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INSIDE

Pitt's CTSI Receives $67.3 Million to Translate Science Into Therapies

By Jennifer C. Yates

A University of Pittsburgh institute aimed at accelerating the pace of translating science into real-life treatments for patients has received $67.3 million from the National Institutes of Health (NIH) to expand its work over the next five years.

Pitt's Clinical and Translational Science Institute (CTSI) is among 10 institutes nationwide to receive renewed funding in recognition of its successes during the first five years of the Clinical and Translational Science Awards (CTSA) program. The program is administered by the NIH's National Center for Research Resources (NCRR).

"This funding validates the important work being done by University of Pittsburgh researchers and physicians who are dedicated to advancing science in a meaningful way," said Arthur S. Levine, Pitt senior vice chancellor for the health sciences and dean of Pitt's School of Medicine.

The renewal underscores the success of Pitt's CTSI, through which researchers have used novel computer software to improve the diagnosis of breast cancer, brought researchers together as part of the Sleep Medicine Institute to advance research into sleep disorders, and funded research into the efficacy of low-cost prescription drug programs, among many other initiatives.

Steven E. Reis

"This funding helps us take science from the laboratory to real life in ways that are useful to people. We're grateful to be a part of the CTSA," said Steven E. Reis, director, CTSI, and Pitt associate vice chancellor for clinical research, health sciences.

The other institutions that received renewed funding are the Columbia University Medical Center; the Mayo Clinic; the Oregon Health & Sciences University; Rockefeller University; the University of California, Davis; the University of California, San Francisco; the University of Pennsylvania; the University of Rochester; and Yale University.

> Pitt's Clinical and Translational Science Institute is among 10 institutes nationwide to receive renewed funding in recognition of its successes during the first five years of the Clinical and Translational Science Awards program.

"These institutes were the pioneers in this program and are to be commended for the work they have done in bridging the traditional divides between laboratory research and medical practice," said NCRR Director Barbara Alving. "They were tasked with transforming the way their institutions coordinate research to make it more proactive and effective in producing real-world results, and, in the process, they have served as innovative models nationwide."

Together, the institutes represent a $498 million renewed commitment on the NIH's part to speed translational research nationwide. The renewal awards endorse the success of Pitt's CTSI and its sister programs in creating a framework for scientists to move beyond the traditional silos of science to collaborate on promising research and find the training and resources to move those projects ahead.

Pitt's CTSI was established in 2006 with an $83.5 million NIH grant. It is a collaboration between Pitt, UPMC, Carnegie Mellon University, and, as community partner, the Urban League of Greater Pittsburgh, among others.

Wang-Led Team Regrows Blood Vessels With a Potent Molecule

By Karen Hoffmann

Ever since the Nobel Prize for nerve growth factor was awarded more than 30 years ago, researchers have been searching for ways to use growth factor clinically.

University of Pittsburgh Professor Yadong Wang has developed a minimally invasive method of delivering growth factor to regrow blood vessels. His research, which could be used to treat heart disease, the most common cause of death in the Western world, was published in the Aug. 1 issue of the journal *Proceedings of the National Academy of Sciences*.

Yadong Wang

Wang is a professor in the Department of Bioengineering in Pitt's Swanson School of Engineering and the Department of Surgery in the University's School of Medicine. He is also affiliated with the Pitt-UPMC McGowan Institute for Regenerative Medicine (MIRM). His coauthors are Johnny Huard, a professor in the Department of Bioengineering and the School of Medicine's Departments of Orthopaedic Surgery, Molecular Genetics, and Pathology, as well as MIRM; graduate student Hunghao Chu and postdoctoral fellow Jin Gao in the Departments of Bioengineering and Surgery; and Chien-Wen Chen, a Ph.D. candidate in bioengineering and surgery.

When the researchers injected their growth factor compound under the skin of mice, they saw something amazing: New blood vessels grew, and large ones, not just tiny capillaries. "We had structures that resembled arterioles—small arteries that lead to a network of capillaries," says Wang.

Moreover, the structures stuck around. At least a month later, after only one injection of the growth factor complex, the new blood vessels were still there.

Powerful in Small Doses

In our bodies, growth factors control many different functions, including cell proliferation, migration, and differentiation. There are even growth factors that inhibit the growth of certain cell types or cause cell suicide. "They are very potent molecules," says Wang.

Being so powerful, growth factor is controlled very tightly by the body, which quickly destroys free-floating growth factor. The half-life for most growth factor injected under the skin is half an hour or less—very short-lived.

