Bronze bust honors former University mathematician Szego

People strolling between Crow and Cupples halls had to be taken aback the April to suddenly see a piece of adorning the courtyard. Facing northward is a permanent fixture on the northeast Hilltop Campus: a five-foot-tall pedestal holding a bronze bust of mathematician Gabor Szego, a 20th-century giant in analysis and one of the most famous academicians ever to teach on a regular basis at Washington University without drawing a University paycheck.

Szego (1895-1985) came to the University in 1934 and taught for four years before joining the faculty at Stanford University and making Stanford an enduring powerhouse in mathematics.

Szego, a native Hungarian Jew, was forced out of his professorship at the University of Königsberg in Germany by the Nazis. Through personal and professional connections in St. Louis, he learned of the quiet return to the University. Szego taught his first two years at the University with the aid of a Rockefeller Foundation grant matched by funds from the St. Louis Emergency Committee in Aid of Displaced German Scholars. The second two years were funded by a local business and citizens committee. Because of the Great Depression, the University’s budget was extremely tight. As a result, the University never was able to make an offer to Szego, whose leadership and wisdom directed the first four doctoral graduates in the Department of Mathematics in Arts and Sciences.

Group effort

The bust of Szego was not dropped by firefighter in helicopter, but the story of Szego’s quiet return to the University is intriguing, if not involved, and it includes mathematics department faculty and alumni. Two years ago, Hungarian artist Gusztáv Zinner created the bust in honor of Szego’s career with the intent of placing it outdoors in Szego’s hometown of Kunhegyes. He made two replicas of the original. It was decided that they should go to the University — the only American institutions with which Szego was affiliated.

Szego came to St. Louis from the world center of mathematical activity. “The math professors here were eager to learn about the latest developments from Szego,” said Gary J. Jensen, Ph.D., professor of mathematics. “In fact, in his first year, he taught mainly the faculty. It seems a shame that we couldn’t have kept him because that would have been a big boon to the University.”

Jensen, along with colleague Steven

Continued on back page

WASHINGTON UNIVERSITY IN ST. LOUIS

Vol. 21 No. 30 May 1, 1997
Nephrologist to give 1997 Beaumont lecture

On Wednesday and Thursday, May 7 and 8, the Department of Medicine will host lectures by the 1997 William Beaumont Visiting Professor, Thomas E. Andreoli, M.D., chair of the Department of Internal Medicine at the University of Arkansas College of Medicine in Little Rock.

Andreoli will deliver a lecture titled “The Medullary Thick Ascending Limb Channel” at 4 p.m. May 7 in the Irwin Room on the first floor of the Barnes-Jewish Hospital North Campus. At 8 a.m. May 8, he will deliver a lecture titled “The Edema Syndromes” in the Clifton Amphitheater of the Barnes-Jewish South Campus.

Medical Center master plan one step closer to reality

Last September, officials at Barnes-Jewish Hospital and the School of Medicine announced plans for a $225-million campus integration project with a vision to change the way health-care services are organized and delivered. Since then, architects have refined the master plan for the Washington University Medical Center. Now, programming committees made up of physicians and staff will work with the architects and design and construction personnel to bring the vision one step closer to reality.

The committees will determine space and functional needs for the Ambulatory Care Center, the Cancer Center, diagnostic labs, the Emergency Department and other new areas during the next several months. Committee members will ensure that the new facilities provide the best possible experience for patients. Members will define fundamental space requirements based on their knowledge of and experience with staffing, systems, and processes.

Medical Update

Viewing cell death by suicide helps researchers solve diabetes mystery

Insulin-dependent, or Type 1, diabetes was once a murder mystery without witnesses. Researchers knew the immune system killed insulin-producing cells in the pancreas, destroying the body's ability to regulate blood sugar. But no one had seen the cells dying, and some couldn't agree on the cause of death.

School of Medicine researchers recently became the first eyewitnesses to the mass death of pancreas cells. Studying genetically engineered mice that develop diabetes in just a few weeks, the researchers isolated cells in the last moment of life.

The death scene, described in a recent issue of the Proceedings of the National Academy of Science, was surprisingly clear and a bit morbid. The cells, following sinister instructions from the immune system, were committed suicide.

