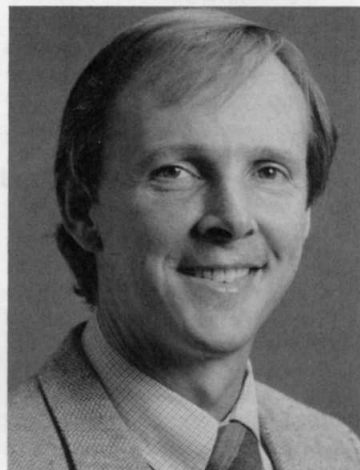
The William H. Stein Memorial Lecture Series was established in 1980 in memory of Rockefeller Professor William H. Stein. Together with his Rockefeller colleague Stanford Moore and Christian Anfinsen of the National Institutes of Health, Stein received the 1972 Nobel Prize in Chemistry for decoding the chemical structure of the enzyme pancreatic ribonuclease. This was the first time the complete chemical structure of an enzyme had been obtained.

Stein came to Rockefeller in 1937, following his graduate research at Columbia University, and joined the laboratory of noted

See *Wells*, page 2



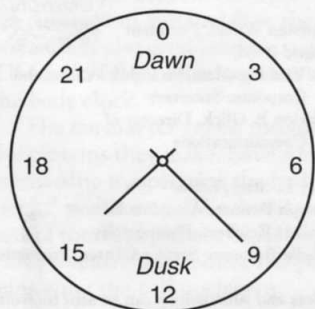
Rockefeller scientist William Stein (left) shared the 1972 Nobel Prize in Chemistry for decoding the chemical structure of the enzyme pancreatic ribonuclease. James Wells, staff scientist at Genentech, gives the Stein memorial lecture today (Nov. 10).



Courtesy of James Wells

## 2 Mind on brain

## 3 Tick and tock, aka per and tim



## 4 Sweats on sale

## Club uses mind to understand brain

Liana Muccio



From left: Graduate fellows Sidarta Ribeiro, Fiona Doetsch, and Cathy Friedman have organized a neuroscience journal club that discusses both experimental and theoretical topics in neurobiology.

In October, three graduate students established an open forum to discuss various aspects of consciousness commonly studied in philosophy, psychology, psychiatry, and anthropology. They hope that this approach will suggest new experimental strategies for examining consciousness.

"In traditional neurobiology, we look at anatomy, electrophysiology, and molecular structure. But the aim of this group is to draw together different disciplines to allow us to explore neurobiology in different ways," said Fiona Doetsch, a graduate fellow in the Alvarez-Buylla lab who organizes the meetings with Sidarta Ribeiro, a graduate fellow in the Nottebohm lab, and Cathy Friedman, a graduate fellow in the Hemmati-Brivanlou lab.

Club participants examine phenomena of mind at alternate sessions of the weekly club. At the other meetings, the journal club follows a more didactic path, with discussions of scientific papers in neurobiology guided by *The Principles of Neuroscience*, whose first author is Columbia University neurobiologist and RU trustee Eric Kandel, and *Histologie du Systeme Nerveux* by Santiago Ramon y Cajal.

"The modular structure of the journal club allows people to attend those units of particular interest," said Ribeiro.

The first unit of the theoretical branch covered philosophy of science, using writings by Paul Feyerabend, Karl Popper, and recently deceased Rockefeller Professor Emeritus Hao Wang. The second unit is now addressing sleep and dreams from four perspectives: anthropology, classical psychoanalysis, dream exploration, and biology. Among the readings are classic papers on dreaming in the

Senoi culture and work by Carlos Castaneda, Sigmund Freud, Carl Jung, and RU Professor Emeritus Jonathan Winson. Club members also focus on integrating these works with neurobiology.

The club will not convene next week because of the Society for Neuroscience meeting in California. It next gathers Mon., Nov. 20, to discuss topics related to diseases and regeneration of the motor unit (chapters 17 and 18 of Kandel). On Mon., Nov. 27, the theme is lucid dreaming. The club meets at 8:00 P.M. in Smith Hall 115. Readings are available in the Library.

For more information, contact Doetsch, x8381, Friedman, x8684, or Ribeiro, x8381.

## Grounds require perpetual care

(continued from page 1)

Many plants are more than 40 years old. To keep the plantings in good shape and preserve their health, the team prunes each fall and winter, when infections are less likely.