With this limitation in mind, the researchers investigated ways to use growth factor efficiently. They hit on a molecule called heparin, one of the molecules that bonds growth factor to its receptor on the cell's surface. When heparin binds to the receptor and the growth factor, it actually increases the activity of growth factor and stabilizes it.

"Our idea was, 'Let's use heparin as is, without any modification, to stabilize the growth factor and also to present it to the receptor,'" says Wang.

But there was only one catch: If you bond heparin to growth factor, the resulting substance is water-soluble. Injected into the body, the complex dissolves within seconds. Humans are made mostly of water, after all.

The team had to figure out a way to keep the complex from dissolving long enough for it to do its work of regenerating blood vessels.

The trick, they discovered, was to use a polycation—a molecule with multiple positive charges. Heparin has many negative charges. If it's neutralized with a polycation, it can be brought out of solution into what is called a coacervate—an aggregate of tiny oil droplets. Many other research teams use heparin in growth factor delivery as well, but the Wang lab is the first to convert the heparin/growth factor complexes into coacervates.

In this first-ever report of using coacervate for the controlled delivery of growth factor, the team delivered fibroblast growth factor-2. This led to extensive and persistent new blood vessel formation. The team used only one growth factor to induce the formation of mature blood vessels. These vessels were stabilized by special

Continued on page 2

Remembering 9/11

About 250 Pitt students will participate in an 11 a.m . Sept. 11 service in Soldiers & Sailors Memorial Hall & Museum, 4141 Fifth Ave., Oakland, commemorating the 10th anniversary of 9/11. As photographs of fallen military service members play on the auditorium's projector screen, Pitt students will carry from the auditorium to the front lawn U.S. flags representing the fallen members, placing them in rows for a tribute that will remain on the lawn for a week. The memorial service is being presented as a partnership between the University and its Office of Student Affairs and the Soldiers & Sailors Memorial Hall & Museum Trust, Inc. Also, at 9 a.m. Sept. 11, 50 firefighters will climb to the 35th floor of the Cathedral of Learning as part of a National Fallen Firefighters Foundation 9/11 Memorial Stair Climb (http://9-11stairclimb.com). Bigelow Boulevard between Fifth and Forbes Avenues will be closed, and fire vehicles will be parked in the street. In the 2002 photo, above, a grieving Pitt student bends over one of the flags placed on the Cathedral lawn as part of the University's first-anniversary observance of 9/11.

Rocky Markets

TIAA-CREF, Vanguard Offer Financial Counsel Services to Pitt Retirement-Fund Participants

Citing the recent stock market upheaval, the University of Pittsburgh's Office of Human Resources and Pitt's two retirement-benefit partners—TIAA-CREF and Vanguard— are urging Pitt faculty and staff to meet with a financial advisor for experienced counsel.

Both TIAA-CREF and Vanguard offer, at no charge, individual retirement counseling sessions to all faculty and staff who participate in either plan, according to an e-mail message from Ronald Frisch, Pitt's associate vice chancellor for human resources, to Pitt department administrators and human-resources managers. The TIAA-CREF and Vanguard counselors are noncommissioned financial managers who work with Pitt faculty and staff to create individual customized action plans.

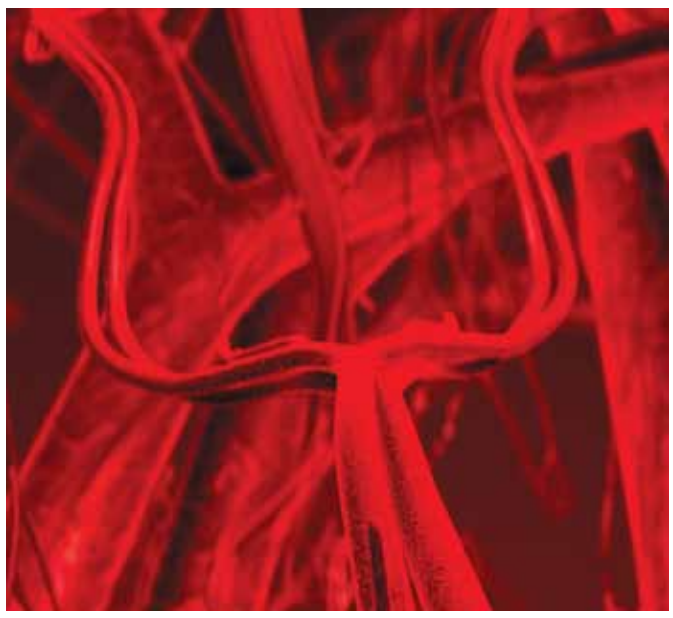
The counseling covers updates on market conditions, as well as advice on rebalancing retirement goals, developing an appropriate investment strategy, and managing retirement plans effectively.