"We wanted to know exactly how the cells died," said Jonathan D. Katz, Ph.D., assistant professor of pathology and lead author of the study. "This is important because once we understand this death and how it's played out, we may be able to inhibit the process.

The study was supported by the American Diabetes Association, the National Institutes of Health and the Juvenile Diabetes Foundation.

The insulin-producing pancreas cells were killing themselves by ripping apart their own DNA. This cell suicide is called apoptosis. The suicides are somewhat orchestrated by T cells, the "security guards" of the immune system responsible for detecting foreign invaders. The T cells might release proteins that trigger apoptosis, or they might encourage the suicide in a less direct way.

Apoptosis plays an important role in the body. As we develop, it helps clear excess cells. Also, the immune system kills a variety of abnormal cells, including cancerous and virally infected cells, by inducing apoptosis. Many researchers suspected T cells killed pancreas cells in the first place. Others thought T cells might surround the pancreas cells and block the flow of blood and nutrients, thus starving them to death.

Cells caught in act of dying

Researchers wanted for many frustrating years to find a pancreas cell in its death throes, a task that seemed to require the first eyewitnesses, the lottery winner. When researchers looked at preserved cells under a microscope, the cells always looked healthy. Once a cell commits itself to apoptosis, it dies quickly, and macrophages immediately degrade the remains. A fleeting death is scattered over several years. Even when researchers used mice that developed diabetes in a few months, the dying cells remained elusive.

Katz solved this problem by using genetically engineered mice that develop diabetes in just a few weeks. These mice had only one kind of T cell, the kind that reacts to pancreas cells. The T cells staged a massive attack concentrating several months of cell death into just a few weeks. Katz and his colleagues were able to catch many cells in the act of suicide.

The fact that pancreas cells through apoptosis may be good news for researchers trying to find a cure for insulin-dependent diabetes. For the future, doctors might be able to use drugs or genetic engineering to block the suicide message from T cells, Katz predicts. Theoretically, it would have been much more difficult to protect pancreas cells from a siege that causes starvation, he says.

For now, Katz wants to answer more immediate questions. He still doesn't know why T cells persuade the pancreas cells to self-destruct. More fundamentally, he wants to understand why T cells turn against the pancreas cells in the first place. They are responding to a specific antigen in the pancreas cell, but which antigen? And does the same antigen cause insulin-dependent diabetes in humans? Now that he's found a way to study the dying moments of pancreas cells, Katz might someday be able to answer these questions.

Jonathan D. Katz

Medical Campus employees: Send to Payroll Department, Washington University, 8017 S. Euclid Ave., St Louis, MO, 63110. Periodicals postage paid at St. Louis, Mo.

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Phillips' career is poetry in motion

There is the career that he planned and the career that's happening on its own. So says Carl Phillips, associate professor of English and of African and Afro-American studies in Arts and Sciences. The Olympian leap from Falmouth, Mass., where Phillips taught high school students Greek and Latin, to Washington University, where he is now director of the notable Creative Writing Program, is nothing short of fate, he says.

If so, destiny has struck a deal with literary success, and the classicist, still a bit confounded by his rapid ascent, is making a Philip Harris gracefully with the agility of a cat.

Phillips' first book of poetry, "In the Blood," received the Samuel French Morse Poetry Prize in 1992. Submitted on the advice of a friend, the collection explores issues of sexuality and mortality. "We write to communicate to other people, but poets also write to communicate something to themselves," Phillips explains. "I was taken attack when the book, a sort of outing of myself, first appeared because it revealed a lot of things that I hadn't yet known about myself."

Critics initially hailed the collection as a bold treatment of highly charged, explosive homoerotic poetry infused with allusion to ancient Greek and Roman texts. Influenced by the metaphysical poets as well, Phillips' work transcends gender to explore the point where the flesh and the spirit interact. He writes of a contradictory world of dreams and desires "in which everything seems to contain its opposite in some disturbing way." He continues: "Happiness doesn't require opposite in some distressing way." He is why I came to the program."

Pinsky "is a wonderful teacher, a learned man, and a tremendously gifted poet who already has established an unmistakable voice and subject, rhythm and cadence." "In the Blood" moved poet Marilyn Hacker to write: "Phillips possesses "mandarin grace and surpassing sensitivity, subtle, strong. He is why I came to the program."