"For some of our shrub species, we prune off a third of the plant in a season, so that within three years, the plant renews," Leibel explained. Other shrub species can be pruned more drastically: Grounds workers recently cut back the Japanese holly hedge by Bronx Laboratory, reducing it from four feet to about eight inches in height. This winter, the gardeners will shape the holly and other garden hedges.

Pruning and tending soil are important, but perhaps a gardener's most joyful task is planting. Because of the drought's uncertain effects, the only plantings planned this fall are of spring-blooming bulbs—crocuses, daffodils, snowdrops, tulips, and more, some 10,600 bulbs in all.

The groundskeeping staff is also busy with year-round duties. A traditional fall task like raking leaves lasts nearly eight months at Rockefeller because of the London Plane trees, which rise with stately grace from the lawns and 66th Street drive but drop leaves from May until late in the fall.

Other ongoing tasks are cleaning the campus and the surrounding sidewalks and streets. As James Sullivan, grounds supervisor, explained, "Most people think that the city

cleans the street. But we are responsible for the sidewalk, the curb, and 18 inches into the street."

Three RU groundskeepers spend about an hour and a half a day, three to five times a week, cleaning from 63rd to 68th Street along York Avenue, including the pedestrian bridge at 63rd Street. The new fence along the York Avenue gardens has helped keep the area clean, said Sullivan.

When the snows fall, the groundskeepers and custodial service will be busy clearing the sidewalks and roadways of the campus. Ever mindful of the plants, they will be using calcium chloride, not salt, to keep ice at bay.

## Wells

(continued from page 1)

biochemist Max Bergmann. There he met Moore and began a lifelong collaboration investigating the fundamental principles governing protein chemistry. The analytical techniques they refined were vital to modern biochemistry.

During the 1940s and 1950s, Stein and Moore developed chromatographic procedures for the separation and identification of the amino acids in proteins. Their automatic fraction collector and automatic amino acid analyzer are now standard equipment in hospitals and research laboratories around the world.

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

## HHMI lab safety video premieres at RU



Attended by some four dozen lab and lab safety workers from the university and neighboring institutions, the premier showing of the Howard Hughes Medical Institute's (HHMI) safety video, "Glassware Washing Hazards," took place at Rockefeller Mon., Nov. 6. "We look for our own staff to share their expertise in this series of safety videos. It's the best way to communicate lab safety information," said Emmett Barkley, director of lab safety for HHMI as he introduced the film, which stars Cliff Sonnenbrot, supervisor of the HHMI Glasswash Facility at RU. The video will be distributed to all 63 HHMI research sites and any university that requests it.

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# Circadian rhythm set by pairing of two proteins

by Marion E. Glick

Like people, fruit flies have a daily cycle—the circadian rhythm—lasting approximately 24 hours. In 1971, scientists at the California Institute of Technology discovered a fly gene, dubbed *period* (*per*), involved in the clock controlling the cycle, but exactly how it worked was unknown. In 1984, RU Professor and Howard Hughes Medical Institute (HHMI) investigator Michael W. Young and collaborators at Rockefeller and a second group of scientists at Brandeis University led by HHMI investigator Michael Rosbash and Jeffrey Hall, cloned the *per* gene and characterized the protein it makes. In 1994, Young's group identified a second clock gene, *timeless* (*tim*).

The molecular control of the circadian rhythm and all its daily cycles lies in the pairing of these two proteins, Young and collaborators reported in a trio of papers in the Nov. 3 *Science*. The findings promise to help scientists better understand human, animal, and plant circadian rhythms, which influence cell and body biochemistry, health, aging, and behavior.