To schedule an appointment with a financial advisor, call TIAA-CREF at 1-877-209-3136 and Vanguard at 1-800-662-0106, ext. 14500, or www.meetvanguard.com.

To make changes in investments, ask questions about an account, or to check balances, call the companies' Participant Services Departments—TIAA-CREF at 1-800-682-9139 and Vanguard at 1-800-523-1188.

Account management may also be done online at www.tiaa-cref.org/pitt and www.vanguard.com.

Wang-Led Team Regrows Blood Vessels With a Potent Molecule



Continued from page 1

cells called mural cells.

Now, Wang has gone on to use his unique delivery platform to study the controlled release of other growth factors that bind heparin: nerve growth factor, vascular endothelial growth factor, epidermal growth factor, bone morphogenetic proteins, and many others. "In all cases, the controlled delivery using coacervate was much more effective," says Wang.

The complex is highly efficient: Since the heparin and growth factor are both active ingredients, and polycation is added only to bring it out of the water, as much growth factor as necessary can be delivered. "High loading efficiency is important because it allows us to reduce the frequency of injections," Wang adds.

The coacervate is not very viscous. This means that "you can use a needle as thin as a hair" to inject it, says Wang. "So if you inject that through tissue, the damage you create is very small." It could be done through a catheter, a long tube with a needle through it. This means the chest wouldn't have to be opened up—a huge advantage over open-heart surgery.

Healing a Broken Heart

During a heart attack, time is muscle. When a blocked blood vessel doesn't allow enough oxygen and nutrients to the heart, the muscle dies.

"After a heart attack, the muscle is dead, and what's replacing it is scar tissue—a lot of collagen, but not many cardiac muscle cells. No muscle, no contraction," says Wang.

Once a heart attack has happened, the patient generally has two choices: Get a stent to open the blockage, or have surgery to bypass it. The heart tries to heal itself, but its self-remodeling efforts can have deleterious effects, like dilating ventricles until they're too big.

"If we can use growth factors to reverse that kind of adverse remodeling process, then we can probably rescue the heart function, which is the most important thing," notes Wang.

> "Our hope would be to reduce scarring, keep as much of the muscle alive as possible, and induce quick blood vessel formation to bring as many nutrients as possible in order to reestablish an environment for muscle growth."
> —*Yadong Wang*

The growth factor complex would be injected at the appropriate time—right after the heart attack, or a few days later—to change how the heart repairs itself.

"Our hope would be to reduce scarring, keep as much of the muscle alive as possible, and induce quick blood vessel formation to bring as many nutrients as possible in order to reestablish an environment for muscle growth," Wang says.

Wang's future research plans include eventual human clinical trials. His team will also use a disease model to investigate the efficiency of the treatment in heart attacks.

He is also interested in commercializing the treatment and is in talks with several clinicians and entrepreneurs. "This treatment is very promising in bench-to-bedside translation," Wang says.

Back to Campus 2011

MIKE DRAZDZINSKI/CIDDE

PHOTOS BY JIM BURKE/CIDDE

MARY JANE BENT/CIDDE

MIKE DRAZDZINSKI/CIDDE

1. Arrival Survival began Aug. 23, and the Pittsburgh campus was overtaken by students, their parents, and lots of moving bins, not to mention traffic. **2.** From left to right: Pitt Chancellor Mark A. Nordenberg, Dean of Students Kathy Humphrey, and Provost and Senior Vice Chancellor Patricia E. Beeson address students during the Aug. 24 Freshman Convocation at the Petersen Events Center. **3.** During the Convocation festivities, all freshmen join in the singing of Pitt's Alma Mater. **4.** Provost Beeson lights a candle as Freshman women celebrate the 91st annual Lantern Night in Heinz Chapel on Aug. 28. Lantern Night for freshman women is a rite of passage for new students and one of the oldest traditions practiced at the University of Pittsburgh.

In our Aug. 23, 2011, issue, incorrect photo credits were placed on two pictures. Photographer Mike Drazdzinski shot both the page 3 photo of Honors College Dean Edward M. Stricker and the page 9 photo of the Staff Association Council inauguration. The Pitt Chronicle *regrets the errors.*

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Awards&More

The University of Pittsburgh Institute of Politics' Health Literacy Project was recognized by UPMC's Center for Inclusion as an Inclusion in the Community Champion. The award was presented during the 3rd Annual Partnership Appreciation Event in July, held in UPMC Shadyside's Herberman Conference Center.