Phillips was named a Lilly Teaching Fellow in 1995 from "Cortege" with the permission of Graywolf Press, St. Paul, Minn.
Exhibitions
Bachelor of Fine Arts Undergraduate Thesis Show. Exhibit runs May 9 through May 23. Gallery of Art, upper and lower galleries, Steinberg Hall. Hours: 10 a.m. to 4:30 p.m. weekdays; 1 to 5 p.m. weekends. 935-6530.

Master of Fine Arts Thesis Show. Through May 24. Gallery of Art, upper and lower galleries, Steinberg Hall. Hours: 10 a.m. to 4:30 p.m. weekdays; 1 to 5 p.m. weekends. 935-6530.

“Seven Days in the Life of a Student.” Student-curated show. “Counter Perceptions: A Student’s Quest” explores the student-curator exhibition of works from the WU art collection that presents different historical perspectives and interpretations of events from the past 150 years. Exhibit runs May 4 through May 10, in the lower gallery, Steinberg Hall. Hours: 10 a.m. to 4:30 p.m. weekdays; 1 to 5 p.m. weekends. (See story on page 3) 935-4523.

Lectures
Thursday, May 1

Wednesday, May 7
4 p.m. Internal medicine renal research seminar. "The Medullary Thick Ascending Limb Channel," Thomas E. Andreoli, the 1997 William Beaumont Visiting Professor in Medicine, Univ. of Arizona College of Medicine, Little Rock. Robert Brigham, chief of internal medicine, Univ. of Kentucky College of Medicine North Campus. (See story on page 2)

Thursday, May 8
8 a.m. Internal Medicine Grand Rounds. "The Edema Syndromes," Thomas E. Andreoli, the 1997 William Beaumont Visiting Professor in Medicine, Univ. of Arizona College of Medicine, Little Rock. Robert Brigham, chief of internal medicine, Univ. of Kentucky College of Medicine North Campus. (See story on page 2)

Monday, May 5
3 p.m. Chemistry seminar. "Chelation-assisted C-O and C=C Bond Cleavage Reactions," Tien-Yau Luh, prof. of chem., Room 212 Enright Hall. 935-4030.

Tuesday, May 6
3 p.m. Chemistry seminar. Topic to be announced. Speaker is Daniel Roch, prof. of biochemistry, U. of Wisconsin School of Pharmacy, Madison. Room 311 McMillan Lab. 935-5619.

Music
Friday, May 2
8 p.m. WU Opera. "Get a Grip on Handel: Excerpts From the Composer’s Operas." Directed by Jolly Stewart, master of operatic music (Also May 3, same time) Umholt Hall Lounge. 935-4841.

Saturday, May 3
8 p.m. Jay Zelenka Trio. Jay Zelenka, saxophone; Greg Mills, keyboard; and Eric Markowitz, bass. Cost: $5; $3 for senior citizens and students. Steinberg Hall Aud. 935-4523.

Sunday, May 4

Miscellany
Thursday, May 1
8 p.m. Poetry reading. Features Kelly Stevens and Doug Sanders, masters of fine arts candidates. Hurst Lounge, Room 301 Demcher Hall. 935-5190.

Friday, May 2

Saturday, May 3

11:30 a.m. WU town hall meeting. "The WU Faculty Practice Plan." William P. Reck, medical school dean, executive vice chancellor for medical affairs and president of the Medical Center, and James P. Crate, medical school asso, vice chancellor for clinical affairs, lead the discussion. The 11:30 a.m. meeting is open to clinical faculty, and the 1:30 p.m. presentation is open to the entire WU community. "The Campus Integration Project — Ambula-

tory Care Center, Cancer Center, Trauma and Emergency Center — and its impact on the University's ambulatory care mission. A special look at the "Value Challenge" and "Quality Challenge."" Eric P. Newell, 935-4841.
**Third Miles Davis conference focuses on jazz and civil rights**

Learns more about one of history’s great jazz musicians and the impact of the civil rights movement on jazz at the conference titled “Miles Davis and American Culture III: Jazz and the Civil Rights Movement.”

