RECENT PUBLICATIONS

[This list reflects publications for which Geisinger employees are recognized as authors and which were published in June, July and August. If we have overlooked a publication, please forward to the citation to Nicole Hunter and it will be included in the next issue.]

Berger P, Skelding K. Review: Rescue percutaneous coronary intervention but not repeated fibrinolysis is effective for failed fibrinolysis in STEMI. *ACP J Club.* 2007;147:11.

Mehilli J, Ndrepepa G, Kastrati A, Neumann FJ, ten Berg J, Bruskina O, Dotzer F, Seyfarth M, Pache J, Kufner S, Dirschinger J, **Berger PB,** Schomig A. Sex and effect of abciximab in patients with acute coronary syndromes treated with percutaneous coronary interventions: Results from Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment 2 trial. *Am Heart J* 2007;154:158.e1-158.e7.

Steinhubl SR, Kastrati A, **Berger PB.** Variation in the definitions of bleeding in clinical trials of patients with acute coronary syndromes and undergoing percutaneous coronary interventions, and its impact on the apparent safety of antithrombotic drugs. *Am Heart J.* 2007;154:3-11.

Boscarino JA. The Postwar Experiences and Health Outcomes of Vietnam Veterans. In: G. Fink (ed), Encyclopedia of Stress, 2nd Edition. New York, NY: Academic Press, 2007, pp. 830-838.

Larson, Sharon, Eyerman, Joseph, Foster, Misty, Gfroerer, Joseph. Worker Substance Use and Workplace Policies and Programs. *DHHS publication No. SMA 07-4273, Analytic series A-29*, June 2007.

Stewart WF, Ricci JA, Chee E, Hirsch AG, Brandenburg NA. Lost Productive Time and Costs Due to Diabetes and Diabetic Neuropathic Pain in the US Workforce. *J Occup Environ Med.* 2007;49:672-679.

Bigal, M E. Litpon, R B. Winner, P. Reed, M L. Diamond, S. **Stewart, W F.** AMPP advisory group. Migraine in adolescents: association with socioeconomic status and family history. Neurology, 2007 Jul 3;69(1).

Zhang K, Prichard JW, Yoder S, De J, Lin F. Utility of SKP2 and MIB-1 in grading follicular lymphoma using quantitative imaging analysis. *Hum Pathol.* 2007;38:878-882. ❄

Highlighting new investigators: Adele Spegman, RN, PhD to lead Institute on Nursing Excellence

Adele Spegman, RN, PhD, has joined Geisinger Health System as director of the Geisinger Institute on Nursing Excellence, where she will promote and facilitate nursing research throughout the health system.

"The Institute is designed to support the Geisinger tradition of exceptional clinical practice," Spegman said. "I'm excited to be among nurses committed to strengthening the quality and outcomes of nursing care. GHS nurses are poised to be national leaders in clinical nursing." The Institute will also foster multi-disciplinary approaches to healthcare research. "Nurses have a unique role in healthcare," Spegman said, "and bring unique perspectives to research activities."

Dr. Spegman brings more than 20 years experience in clinical, educational and research settings. With expertise in early child development and family-centered care, her research work has also included care-giving for elders with Alzheimer's disease, family responses to a child's diagnosis of ADHD, and low back pain.

Prior to coming to Geisinger, Dr. Spegman held faculty appointments at Western States Chiropractic College, the University of Portland and the University of New Hampshire, and was a senior research associate at Oregon Health & Science University. ❄

Adele Spegman, RN, PhD

RECENT EXTERNAL AWARDS

[This list reflects awards to Geisinger received in June, July and August. The listing includes new awards and competitive renewals. To protect the sponsor's confidential information contained in study titles, it does not include clinical trial agreements; dollars are not listed for industry agreements. If an award is overlooked, please forward the relevant information to researchconnections@geisinger.edu and it will be included in the next issue.]

Marilyn Haupt, MD,
The ABATE Study, Queens University and Astra Zeneca.

Stuart Hoffman, DO,
Describing Non-Adherence to Anti-Epileptic Drugs (AED's), and Developing a Model that Describes Events associated with Non-Adherence Outcomes (Morbidity and Mortality), GlaxoSmithKline.

Robert Langer, MD,
Stage III Colon Cancer Study, American Cancer Society, $16,000

Tooraj Mirshahi, Ph.D.,
Protein Signaling to Cardiac Potassium Channels, American Heart Association, $100,000.