Mary E. Besterfield-Sacre

Mary E. Besterfield-Sacre, a University of Pittsburgh professor and Fulton C. Noss Faculty Fellow in Pitt's Department of Industrial Engineering, has been named one of 12 new fellows of the American Society for Engineering Education (ASEE); the group was inducted at a special awards ceremony June 29 at the ASEE Annual Conference and Exposition in Vancouver, B.C., Canada.


Michael Beach

Ann Dugan, founder and director of the University of Pittsburgh's Institute for Entrepreneurial Excellence (IEE) in the Joseph M. Katz Graduate School of Business, was recently elected to the Team Pennsylvania Foundation Board of Directors. Dugan is one of only two Western Pennsylvanians elected to the 36-member board. The newly elected members will serve through June 2014.


Eva Tansky Blum

The following faculty and staff of the University of Pittsburgh Schools of Dental Medicine, Nursing, and Pharmacy have been recognized for their academic achievements and leadership.

Michael Beach, an assistant professor in the School of Nursing, received a $100,000 award from the Robert Wood Johnson Foundation to provide 10 scholarships of $10,000 each for second-degree students for next fall and spring.

Lora E. Burke, a professor in the School of Nursing, received a $699,897 award from the National Institutes of Health for a four-year project titled "Advancing Real Time Data Collection: Adaptive Sampling and Innovative Technology."

Paul A. Moore, a professor in the School of Dental Medicine, was invited to represent the dental profession on a U.S. Surgeon General's Expert Panel, "Prescription Drug Abuse in Youth", held recently in Washington, D.C. He discussed abuse issues in the health care setting.

Alexandre Vieira, an assistant professor in the School of Dental Medicine, was appointed to the board of directors of the Society for Clinical and Translational Science.

Pitt alumnus and trustee **Eva Tansky Blum** (A&S '70, LAW '73) received the Allerton Award for Lifetime Achievement from the YWCA Greater Pittsburgh during the 29th annual *Tribute to Women* Leadership Awards Luncheon held May 25 at the Westin Hotel, Downtown. Blum is senior vice president and director of community affairs, PNC Bank. Two other Pitt alumnae were award winners as well: **Yvonne Cook** (CGS '91), president of the Highmark Foundation, a private corporate foundation that is funded by insurer Highmark, Inc., won in the Business & Industry category; and **Bonnie W. VanKirk** (SIS '2002), a community volunteer, won the Civic & Community Service Award

Elena Constantin, a University of Pittsburgh at Johnstown assistant professor of mathematics, received the Pitt-Johnstown President's Award for Teaching Excellence. Pitt-Johnstown President Jem Spectar said Constantin's "strong interactions with students and her mentoring of them through extracurricular activities clearly demonstrate her dedication and passion for teaching."

Ralph Roskies Appointed to National Library of Medicine Board of Regents

Pitt professor of physics Ralph Roskies, scientific codirector of the Pittsburgh Supercomputing Center (PSC) since 1986, has been appointed to the National Library of Medicine's Board of Regents. The appointment, for a four-year term, was made by Kathleen Sebelius, U.S. Secretary of Health and Human Services.

In 1984, Roskies, together with Professor Michael Levine of Carnegie Mellon University and James Kasdorf, then facilities manager of Westinghouse Electric Co., developed the proposal, submitted to the National Science Foundation, for what eventually became the PSC. Roskies is the author of more than 60 papers on theoretical elementary particle physics.

The PSC—a joint effort of Pitt, CMU, and Westinghouse— performs work that is pertinent to the National Library of Medicine, including the development of file systems, large-scale data storage, and wide-area networking.

At PSC, Roskies was principal investigator of the National Resource for Biomedical Supercomputing, the first external biomedical supercomputing program funded by the National Institutes of Health.

The National Resource for Biomedical Supercomputing, a part of PSC, has developed software tools used with the National Library of Medicine's Visible Human project, which enhances anatomy training through innovative, interactive viewing. The National Resource for Biomedical Supercomputing's volumetric visualization software also enables researchers to view and analyze the extremely large datasets obtained from light and electron microscopes and CAT and MRI scanners.