The conference, which is free and open to the public, will be held Saturday and Sunday, May 3 and 4, at the West Campus Conference Center. The conference runs from 9:45 a.m. to 3:45 p.m. May 3 and from 10 a.m. to 4 p.m. May 4. No advanced registration is required.

This third conference on Miles Davis explores the relationship between the historical context of the civil rights movement and the history of jazz. Musicians, critics and record producers who were active in the jazz scene between 1954 and 1965 will present their recollections and analysis of the role of historical events in shaping everyday life in the music industry.

A special concert featuring artists who worked with Miles Davis will be presented. May 3 in the Shoenberg Auditorium of the Missouri Botanical Garden. Tickets are $15 at the door. For more information, call (314) 935-4841.

**Sports**

Compiled by Mike Wolf, director, and Kevin Bergquist, ass. director, sports information.

**Women’s tennis earns first-ever NCAA bid**

Washington University’s women’s tennis team earned the first postseason bid in the program’s 22-year history. The Bears compete May 6-12 at the NCAA Division III Championships at Claremont-Mudd-Scripps Colleges (Calif.).

The Bears ranked No. 12 in the latest Division III rankings. Face fourth-ranked Trinity University (San Antonio, Texas) in the first round. Seniors Maria Lonard and Nina Poursafar were named as alternates for the doubles competition.

The Bears opened the spring season 1-6 against a brutal schedule but rebounded to win 12 of their final 14 matches.

Next week: 3 p.m. PDT Tuesday, May 6, vs. Trinity University at NCAA Division III Championships, Claremont, Calif.

**Men sweep UAA track; women break records**

Several Bears posted school-record and NCAA Division III national qualifying times at the University Athletic Association outdoor track meet last week at Bushyhead Track and Francis Field.

**Rain cancels four baseball games**

Morgan said that he and other members of the group — made up of art history, School of Art and other students — were excited to have the opportunity to use it and present it to the rest of the campus. It was fairly easy to find the works that fit our idea. Hayden said that he and other members of the group — made up of art history, School of Art and other students — were excited to have the opportunity to use it and present it to the rest of the campus. It was fairly easy to find the works that fit our idea. Hayden said that he and other members of the group — made up of art history, School of Art and other students — were excited to have the opportunity to use it and present it to the rest of the campus. It was fairly easy to find the works that fit our idea.
Faculty members help bring memorial to campus — from page 1

Krantz, Ph.D., professor of mathematics, played a major role among the faculty in bringing the bust here. The two organized a fund-raising drive that brought in $1,600 for the bust itself plus another $4,000 for shipping and $2,000 for the pedestal, which Krantz contracted through Weis and Weis Marble Inc. in St. Louis.

Alumnus Richard Askey, Ph.D., professor of mathematics at the University of Wisconsin in Madison, was Instrumental in getting the bust to Washington University, along with Hungarian-born Paul Nevius, Ph.D., professor of mathematics at Ohio State University. Both men were influenced by Szego’s work, and Askey knew him from Askey’s days as an instructor at Washington University in the 1950s.

A champagne dedication The bust will be officially dedicated in a ceremony beginning at 3 p.m. Thursday, May 8, in Room 199 Cupples I Hall. Askey and Nevi will speak at the event. At 5 p.m., there will be a champagne toast to the Szego bust in the courtyard. The University community is invited to join this gathering, which is expected to attract visitors from throughout the country.

“It’s been a satisfying though hectic process,” Jensen said. “The bust has charm and dignity and honors a great mathematician.” It also joins a similar tribute to William Chauvenet, another great mathematician and the University’s second chancellor (1862-69). “I think of the Szego bust the same way I think of the Chauvenet bust in the portico of Holmes Lounge,” said Krantz. “The sculptures are definitely something I’ll point out to visitors because we now have two bronze works of art recognizing mathematicians of historical importance.”

Krantz, who has a view of the Szego bust from his office in Cupples I Hall, said, “It’s a pleasure to look out the window and see people admiring it.”

Signature collection lets design students study the real thing

In any academic endeavor, there is nothing quite like having a tangible example of what is being studied to make the subject come alive. The students in the fashion design program at the School of Art recently obtained a wealth of such real-life examples in the form of pieces of clothing.