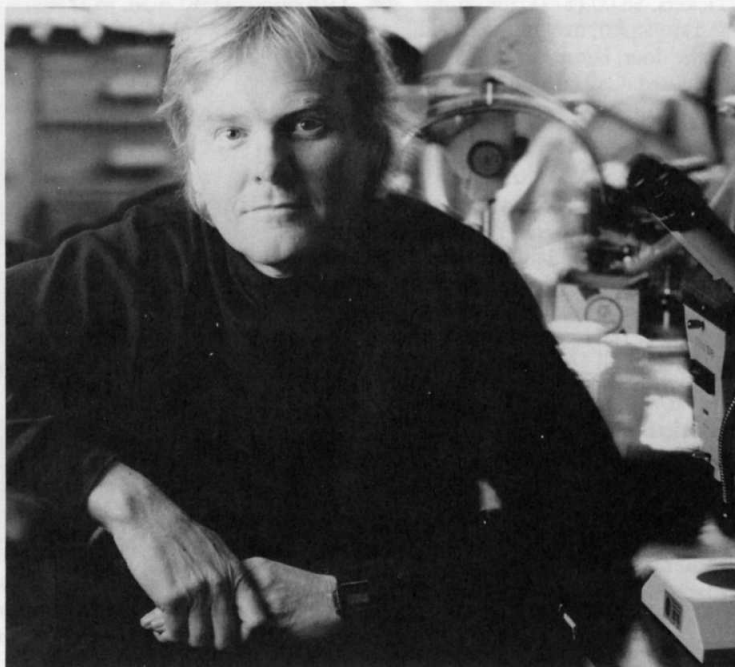
## Pacemaking partnership

"Our data show the setting and running of the daily body clock comes from the delicate affinity of two proteins," said Young, head of the Laboratory of Genetics and director of the National Science Foundation (NSF) Science and Technology Center for Biological Timing at Rockefeller. NSF supported the studies.

In the new studies, Young and colleagues from Rockefeller, the University of Pennsylvania, and Harvard Medical School cloned the *tim* gene, determined the order of nucleic acids in its DNA structure and characterized the protein it makes, TIM. By investigating what happens when *tim* and *per* are damaged in mutated flies, the researchers also established how the TIM and PER proteins together set the body clock.

"The *tim* and *per* genes, through the proteins they make, have a true partnership in operating the body's clock," said Young. "We found that part of the TIM protein binds to the PER protein. Once joined, the proteins enter the cell nucleus, a process that sets the time and duration of the circadian cycle."

All cells in the fly have *per* and *tim* genes, but the cells in the fly's brain set the body's clock. "The two genes become active at midday," explained collaborator Amita



Michael W. Young, Rockefeller professor and HHMI investigator, published three papers in the Nov. 3 *Science* on the role of two proteins, PER and TIM, in controlling circadian rhythm.

Sehgal, of the Department of Neuroscience and Center for Sleep and Respiratory Neurobiology at the University of Pennsylvania School of Medicine. "In the cell's nucleus, the genes' DNA code is transcribed into two RNA molecules, *per* RNA and *tim* RNA, which accumulate over several hours in the cell."

## Waxing and waning from dusk to dawn

At dusk, the levels of RNAs peak and only then does the cell use the RNAs to stockpile PER and TIM proteins. In the evening, the proteins join and cross into the cell's nucleus. About four hours before dawn, the PER and, presumably, TIM proteins in the nucleus reach their maximum amounts, an achievement that signals the *per* and *tim* genes to stop making the RNA. Near dawn, the nuclear proteins begin disintegrating, the cycle begins again and throughout the daylight hours the *per* and *tim* genes produce new RNA to make replacement proteins.

The pace of the clock appears to stem from the gradual, coordinated accumulation of the *tim* and *per* RNAs during several hours, as well as from the attraction of the PER and TIM proteins for each other, Young reports.

"The PER and TIM proteins have an affinity for each other, but it is not a strong link," Young said. "Only if the two proteins are available in sufficient quantities do they

begin to bind. Most importantly, the proteins can only survive and enter the cell nucleus when they are bound to each other. Therefore, about six to eight hours lapse between the time of peak RNA accumulation, which occurs around dusk, and the peak in the nuclear protein levels, shortly before dawn."

## Binding begins the cycle

This pattern of late binding of the proteins sets up daily cycles of RNA and protein production, because only after the bound proteins enter the cell nucleus can they turn off further synthesis of RNA from the *per* and *tim* genes. Further evidence of the power of the binding pattern comes from studies of mutant fruit flies who have 29-hour body clocks that slow even further when their temperature rises. Young and his colleagues found that these flies have a mutated form of the PER protein that binds improperly to the TIM protein. The two proteins bind more poorly as temperatures rise, consequently delaying the PER protein's entry into the nucleus and slowing the clock.

Additional mechanisms and other, as yet unidentified, proteins also may influence the interaction between the PER and TIM proteins, which could affect the timing, Young adds. For example, scientists know that light affects circadian rhythms, and, Young notes, evidence exists that the PER/TIM protein union is affected by light. This sensitivity may help explain how

body clocks are reset after a period of jet lag that occurs as a traveler crosses time zones.

