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 and patients together at 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. “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 CTSI,” 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, San Francisco; the University of Pennsylvania; the University of Rochester; and Yale University. “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 care,” 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.

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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 coauthors for ways to use growth factor clinically.

Moreover, the structures stuck around. When the researchers injected their 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 the 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 can neutralize 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.

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Vessels With a Potent Molecule
Wang-Led Team Regrows Blood

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.

But 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.

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.

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,” 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,” says Wang.

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,” says Wang.

In our Aug. 23, 2011, issue, incorrect photo credits were placed on two pictures. Photographer Mike Drazdinski shot both the page 3 photo of Honors College Dean Edward M. Stocker and the page 9 photo of the Staff Association Council inauguration. The Pitt Chronicle regrets the errors.
The classic symptoms of schizophrenia—paranoia, hallucinations, the inability to function socially—can be managed with antipsychotic drugs. But paradoxically, how these drugs work has long been a mystery.

Now, researchers at Pitt have discovered that antipsychotic drugs target 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.

“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 Schools 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 involve an overactive “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 and what’s called cognitive or 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.

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 Schools of Arts and Sciences and professor of psychiatry in the Pitt School of Medicine, who is senior author of the paper. Grace has been studying the role dopamine plays in the schizophrenic brain since 1978. It’s been known that after several weeks of treatment with antipsychotic drugs, dopamine is reduced. “But it was 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 overactive dopamine system is turned up too high,” says Grace. “That fits with human imaging studies in schizophrenias 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.”

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

By Karen Hoffmann

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 Kosdorff, 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—joint effort of PSC, 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 externally biomedical supercomputing program funded by the National Library of Medicine.

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.

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 billions of bytes of data to millions of users every day.

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

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—Anthony Grace
Happenings

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, 412-648-2450.


Lectures/Seminars/Readings

“Lifeline as Mechanist and Mechanism,” Nicholas Rescher, Distinguished University Professor of Philosophy and cochair of Pitt’s Center for Philosophy of Science, 12:05 p.m. Sept. 6, 417 Cathedral of Learning, 412-622-1052, www.philosophy.pitt.edu-
present.

“Trains 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.

“Leibniz as Mechanist and Mechanic,” Nicholas Rescher, Distinguished University Professor of Philosophy and cochair of Pitt’s Center for Philosophy of Science, 12:05 p.m. Sept. 6, 417 Cathedral of Learning, 412-622-1052, www.philosophy.pitt.edu-
present.

Pitt PhD Dissertation Defenses

Tarek W. Elnaccash, Department of Biological Sciences, 2:15 p.m. Sept. 9, A219B Langley Hall.

Opera/ Theaters/Dance


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 412-624-3033 or e-mail robinet@pitt.edu.