The garments, which span the past four decades, were donated by the estate of Esia Fulton, a well-known buyer for Famous-Barr department stores for 40 years who helped launch the careers of many young designers. Fulton died in February at age 81.

This collection of trend-setting clothes from Fulton’s personal wardrobe allows the students to see firsthand how fashions change and evolve over the years, said Jeigh Singleton, associate professor of art and head of the fashion design program. “She could spot trends and had this knack for knowing what was new and different and happening,” Singleton said as he displayed some of the clothes to his students. “That is the spirit of your signature collection,” he told them, “being avant-garde and different and not being afraid to put your own point of view into your designs. For us, we served as the inspiration for the signature collection segment of the annual Fashion Design Show, which takes place Sunday, May 4, at the Saint Louis Galleria.”

Terri Basco, a senior in the fashion design program, said the clothes have given her and other students a chance to examine garments they might not ordinarily see. “You don’t normally see featured couture and historical clothing like you do here,” Basco said. “This is fantastic. It’s in fabulous condition.”

Michael Schwarz agrees. “It gives you the opportunity not only to look for inspiration from a certain time period, but you can actually see how the clothes were constructed,” said Schwarz, a senior in the program. “At the same time, it gives you the opportunity to see the history and see the way things have developed. You can see what really has happened and what either worked or didn’t work. From that, you can decide whether or not you want to do it again.” — Neil Learner

Fashion show launches careers — from page 1

size and prominence over the years and has been held at various locations both on and off campus. In the 1950s and 1960s, employers in the bustling St. Louis garment district sought to attract the student body and head of the fashion design program. “They are surrounded by the stores where their clothes will eventually be sold.” Singleton, who himself has achieved wide recognition in the fashion industry, says he gets great pleasure out of watching his students succeed. “These young people go on to fame and fortune, and sometimes you find their names on your back,” he said. “And then there are those who work quietly, but you are still wearing their creations.”

Tickets are $45 for general seating. Special seating and recognition in the program costs from $75 to $3,000. A limited number of tickets will be available at the door. For tickets or more information, call (314) 935-6515.

— Neil Learner

Women faculty group recognizes two graduate students

H ester Baer, a doctoral candidate in German, and Julie Miller-Cribbs, a doctoral candidate in social work, have received the first annual Graduate Student Award from the Association of Women Faculty (AWF). The award was established by AWF to put into practice the organization’s commitment to mentoring women in the academic profession. Each year, the award will recognize two graduate students—one from Arts and Sciences and one from the professional schools—for exceptional scholarly accomplishment and promise.

Baer is an Oliver Fellow working on the influence of feminist film theory on film production in Germany. In receiving the award, she cited the importance of greater student-faculty intellectual interaction and for encouraging the professional development of her peers in the Department of Germanic Languages and Literatures in Arts and Sciences. Baer has served as a representative to the Graduate Student Senate.

Miller-Cribbs has contributed significantly to course development in the George Warren Brown School of Social Work and has enhanced her peers’ capacity by designing integrative teaching and research interactions and for resources for the social work profession. Her area of scholarly expertise is social literature on human diversity.

The Association of Women Faculty was established on the Hilltop Campus in 1995 to promote professional and social interactions and to promote the careers of women at the University. It promotes these interactions by soliciting and reviewing faculty awards, providing an opportunity for contact with the University administration and by working with the Academic Women’s Network in the School of Medicine.

The annual fall and spring semester women faculty convocation and track-and-field tenure track women faculty members are eligible for membership. Membership in the organization is open to all members of the academic community, which represents more than one-third of faculty women on the Hilltop Campus.

For more information about the organization, call Mary Ann Druback, Ph.D., adjunct professor of history and associate professor in the Women’s Studies Program and in the Department of Education and Human Development, at (314) 935-4160, or Maria Ines Lagos, Ph.D., associate professor in the Department of Romance Languages and Literatures in Arts and Sciences, at (314) 935-5002.

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Campus Watch

The following incidents were reported to the University Police Department from April 19-27. Readers with information that could assist the investigation of these incidents are urged to call (314) 935-5555. This release is provided as a public service to promote safety-awareness on campus.