Anthony Petrick, MD,
Hepatic Iron Overload, Society of American Gastrointestinal and Endoscopic Surgeons, $20,000

Mohammed M. Shareef, Ph.D.,
Therapeutic Implications of Oxygen-Sensitive Notch Signaling in Breast Carcinoma. Department of Defense, $115,350

Walter Stewart, PhD, MPH,
and **Ronald Harris, MD,**
E-Diabetes, Merck/Schering-Plough Joint Venture

Mark Selna, MD,
Inpatient-Outpatient Transitions: Reducing the Rate of Readmission, Agency for Health Care Research and Quality, $199,486

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IN THE NEXT ISSUES OF RESEARCH CONNECTIONS: Genomics Initiatives

GEISINGER

RESEARCH CONNECTIONS

LINKING THE RESEARCH COMMUNITY

SEPTEMBER 2007

Newsletter links research community

Research Connections is a new vehicle to link researchers throughout Geisinger Health System.

TO CONTINUE TO RECEIVE THIS PUBLICATION:

Click here to sign up
www.geisinger.org/researchconnections.

HAVE SOMETHING TO SAY?

Comments, content suggestions and request for more information may be submitted to researchconnections@geisinger.edu.

HOLD THE DATE

Fox Chase and Geisinger Population Studies Workshop

November 16, 2007
Geisinger Center for Health Research

More details and an agenda to come. For more information contact Nikki Poe at 570-214-9410.

G protein-coupled receptor signaling: The search for novel drug targets

As a result of their understanding of G protein-coupled receptor (GPCR) signaling, Geisinger scientist are now able to better understand how drugs, like those that treat obesity, regulate appetite.

GPCRs belong to a large protein family of transmembrane receptors that sense molecules outside the cell and activate signal transduction pathways inside the cell and, ultimately, cellular responses. There are nearly 1,000 different G protein coupled receptors throughout the body. The agents that activate these receptors include light,odors, pheromones, hormones and neurotransmitters.

GPCRs are one of the keys to regulation of all functions in every cell of the body. When GPCRs fail to work, they can lead to schizophrenia, bipolar disease, depression, hypertension and renal disease, as well as other disorders. GPCRs are also the target of approximately half of all modern drugs. Scientists studying GPCRs are focused on predicting how cells will respond to different combinations of signals. Appetite regulation, for example, is controlled by more than 25 GPCR-signaling pathways in the brain. Scientists predicted that targeting these pathways would result in turning off the

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UPCOMING SIGNALING SYMPOSIUM

G Protein Coupled Receptor Signaling: Bench to Bedside

September 21, 2007 ■ 8:30 am to 5 pm
Geisinger Medical Center campus, Danville, PA

As part of the Weis Center's 20th anniversary celebration, investigators are hosting a symposium focused on the role of G-proteins in the etiology and treatment of complex diseases. Internationally renowned speakers will highlight new signaling paradigms and their implications for developing innovative treatments.
For program details or to register:
www.geisinger.org/signalingsymposium
or call 570-271-6659,
or email signalingsymposium@geisinger.edu.

Weis Center for Research celebrates 20 year anniversary

The Sigfried and Janet Weis Center for Research, dedicated in 1987, has 77 employees, including scientists and support staff.

When the George F. Geisinger Memorial Hospital opened its doors in September 1915, it had one operating room, one physician, seven nurses and 70 beds. That hospital has since grown into one of the country's foremost integrated health delivery systems. One of the key moments on Geisinger's road to success was when former President & CEO Henry Hood, MD, brought his vision for a basic science research program to then chairman of the Geisinger Foundation Sigfried Weis. Together, they determined that Geisinger needed a research facility to further health-related knowledge and draw some of this country's brightest minds to Geisinger.

Understanding that a strong and visionary leader was needed to make their vision a reality, Dr. Hood and Mr. Weis recruited one of this country's foremost experimental cardiologists, Howard Morgan, MD to Danville. Dr. Morgan, a former president of the American Heart Association, laid the groundwork for a program that attracted a cadre of outstanding scientists.

With the backing and leadership of Drs. Hood and Morgan, and through the generosity of the Weis family, the 65,000-square foot Sigfried and Janet Weis Center for Research was dedicated in Sept. 1987.

As Senior Vice President for Research and Director of the Weis Center, Dr. Morgan established the standards and policies for a flourishing research program at Geisinger.

Moving from his position as one of the original senior investigators, David J. Carey, PhD, was named Director of the Weis Center for Research and Associate Chief Research Officer in 2000.

Dr. Carey has concentrated on strengthening research, science education and community service while expanding the collaborative initiative with clinicians and the scientists in the newly dedicated Center for Health Research.

Today, at the Weis Center 21 senior and research scientists supported by a staff of about 50 professionals conduct important basic and translational research in cardiovascular biology, cancer, neuroscience, obesity and other areas. The program brings together scientists and physicians in projects that directly improve care at the patients' bedside. These projects advance translational medicine today and draw international recognition to the system. ❄

Howard Morgan, MD, the founding director of the Weis Center for Research and one of the nation's foremost cardiology researchers, lead a program that diversified into biochemistry, molecular biology, and cancer research.

The search for novel drug targets

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body's craving for food. Scientists at the Sigfried and Janet Weis Center of Research are working on studies that show that targeting the G protein rather than the GPCR may be the key to developing a family of drugs to treat obesity.

For example, the Robishaw laboratory has generated a mouse missing the G protein γ3 subunit, which limits weight gain on a high-fat diet, primarily by reducing food intake. Targeting the G protein rather than the GPCR blocks input from many GPCRs, thus blocking the effects of hormones that increases appetite and decreases metabolism. Interestingly, the mice also show a decreased response to morphine and other potentially addictive medications, suggesting the G protein γ3 subunit may also be a target for the design of a new class of drugs to treat alcohol and drug addiction.

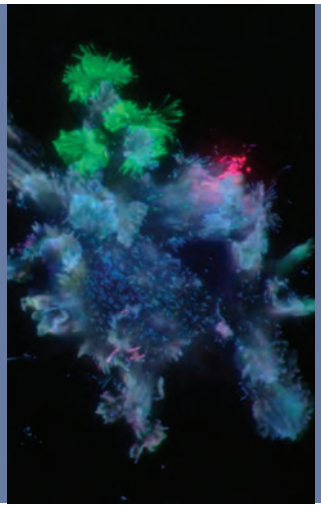
Four Weis Center laboratories are devoted to different, but complementary, research on G proteins and GPCRs. Drs. Janet Robishaw, Gerda Breitwieser, Catherine Berlot and Tooraj Mirshahi utilize a range of tools – from genetic studies in zebra fish and mice to sophisticated molecular imaging technology such as total internal reflection fluorescence microscopy – to examine the molecular dynamics of the GPCR–G protein interaction and how to activate signaling pathways. These researchers are working with their clinical colleagues to identify the link between genetic variations in specific GPCRs and G proteins and disease risk factors, with the goal of improving diagnosis and optimizing treatment.

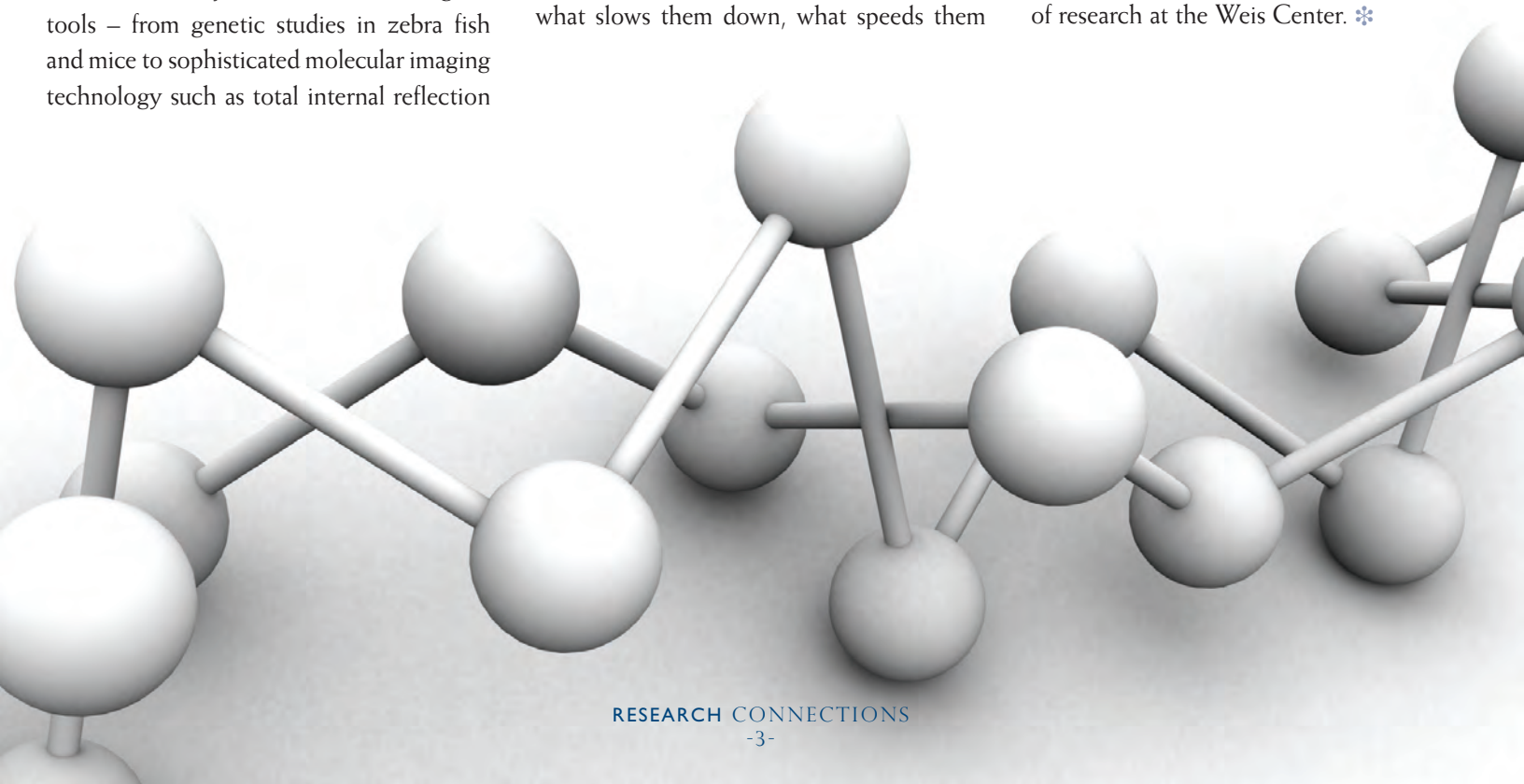
Scientists at the Weis Center are studying the strength and timing of GPCR function – what slows them down, what speeds them up, what turns them on and what turns them off entirely. A key GPCR binds to ghrelin, which causes increases in hunger and decreases in metabolism. If the Weis Center researchers can determine how to block the effects of ghrelin, they can possibly determine how to limit appetite in obese individuals through drug therapy.

"Its an asset to have so many investigators dedicated to this area of research in one facility," noted David Carey, PhD, director of research at the Weis Center. ❄

G Protein Coupled Receptor Signaling as Art

To capture G protein-coupled signaling pathways in the act of signaling, researchers at the Weis Center "tag" the GPCR, G protein and other potential interacting proteins with distinct colors to allow time-lapse imaging. Such approaches will help the investigators understand the dynamics of the assembly and disassembly of signaling complexes at the membrane.





Weis Center G Protein Signaling Laboratories

Catherine H. Berlot, MD, PhD
Staff Scientist

PhD and MD, Stanford University
Postdoctoral Research: University of California at San Francisco

Studying how G proteins and their receptors communicate in live cells under a variety of conditions.

Gerda E. Breitwieser, PhD
Senior Scientist

PhD, Washington University at St. Louis
Postdoctoral Research: University of Texas Medical Branch

Studying the life cycle of GPCRs, from synthesis to plasma membrane targeting and signaling to degradation.

Tooraj Mirshani, PhD
Staff Scientist

PhD, Virginia Commonwealth University
Postdoctoral Research: Mt. Sinai School of Medicine

Studying the interaction between G proteins and potassium channels.

Janet D. Robishaw, PhD
Associate Director and Senior Scientist

PhD, The Pennsylvania State University
Postdoctoral Research: University of Texas Health Sciences

Studying how G proteins switch cell activity on and off and control cellular development and/or differentiation.

Geisinger partners with local hospitals to share data

Shamokin and Bloomsburg Hospitals are onboard

Geisinger is working with Shamokin Area Community Hospital and Bloomsburg Hospital to share critically important health information electronically. The initiative, which started in 2005 and is

> *"The first step to successful health information exchange is the ability to accurately identify a patient across multiple facilities..."*

funded by a three-year $1.5 million grant from the Agency for Healthcare Research and Quality, is expected to grow to a much larger collaboration that will include additional regional hospitals. The three collaborating hospitals have added additional support to this effort, for a total project cost of $3 million.

The first step to successful health information exchange is the ability to accurately identify a patient across multiple facilities through an index that has about 2.6 million patients from Geisinger Health System and the Bloomsburg and Shamokin hospitals. The next phase of the project will focus on ensuring that the hospitals' computer systems are compatible. This includes sharing laboratory results and starting a regional health information exchange.

The initiative is starting in emergency departments and will provide emergency physicians at all three hospitals with valuable and timely information to make better-informed decisions. All shared data is HIPAA-compliant; patients wishing to participate sign a Universal Authorization to release information for the purpose of treatment.

This project sets the groundwork for an even larger collaboration known as a Regional Health Information Organization (RHIO). Joining Geisinger in the central Pennsylvania's RHIO are four additional hospitals and a physician group practice. The long-term plan is to accommodate more than 50 hospitals and an additional 9,000 physicians. An additional $500,000 in state funds has been committed to foster expansion to this larger regional group. ❄