In addition, the scientists are searching for the genes of the human body clock. "In general, the genes that control fundamental body mechanisms are passed on in evolution," Young explains. "Now that we know the mechanisms in the fly's body clock that produce the TIM and PER proteins, and the feedback loops involved, we expect to find a similar process in the body clocks of humans."

## In the absence of light

In humans, daily circadian rhythms underlie many functions, including the sleep/wake cycle, body temperature, mental alertness, pain sensitivity, and hormone production. In natural conditions, many rhythms have a 24-hour period related to sunlight, but though light can affect the rhythm, it does not cause the cycle. In fact, in the absence of light or other environmental clues, rhythms continue and most adapt to periods slightly longer or shorter than 24 hours, Young noted.

During the fly study, the team measured for four days the levels of RNA in the absence of light. Both *tim* and *per* RNA accumulated at the same pace, peaking together once every 23 hours. On some days, the peak amount of RNA could be as much as 15 times greater than the lowest level.

Young's coauthors on the first paper, *Positional Cloning and Sequence Analysis of the Drosophila Clock Gene*, *timeless*, are Michael P. Myers, Karen Wagner-Smith, and Cedric S. Wesley, of Rockefeller and HHMI, and Sehgal of the University of Pennsylvania.

Young's collaborators on the second paper, *Rhythmic Expression of timeless: A Basis for Promoting Circadian Cycles in Period Gene Autoregulation*, are Adrian Rothenfluh-Hilfiker and Myers of Rockefeller and HHMI, and Melissa Hunter-Ensor, Yifeng Chen, and Sehgal of the University of Pennsylvania.

Young's coinvestigators on the third paper, *Isolation of timeless by PER Protein Interaction: Defective Interaction between timeless Protein and Long-Period Mutant PERL*, are Lino Saez, and Myers of Rockefeller and HHMI; Sehgal of the University of Pennsylvania; and Nicholas Gekakis, Anne-Marie Delahaye-Brown, and Charles J. Weitz, of the Department of Neurobiology at Harvard Medical School.

# Potpourri

Pete Checchia and Allen Cohn



**Violinist Jennifer Koh, silver medalist at the 1994 International Tchaikovsky Competition, performs the works of Bach, Ysaÿe, and Paganini at the Tri-Institutional Noon Recital today (Nov. 10). The concert, to be held at noon in Caspary Auditorium, is free. All are welcome.**

## Friday film

*Paths of Glory* (USA, 1957), directed by Stanley Kubrick, will be shown today (Nov. 10) at 8:00 P.M. in Caspary Auditorium. In one of Kubrick's milestones in his journey through the constraints to mass and individual freedom, Kirk Douglas portrays a man of peace who answers his country's call to war. Admission is free and all are welcome.

## Science outreach ceremony

The Science Outreach Program will give certificates to last summer's program participants at a convocation in Caspary Auditorium Sat., Nov. 11 at 10:30 A.M. All are invited. For information, contact Bonnie Kaiser, program coordinator, x7431 or e-mail bonnie.

## Lecture on Samuel Morse

Thomas Bender, dean of humanities, New York University, will lecture on "Samuel Morse and the Intellectual Life of New York, 1820s to 1830s" at the Abigail Adams Smith Museum Tues., Nov. 14 at 6:30 P.M. The museum

is located at 417 East 61st St. Tickets, \$8.00 (\$7.00 for seniors and students), may be purchased at the door, but reservations are requested. Call 838-6878.

## Free concert

Soprano Olga Makarina will perform in Caspary Auditorium Tues., Nov. 14 at 7:30 P.M., accompanied by pianist Elaine Rinaldi. Sponsored by the Rogosin Institute, the concert is free but reservations are required. Call 746-1552.

## Clinical Research Seminar

Melissa Jane Pope, research associate in the Steinman lab, gives a talk entitled "Dendritic Cells Promote HIV-1 Replication" at the Clinical Research Seminar Wed., Nov. 15 at noon in Nurses Residence 110B.

