

# GEISINGER Research Connections



August 2010

Linking the Research Community

## Research for Tomorrow

*An interview with CEO Glenn D. Steele Jr., MD, PhD*

Geisinger President and Chief Executive Officer Glenn D. Steele, Jr., M.D., Ph.D. talks with *Research Connections* about critical elements of the new research strategic plan and how research fits into Geisinger's mission and strategic vision for the future.



**Glenn D. Steele  
M.D., Ph.D.**

**Q. Why is research important to Geisinger?**

**A.** Research is important in any health care venue, particularly in an environment increasingly focused on identifying and implementing best practices. At Geisinger, we have a unique environment that provides ample opportunity to explore different ways of caring for our patients. Research helps optimize patient care by allowing us to

study the effects – both short- and long-term of reengineering that care. Then, we take what we've learned and feed it back to the clinicians, so we can enhance the way we treat our patients. It's a perfect linkage to the clinical improvement commitment we've made. Investing in the intellectual dimension that research represents will help us demonstrate benefits to everyone we serve in a more formal way.

Establishing a world-class research infrastructure is critical in two distinct areas – the clinical and the intellectual – and the two are undeniably linked. By committing resources today to raising the bar in research endeavors across all components of our health system, we will position Geisinger to reach new heights in clinical excellence, not to mention scientific and thought leadership. This, in turn,

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## Research Plan Leverages Existing Strengths and Sets Course for Personalized Healthcare

Based on the principle that research contributes fundamentally to clinical excellence, Geisinger has embraced an ambitious and strategic vision that will guide the institution's efforts for the next 10 years. The research plan is specifically designed to leverage Geisinger's existing institutional strengths. It will help fulfill a separate but related mission to implement personalized health care, a concept based on the principle that pathologic states, defined by specific genetic and environmental variables, are unique to each individual.

"The research plan is core to our mission. It enhances clinical care, supports innovation, and is essential to our training programs," explained Dennis Torretti, M.D., a member of the Research Advisory Task Force responsible for the plan. Dr. Torretti, chairman of medicine and a practicing rheumatologist, emphasized that the plan was a team effort by researchers and clinicians. Titled "The Strategic Vision for Research at Geisinger 2010-2020," the plan provides a pathway to incorporate many recent

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## Personalized Healthcare to Change Patient Care

As Geisinger continues its journey to shift the healthcare delivery model from reactive to predictive, preventative, and patient participatory, its major research initiative will focus on building a comprehensive personalized healthcare program.

Based on two intersecting phenomena: rapid progress in understanding the genetic and molecular processes of disease and better data collection allowing patient-specific information to be thoroughly dredged, personalized healthcare will provide meaningful insights and therapies for individual patients.

Geisinger will approach personalized healthcare from several fronts:

- Genomics
- The Science of Healthcare Delivery
- