Looking ahead to the next five years in health sciences research

From the Interim EVPHA

Wright Caughman

Thanks to all who make us leaders in research

At a time when so much of the economic news we hear is grim, the Woodruff Health Sciences Center has...
neurology to identify biomarkers for ALS.

A new five-year strategic plan for research in the WHSC, initiated in fall 2008, is nearing completion after much hard work by an executive committee and eight working groups from the WHSC Research Advisory Council. The plan highlights tremendous growth in research funding over the past three decades to more than half a billion dollars in fiscal year 2009-2010.

The schools of nursing, public health, and medicine all have launched new research plans of their own, which will work hand in hand with the WHSC overall plan. All the plans acknowledge that attracting research funding, which has never been easy, will be even more difficult in the future, with constrained foundation and federal budgets.

To prosper and grow, the WHSC report says, Emory University and the WHSC must first embrace research as the foundation and fundamental driver of the creation of new knowledge, which ultimately distinguishes the really great from the merely good universities.

Research has a major impact for Emory and its many constituents by doing the following:

- Generating value in intellectual capital and institutional distinction
- Placing Emory among the top research intensive academic institutions
- Driving recruitment and retention of the highest-quality faculty
- Attracting the brightest and best students and trainees
- Developing a dynamic economic engine for Atlanta, Georgia, and the region
- Creating clinical competitive advantage for Emory Healthcare and its partners
- Laying a foundation for philanthropy and fundraising
- Leveraging investment by federal, state, and local governments and foundations
- Creating commercializable intellectual property

The value of research will be tracked through programs like STAR METRICS, a federal and university partnership measuring the outcomes and impact of science investments and demonstrating benefits of those investments to the public. The NIH and the NSF are leading development of the program through the Office of Science and Technology Policy.

Key elements of the WHSC research strategic plan emphasize interdisciplinary research, integrating research and health care, streamlining research by developing cutting-edge core labs and enhancing IT connectivity, developing intellectual property, commercializing new discoveries, and promoting a culture that values training and mentorship.

The final plan is scheduled to be completed by the end of this year. —Holly Korschun
Developing a treasure trove of new drugs

Drug discovery is often described as prospecting or mining because researchers have to search through thousands of inert substances to find something valuable. After several years of sifting and screening, scientists Stephen Traynelis and Ray Dingledine (pharmacology), Dennis Liotta (chemistry), and other collaborators now have a treasure trove of compounds that can modify the activity of NMDA receptors, critical players in communication between brain cells. This work may lead to new drug treatments for schizophrenia, Parkinson’s disease, and other disorders.

Receptors for NMDA (N-methyl-D-aspartate) act as gates, allowing electrical charges to flow into neurons in response to the chemical messenger glutamate. NMDA receptors play important roles in learning and memory and in several disease states. They come in four varieties, depending on the part of the brain being investigated.

The research team has focused on compounds that can target different types of NMDA receptors selectively to either enhance or block them.

Last month, they reported in Nature Communications about effects of the
compound CIQ, which selectively enhances the NR2C and NR2D forms of the NMDA receptor. Because these forms are altered in patients with schizophrenia, a compound that could enhance them potentially could help relieve schizophrenia symptoms.

In July, the team reported in the *Journal of Medicinal Chemistry* on compounds that, conversely, selectively block these two forms of the NMDA receptor.

Experiments with animal models of Parkinson’s suggest that blocking NMDA receptors could compensate for circuit changes that accompany the neurodegeneration associated with the disease. The selectivity of the team's compounds could be especially useful because the NR2D form of the NMDA receptor is highly active in the parts of the brain that are most affected by the degeneration from Parkinson’s. Additionally, the compounds' ability to block NMDA receptors selectively could avoid side effects (symptoms that simulate schizophrenia, for example) seen with nonselective drugs like PCP that block NMDA receptors everywhere in the brain.

NeurOp, an Emory start-up company founded in 2002, is developing compounds to mitigate brain damage from stroke. Another variety of selective NMDA receptor blockers is the focus of NeurOp, a start-up company founded by Traynelis and Dingledine in 2002 along with Duke’s James McNamara. NMDA receptor blockers have been proposed as potential neuroprotective agents because loss of blood flow to the brain (such as that seen in stroke) leads to an “excitotoxic” state involving over-activation of NMDA receptors. In an effort to steer clear of potential side effects of nonselective NMDA receptor blockers, NeurOp is developing compounds that are active only in the acidic environment of injured brain tissue. This spring, the firm was named Start-Up Company of the Year by Emory’s Office of Technology Transfer and announced a two-year research collaboration with Bristol-Myers Squibb. —Quinn Eastman

**Reducing effects of stress in cancer and heart disease**

Susan Bauer-Wu has had her share of life-changing moments. As a nursing student in New York, she learned that her mother had breast cancer. As she helped her mother cope with the emotional and physical stress of the disease, her studies took on an intense personal focus. Now a Georgia Cancer Coalition Distinguished Cancer Scholar in the nursing school, she is regarded as a national leader in palliative medicine and integrative health.

Bauer-Wu’s studies focus on the effects of meditation and other stress-relieving activities on cancer patients. She currently leads a large randomized clinical trial that looks at whether meditation affects subjective symptoms as well as laboratory findings such as stress hormone levels or length of time required for a patient's white blood cells to recover after a bone marrow transplant. Funded by NIH, the study involves 241 patients at Emory and Dana-Farber Cancer Institute, where Bauer-Wu previously served as director of the Cantor Center for Research in Nursing and Patient Care.

And of course we recognize the school and unit financial officers and their staffs who keep our research dollars flowing smoothly. These include, among others, Barbara Schroeder in medicine, Dean Surby in public health, Martha Walsh at Yerkes, and Rob Hoover in nursing.

Our research enterprise is made more promising by our partnerships. These include the Georgia Research Alliance and the Georgia Cancer Coalition, which help us recruit faculty and develop collaborations with neighboring institutions. Other partners—Georgia Tech, Morehouse School of Medicine, Children’s Healthcare of Atlanta, Grady Health System, the Atlanta VA Medical Center, and the CDC—are also a large part of what makes Emory great and Georgia unique in its biomedical research.

Finally, thanks to the tremendous medical, nursing, and administrative leadership and staff in Emory Healthcare, who not only allow us to provide the best care available but also help differentiate Emory from its local peers in our ability to offer patients leading-edge clinical trials that move research from the laboratory to the bedside.

Transforming health and healing means pioneering discoveries that advance our understanding of disease to improve lives locally, nationally, and globally. It takes a hugely talented team to make that happen, but as you’ll discover when you read the stories in this issue, that’s just what we’re doing. Thanks for all you do to make Emory and WHSC leaders in research and discovery.

_Please let me know your thoughts and suggestions at evphafeedback@emory.edu._

**In brief**

Notable

Anne Adams is interim AVP for clinical trial...
Services. In a related study, she is using neuroimaging to see what parts of the brain respond to such interventions.

Just recently, she received a $3.5 million NIH grant for studies to reduce heart disease risk and improve the health and well-being of family caregivers for patients experiencing dementia or heart failure (read related story).

Bauer-Wu was inducted last fall as a fellow of the American Academy of Nursing (AAN), one of the highest honors in the profession. Read more. —Pam Auchmutey

Top

Construction of new research building to begin next spring

The WHSC continues to invest in researchers and research space, as evidenced by a new 200,000-square-foot research building on Haygood Drive, currently in the design development phase. It will be on the site of the old Turman residence hall, demolition of which is scheduled for completion in March 2011, to be followed by excavation and foundation work. Construction is expected to take 22 to 24 months, with completion in March 2013.

The building, with a total cost of $89.9 million, will include four stories of laboratories above grade and one basement level with a vivarium and mechanical plant. A two-level bridge, including research offices and “dry” research space, will span Haygood Drive, connecting the building to the Emory-Children’s Center.

The building is designed to accommodate 65 principal investigators, with about 115,000 gross square feet dedicated to pediatric research. Other research space will focus on cancer, immunology, and drug discovery, among other areas. Core laboratories will include a BSL-3 containment lab, flow cytometry, genomics, and cellular imaging. —Holly Korschun

Ray Dingledine (pharmacology chair and executive associate dean for research in the medical school) has been elected to the Institute of Medicine. His work has laid groundwork for new drug therapies for epilepsy and has broad implications for other brain disorders, including stroke and schizophrenia. Read more. Listen to an interview podcast with Dingledine.

Michael Hart (pulmonology) recently was named the new associate chief of staff for research at the Atlanta VA Medical Center after serving in an acting role in this position over the past year. Read more about his research in internal medicine faculty profiles.

James Hughes (infectious disease, medicine and public health) has been elected president of the Infectious Diseases Society of America. He took office during the organization’s 48th meeting held recently in Vancouver, British Columbia. Read more.

Ami Klin has
The process of fear learning

Kerry Ressler gleans information about mental distress not only from the patients he sees as a psychiatrist but also in his role as a neuroscientist, studying the phenomenon of fear learning in both humans and animals.

In a study involving patients, for example, Ressler, who is the first practicing psychiatrist to have been named as a Howard Hughes Medical Institute investigator, works with a team of colleagues on the Grady Trauma Project.

This is a study of risk factors for post-traumatic stress disorder (PTSD) in nonpsychiatric patients seen in Grady Hospital's General Medical Clinic. Pilot data from these patients suggests that more than 80% have suffered significant trauma and about 30% have PTSD. Ressler's team has evaluated some 4,000 patients thus far, with a goal of including 8,000 total. The study's funding from the National Institute of Mental Health was recently renewed at an annual rate of more than $1 million.

The investigators, who include psychologist Bekh Bradley and geneticists Joseph Cubells and Alicia Smith, are looking at both genetic and environmental influences on PTSD. They are gathering demographic data and information about participants' history of child abuse or trauma, adult depression, and PTSD symptoms. They also are collecting saliva and blood samples to determine genetic and biologic risk markers, along with measurements of startle response and heart rate.

"Our data suggests that there seems to be a critical period of development for emotional memory systems," Ressler says. "During this period, stress alters the sensitivity of genes involved in the stress response, leading to an altered stress...

Ami Klin

Alliance Eminent Scholar, Klin is an internationally recognized psychologist and researcher. He comes to Emory and Children's Healthcare of Atlanta from Yale, where he headed the Yale Autism Program. At Emory, Klin will create a comprehensive autism program focusing on research, clinical care, training, and advocacy. A primary goal for Klin and his team will be to implement universal screening for autism spectrum disorder (ASD) in the first year of an infant's life. Klin's previous research has found that early intervention substantially optimizes outcomes and improves quality of life for children diagnosed with ASD. "Our most exciting goal is to make Atlanta the nation's capital of early autism diagnosis and intervention," says Klin. Read more.

Jean Khoury

(Winship, hem-onc) is the first holder of the R. Randall Rollins Chair in Oncology, established recently with a gift of $2 million from the O. Wayne Rollins Foundation. Khoury's research focuses on novel targeted agents for treating leukemia and other blood disorders. He also studies genetic profile changes in cancer cells to help better tailor anti-cancer treatments. An academic chair such as this one is the most prestigious of named academic positions and helps Emory recruit and retain top-level faculty. Read more.

Rebecca Pentz

(Winship, research ethics, hem-onc) has been appointed to serve on an external scientific panel to provide input to the NIH's new genotype tissue-expression project, which is designed to study how genetic...
sensitivity for the rest of the person's life."

In addition to his research with humans at the Grady clinic, Ressler works with colleagues at Yerkes to study brain chemistry of fear learning in mice. One recent focus has been BDNF, a brain growth factor believed to be one of the critical molecules involved in fear learning. After pathologist Keqiang Ye discovered several compounds that mimic BDNF, Ressler’s team at Yerkes tested their effects. In February, they reported in *Proceedings of the National Academy of Sciences* that one BDNF-like compound, 7,8-DHF, restored behavioral effects of BDNF in mice bred genetically to lack the growth factor. In July, the investigators reported in *PLoS One* journal that another BDNF-like compound, deoxygedunin, has antidepressant and neuroprotective effects on the brain but that it also enhances fear learning under certain conditions.

"Together with other experiments, these findings suggest that BDNF is required both to form fear memories and to inhibit them," Ressler says. "So new drugs that block BDNF might be useful shortly after a trauma to prevent the normal consolidation of fear memory associated with that trauma. Alternatively, drugs that mimic BDNF function may enhance the emotional learning process of talk therapy in treating already-existing PTSD." —Quinn Eastman

Seeking links between genes and social risk factors

**Gene Brody** is a behavioral scientist in public health whose research focuses on better ways to prevent risky behavior. He leads the Center for Contextual Genetics and Prevention Science (CGAPS) at Emory and University of Georgia (UGA), which is one of six core centers supported by the National Institute on Drug Abuse and is funded by a five-year $5.6 million grant.

Researchers in CGAPS are looking at both genetics and social determinants of health, particularly among African American children, youths, and families.

"There is abundant data on how families can prevent risky behaviors," says Brody. "Recent research by our team has shown that the protective family process can ameliorate genetic risks for youths’ involvement in risky behavior. Our goal at CGAPS is to improve the quality of prevention programs to make them more effective."

CGAPS will fund pilot studies for start-up projects and train future investigators. It also will serve as a repository for genetic and environmental data gathered from 4,000 African American families in Atlanta and rural Georgia. A laboratory at the University of Iowa will analyze the genetic and epigenetic (nongenetic causes of gene expression) data provided by these families. Researchers then will tap into this data to analyze how the interplay of genetics and social determinants affect the health and well-being of children, adolescents, and young adults.

The idea for the center evolved from discussions among Brody’s colleagues at Emory, UGA, University of Iowa, and Washington University in St. Louis. Center variation may control gene activity and its relationship to disease. This project will create a resource for researchers to study inherited susceptibility to illness and will establish a tissue bank for future biologic studies. Read more.

**Guido Silvestri**, a leading HIV/AIDS investigator, recently joined the faculty at Yerkes (chief of microbiology and immunology) and the medical school (pathology) as a Georgia Research Alliance Eminent Scholar. He came from Penn, where he developed a highly collaborative research program that spans nonhuman primates and humans. Here, Silvestri will work to develop new therapeutic approaches to HIV that modulate inflammatory immune responses, as well as vaccines for chronic disease. Read more. Listen to a recent *Sound Science* podcast in which Silvestri compares HIV in humans with its equivalent in nonhuman primates.

**Jack Tillman** was recently appointed assistant VP for research in the WHSC. He works closely with WHSC VP for Research **David Stephens**, facilitating, coordinating, and administering strategic research plans, clinical and translational research initiatives, local and national research partnerships, and WHSC interdisciplinary activities. Tillman also promotes the WHSC research enterprise and provides support for the WHSC research infrastructure.

**Events**

**Dec. 13-14:** Sixth Annual National Predictive Health Symposium: Molecules to Mankind. Emory Conference Center. More info.

**Feb. 24:** 2011 State-of-the-WHSC address. 4:30 p.m. WHSCAB auditorium. Reception to follow.
researchers from Emory include behavioral scientists Michael Windle, Ralph DiClemente, Gina Wingood, and Jessica Sales in public health and geneticist Joseph Cubells in the medical school. —Pam Auchmutey