## Lecture and film on Pasteur

Bert Hansen, professor of History at Baruch College/CUNY, will speak on "Louis Pasteur: America's First Medical Hero" at Florence Gould Hall Wed., Nov. 15 at 7:00 P.M. A screening of the Jean Epstein film, *Pasteur* (1922), will follow. The event is part of the International Year of Louis Pasteur celebration. To reserve tickets, call Mary Jo Palencia at 355-6100, x255 by Mon., Nov. 13.

## RU concert

Daniel Smith, with Michael Rabinowitz and Jazz Combo, performs at the Rockefeller University Concert Wed., Nov. 15 at 8:00 P.M. in Caspary Auditorium. For ticket availability and information, contact Cathy Rogers, x8437.

## Retirement annuities seminar

A representative from TIAA CREF will be on campus Tues., Nov. 14 to discuss supplemental retirement annuities (SRA). Two seminars

will be held in Nurses Residence 110B: from 11:30 A.M. to 12:30 P.M. and from 1:00 P.M. to 2:00 P.M. All are welcome.

## Open enrollment deadline

The open enrollment period, which allows employees to join or make changes to the university's health insurance and voluntary accidental death and dismemberment plans, ends Fri., Nov. 17. This is also the only time to sign up for the 1996 flexible spending account (FSA). Prior FSA elections do not roll over each year. For further information, contact Kristin Gross, x8297, or Ginny Hansen, x8299.

## Arrivals

*Visiting Professor:* Mary Dratman, Pfaff lab.

*Research Associates:* James T. Liu and Zoltan Sarnyai, McEwen lab.

*Postdoctoral Associates:* Doo-Il Jeoung, F. Cross lab; Bahram Houshmandzadeh, Libchaber lab; Vincenzo Nardi-Dei, Manning lab; Hua Xiao, Roeder lab; Ilya Vakser, Sali lab.

*Postdoctoral Fellows:* Cordelia Bolle, Chua lab; Rong Xu, Cowburn lab; Xue jun Zhu, J. Darnell lab; Masayuki Matsushita, Greengard lab; Anne Vassalli, Mombaerts lab; Arnaud Nicot, Pfaff lab; Asesh Bandopadhyay, Tuomanen lab.

*Guest Investigators:* Dora Raventos, Chua lab; Masao Yoshinaga, Fischetti lab; Mark Li, Hatten lab; Uwe Kordes, Heintz lab; Berthold Rutz, Konraska lab; Ioannis Giannakis, Khuri lab.

*Adjunct Faculty:* Khosrow Kashfi, Hirsch-Leibel lab; Parameswaran Nair, Khuri lab.

*Fellow:* Mark Goulian, Center for Studies in Physics and Biology.

## Departures

*Visiting Professor:* David Shub, Zinder-Model lab.

# Go for the glass



The RU Media and Glassware Service will be giving away scientific glassware at an open house Wed., Nov. 15 in FHE A10 from 10:00 AM to 4:00 PM. Items include: boiling and Erlenmeyer flasks, petri dishes, tissue staining plates, pipettes and tubes, and assorted bottles, jars, and caps. Supervisor Hyuna Ham-Stoopack said, "Browsers are welcome. These items are commonly used in the laboratories. Some items have never been used. We no longer need this stuff, which can be useful to many others."

*Research Associate:* T.S.R. Krishna, Kuriyan lab.

*Postdoctoral Associates:* Ashis Mukherjee, Agosta lab; Xin Ye, Hanafusa lab; Boyana Konforti, Konarska lab; Jason Bannan, Zabriskie lab.

*Postdoctoral Fellows:* Elizabeth Vallen, F. Cross lab; Harumi Shirakawa, Hall lab; Enal Razvi, Steinman lab; Sahng-June Kwak, Hanafusa lab; Hui Ge, Roeder lab; Agapito Tarasi, Tomasz lab; Diana Cundell, Tuomanen lab.

*Guest Investigators:* Bernd Kisilowski, Agosta lab; Chun-Hai Dong, Chua lab; Stefan Oelmann, de Lange lab; Qingfang Wang, Goulianos lab; Ken-ichi Mitsui, Greengard lab; Wei Chen, Lederberg lab; Barbara Pearce, Tuomanen lab.

## Holiday Extravaganza

Adult sweatshirts  
small and medium

only \$10.00 from now until Christmas

## Children's School Sweat Shirt Shop

Open: Tuesdays and Thursdays, 11:30 A.M. to 1:30 P.M.

Location: RRB Tunnel

The shop now accepts American Express, Mastercard, and Visa.