Ralph Roskies

In other work related to the National Library of Medicine's mission, the National Resource for Biomedical Supercomputing conducts research and training in bioinformatics. It also led innovative early work using high-speed networks to link an MRI scanner with a supercomputer to produce, almost instantaneously, an animated 3-D image of brain activity.

Part of the National Institutes of Health, the National Library of Medicine, located in Bethesda, Md., is the world's largest biomedical library. As a developer of electronic information services, it delivers trillions of bytes of data to millions of users every day.

Working to Build Better Antipsychotic Drug by Treating Schizophrenia's Cause

By Karen Hoffmann

The classic symptoms of schizophrenia—paranoia, hallucinations, the inability to function socially—can be managed with antipsychotic drugs. But exactly how these drugs work has long been a mystery.

Now, researchers at Pitt have discovered that antipsychotic drugs work akin to a Rube Goldberg machine—that is, they suppress something that in turn suppresses the bad effects of schizophrenia, but not the exact cause itself. In a paper published in the Aug. 24 *Journal of Neuroscience*, they say that pinpointing what's actually causing the problem could lead to better avenues of schizophrenia treatment that more directly and efficiently target the disease.


Anthony Grace

"In the past five years or so, we've really started to understand what may be going wrong with the schizophrenic brain," says Anthony Grace, Distinguished Professor of Neuroscience and professor of psychology in Pitt's School of Arts and Sciences and professor of psychiatry in the Pitt School of Medicine, who is senior author of the paper.

Schizophrenia is made up of three different types of symptoms. Positive symptoms, which are added onto a "normal" personality, include hallucinations and delusions, such as hearing voices, thinking people are after you, or thinking you're being targeted by aliens. Those are the classic symptoms of schizophrenia and the ones antipsychotic medications work on best. Grace says these are the symptoms most likely related to a neurotransmitter called dopamine.

The other two categories of symptoms are negative (what's missing from the normal personality—the ability to interact socially or hold down a job; some emotional flattening) and cognitive (the ability to think linearly or concentrate on one thing at a time). These two really aren't addressed well by antipsychotic drugs. "Blocking the dopamine system seems to fix classic hallucinations and delusions a whole lot better than it fixes the other problems," says Grace.

Grace has been studying the role dopamine plays in the schizophrenic brain since 1978. It's long been known that after several weeks of treatment with antipsychotic drugs, dopamine-producing neurons are inactivated. "It would suggest to us that in schizophrenia there is not too much dopamine, but rather the dopamine system is too responsive," says Grace.

Therefore, by inactivating the neurons, this overresponsivity should be able to be treated. "If there were just too much dopamine in the brain, one would expect the biggest treatment effect would be at the beginning and then it would diminish," Grace says.

But the actual effect is different—it builds over a couple days and then is constant; you don't get the tolerance you'd get with other drug treatments. This didn't fit with clinical observation. "Patients respond in the first few days, but we took weeks to see results in our normal animals," Grace says.

> "In the past five years or so, we've really started to understand what may be going wrong with the schizophrenic brain."
> —*Anthony Grace*

Grace's team developed a rat model that approximates some of the key features of schizophrenia. Rats exhibit the same symptoms one would expect from schizophrenia: sensory processing, cognition, and hyperresponsivity to amphetamines. When team members looked at this animal model and used these antipsychotic drugs, they found that what takes weeks to occur in a normal rat happens in a couple days in these schizophrenia-model rats. "It fits very well with the time course we see in human patients," says Grace.

What causes this to be the case? Grace hypothesizes that it's the schizophrenic brain's dopamine system working overtime. "Our recordings of dopamine neurons suggest that the dopamine system is turned up too high," says Grace. "That fits with human imaging studies in schizophrenics showing the dopamine system is overreacting."

Currently available antipsychotic drugs work by blocking dopamine receptors and stopping dopamine neurons from firing. "Using these drugs, we're fixing the overreactivity by causing the neurons to be inactive," says Grace. "It would be better to fix overreactivity by correcting what causes it.

"It's like fixing a car that's going too fast by taking out the engine instead of lifting your foot off the gas."

"What we're doing today, using antipsychotic drugs currently available, is putting a sort of patch several steps downstream from where we think the problem is," says Grace. "By using these animal models, we can start to work backwards to figure out why the drugs are having the effects they do. The next step to look further back and try to fix the problem at its source.

"This is consistent with the hypothesis that the hippocampus is overdriving the system, and antipsychotics are just pushing it over the edge to shut it down," he says. "This gives us an idea of where to go to make a better antipsychotic drug.