April 21
10:43 a.m. — A staff member reported that initials were carved in a century-old elm tree on Brookings Quadrangle.

1:15 p.m. — A staff member reported that a jacket was stolen from an office in the facilities department.

April 22
4:13 a.m. — A student reported receiving a harassing telephone call in Beaumont Residence Hall.

2:47 p.m. — A staff member reported that a cordless drill and accessories were stolen from the mail room in Olin Library.

April 23
6:34 p.m. — A maintenance van reported stolen from the office in Olin Library.

April 24
8:23 a.m. — A staff member reported that graffiti was spray-painted in the basement corridor of Lee Residence Hall.

5:55 p.m. — A student reported that a wallet containing credit cards and personal items was stolen from an unsecured locker in the men’s locker room at the Recreation Complex.

April 25
8:28 a.m. — A staff member reported that two telephones and a stapler were stolen from the Athletic Complex.

9:24 p.m. — A student reported that several harassing messages were left on a door in Shepley Residence Hall. Further investigation revealed messages on at least six other doors on the same floor.

April 27
10:04 a.m. — A University Police officer discovered a house of fire on the grounds by the Rutledge Residence Hall.

4:34 p.m. — A student reported that two taillights were stolen from a car in a parking area in Lee Residence Hall.

University Police also responded to one additional report of theft; two additional reports of vandalism; one automobile accident; and two reports of peace disturbance.
Ernst Zinner received two prestigious honors

Washington University physician Ernst K. Zinner, Ph.D., a pioneer in the analysis of stellar dust found in primitive meteorites, is being recognized for his outstanding contributions to science with two prestigious awards. The National Academy of Sciences presented Zinner with the J. Lawrence Smith Fund by a gift from Sara Julia Smith. Among those singled out for honors were...
Hilltop Campus

The following is a partial list of positions available on the Hilltop Campus open to all faculty, staff, and students. These positions and others may be viewed at the University's Career Resource Rooms, Room 1070C, or by calling (314) 935-5235. All positions are also accessible via the World Wide Web at www.wustl.edu/careers.

System Administrator 970-2492
Engineering Computer Lab. Re- quirement: master's degree in computer science; knowledge of network administration and/or security; Windows and UNIX experience; excellent written communications skills.

Coordinator of Campus Leadership Programs 970-2471
Student Activities: Requirements: master's degree in student affairs; thro- ough grounding in student-development theory, experience in student programming, entertain- ment industry and student participa- tion advisement; experience with large and small audiences; understanding of organizational and communication skills; experience in event planning and execution.

Coordinator of Programming and All Campus Events 970-2486
Student Activities: Requirements: bachelor's degree in student development/ research or psychology; experience in student leadership programs and the student group council; providing ongoing counsel and targeted assistance to student groups; coordinating campus-wide student opportunities. Application required.

Professional and Technical Staff

Accountant 970-2352
Requirements: bachelor's degree, excellent interpersonal and written communication skills, energy, ability to work independently; ability to meet deadlines; ability to organize and prioritize work; strong troubleshooting skills; attention to detail and accuracy; strong computer skills, a working knowledge of accounting applications. Application required.

Accountant Payable and Computer Re- presentative 970-2845
Requirements: bachelor's degree, excellent interpersonal and written communication skills, energy, ability to work independently; ability to meet deadlines; ability to organize and prioritize work; strong troubleshooting skills; attention to detail and accuracy; strong computer skills, a working knowledge of accounting applications. Application required.

Laboratory Technician

Transgenic Mice Rock FELT
Laboratory Animal Resource Center: Requirements: bachelor's degree, animal husbandry or biology with a strong emphasis on regula- tory issues. Animal experience and/or training in transgenic animal production preferred; good written and oral communication skills; ability to take initiative and complete assigned work; ability to maintain records and report results. Application required.

Statistical Data Analyst 970-2161
Requirements: master's degree in biostatistics, experience in SAS programming. Responsibilities include serving as a member of an interdisciplinary team responsible for interpreting and evaluating the results of data analysis; review- ing the literature and understanding data systems; developing and participating in the development of op- erating procedures and query languages. Responsibilities also include participating in the development of scientific software. Programming experience required in SAS, Fortran, or other statistical programming languages. Application required.