The coauthors of the paper are Kathryn Gill, a postdoctoral fellow in Pitt's Department of Neuroscience; and Pierangelo Cifelli and Ornella Valenti, researchers who have since left the University to return to positions they hold in Italy.

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Happenings

University Art Gallery,
On a Lucky Day a Surprising Balance of Form and Spaces Will Appear,
September 8-October 21

Exhibitions

University Art Gallery, *On a Lucky Day a Surprising Balance of Forms and Spaces will Appear,* **Sept. 8-Oct. 21,** exhibition comprising work of 14 faculty members in Pitt's Department of Studio Arts, Frick Fine Arts Building, 412-648-2430.

Carnegie Museum of Art, *Pittsburgh Biennial,* **through Sept. 18;** *Ragnar Kjartansson: Song,* **through Sept. 24;** *Hand Made: Contemporary Craft in Ceramic, Glass, and Wood,* **ongoing;** *Past Meets Present: Decorative Arts and Design at Carnegie Museum of Art,* **ongoing,** 4400 Forbes Ave., Oakland, 412-622-3131, www.cmoa.org.

The Warhol, *I Just Want to Watch: Warhol's Film, Video, and Television,* **ongoing,** 117 Sandusky St., North Side, 412-237-8300, www.warhol.org.

The Frick Art & Historical Center, Fin de Siécle *Prints: Art Nouveau on Paper*, **through Sept. 11,** free and open to the public, 7227 Reynolds St., Point Breeze, 412-371-0600, www.thefrickpittsburgh.org.

Heinz History Center, *America's Best Weekly: A Century of* The Pittsburgh Courier, **through Oct. 2;** 1212 Smallman St., Strip District, 412-454-6000, www.heinzhistorycenter.org.

Wood Street Galleries, *Cell Phone Disco,* **ongoing,** Tito Way, Downtown, 412-456-6666, www.pgharts.org.

Lectures/Seminars/Readings

"Leibniz as Mechanist and Mechanician," Nicholas Rescher, Distinguished University Professor of Philosophy and cochair of Pitt's Center for Philosophy of Science, 12:05 p.m. **Sept. 6,** 817 Cathedral of Learning, 412-624-1052, www.pitt.edu/~pittcntr.

"Trainees in Distress: Becoming a Doctor Is an Occupational Hazard," Lotte Dyrbye, associate director, Research Applications, Department of Medicine Program on Physician Well-Being, Mayo Clinic, noon **Sept. 9,** Scaife Hall 4th Floor, Lecture Room 3, Medical Education Grand Rounds, Office of the Vice Dean, Pitt School of Medicine, 412-648-9000, www.megr.pitt.edu.

Opera/Theater/Dance

The Marvelous Wonderettes by Roger Bean, a return to the 1950s and '60s, **through Oct. 2,** Cabaret at Theater Square, 655 Penn Ave., Downtown, 412-281-3973, www.pittsburghclo.org, PITT ARTS Cheap Seats, 412-624-4498, www.pittarts.pitt.edu.

Wicked, story of the Wicked Witch of the West and Glinda the Good before they came to Oz, **Sept. 7-Oct. 2,** Benedum Center, 719 Liberty Ave., Downtown, PNC Broadway Across America-Pittsburgh, 412-456-6666, www.pgharts.org, PITT ARTS Cheap Seats, 412-624-4498, www.pittarts.pitt.edu.

Pitt PhD Dissertation Defenses

Tarek W. Elnaccash, Department of Biological Sciences, 2:15 p.m. **Sept. 9,** "Evolvability in a Variable World: Genetic Architecture of *Arabidopsis thaliana* and its Implications for Adaptation," A219B Langley Hall.

Eartha Kitt visits Pittsburgh's Hill District by Charles "Teenie" Harris

Heinz History Center,
***America's Best Weekly: A Century of* The Pittsburgh Courier,**
through Oct. 2

Carnegie Museum of Art,
Hand Made: Contemporary Craft in Ceramic, Glass, and Wood,
ongoing

PUBLICATION NOTICE The next edition of *Pitt Chronicle* will be published Sept. 12. Items for publication in the newspaper's *Happenings* calendar (See page 3) should be received at least two weeks prior to the event date. *Happenings* items should include the following information: title of the event, name and title of speaker(s), date, time, location, sponsor(s), and a phone number and Web site for additional information. Items may be e-mailed to chron@pitt.edu, or sent by campus mail to 422 Craig Hall. For more information, call 412-624-1033 or e-mail robinet@pitt.edu.