Director of Accounting Services 970-2840
Requirements: bachelor's degree, additional accounting and information systems coursework; strong written and verbal communication skills; knowledge of computer applications; ability to manage a team and work independently.

Summary

The University of Missouri is an Equal Opportunity/Affirmative Action Institution. Questions that have broad appeal to the University community should be submitted to Martha Everett, Campus Box 1070, or pr72245@umail.wustl.edu. Questions may be answered by the appropriate administrator. Though employee questions will be answered anonymously in the Record, please submit your full name, department and telephone number with your typed question. For information, call (314) 935-5235.

Addressing employee questions concerning the Washington University community

Whillow's work could lead to a "whole new class of antibiotics from page 1

Adhesive-based vaccines offer a novel approach to ward off infectious disease. "The idea is very attractive because such a vaccine would give bacteria a double whammy — antibodies against the protein would both block attachment and mark the bacteria for destruction by the immune system," Hillgren said.

Linden and his colleagues analyzed bacterial samples from cystitis patients across the United States. They found that FimH, an adhesin that promotes the adherence of E. coli, is more than twice as prevalent as P. mirabilis, the protein that makes bladder-loving E. coli, hardly varies from strain to strain. The whole-bacterial cross-reacted with more than 95 percent of the strains and prevented binding to bladder cells, Linden said. These cells might prevent recurrent bladder infection, even after success of treatments was involved.

By removing the FimH gene from E. coli, Linden showed that a bacterium without sticky pili is as useless as a Post-it Note without gum. "So the binding event is absolutely critical to the bacterium's ability to cause disease," Hillgren said.

Painstaking studies of pili assembly allowed Hillgren's team to produce cor- rectly folded adhesin that could be used as vaccine. "This is a nice example of how basic science can promote advances in clinical care," Hillgren said.

Over the past decade, his group has shown that the pili assembly begins with adhesin molecules that are assembled into protein complexes that surround E. coli, Boomerang-shaped proteins called chaperones that help release the adhesin from the bacteria and mold adhesion into shape. When the chaperones are assembled into complexes on the outer membrane, the chaperones release their cargo to tunnel-shaped proteases, which process and fold the adhesin. The chaperones are then disposed of by a "chaperoneusher" complex that assembles and extrudes the pili into the bacterial cell en masse.

To obtain FimH for purification, the researchers stepped up adherence produc- tion. They attached "switches" on chaper- one and adhesin genes, inserted the resulting complexes into E. coli, and deleted the usher gene. The product is a bacterium that overproduces chaperones and correctly folded adhesin molecules. These complexes accumulate in the periplasm, staying soluble instead of plaing through the bacterial "pili tips." By getting rid of the usher, you end up with chaperone-adhesin complexes that are easy to purify in large amounts," Hillgren said.

The researchers purified FimH to Cancermag, where they showed that the adhesion triggers a strong, long-lasting immune response when injected into mice. The Medimmun researchers also explored the potential of this adhesion as a vaccine, and cultured cells from the bladder lining, finding that FimH can induce protection in the urinary tract of mice. (The human bladder has the same receptor as that of mice.)

The animals developed full-blown cystitis, but FimH protected some of them, lacking the gene for FimH. But vaccina- tion with FimH allowed normal mice to resist infection — the linings of their bladders had 100 to 1,000 times fewer bacteria than those of unvaccinated mice. The anti-adhesion antibodies also prevented bladder infection when they were introduced into the bloodstream via the abdominal cavity, Linden said. "This is the first demonstration that antibodies targeted against bacterial adhesin offer protection," Langenbrandt said. "It also suggests that by targeting proteins such as adhesins, one might be able to induce protection through systemic immunization.

The FimH vaccine is being tested on monkeys at the Karolinska Institute in Sweden by Linda Sage, Ph.D., who identified adhesins as minor targets of the immune system. "If key trials are successful, the vaccine will be tested in humans," Langenbrandt said.

Linden's group has shown that nearly 30 different kinds of adhesins or "pili tips" can be used to induce protection against cystitis. "This is a new approach in designing vaccines," Linden said. "The idea is to use a vaccine that produces many different adhesins, each with different binding sites on the bladder wall, so that the immune system will be able to recognize and fight any of these."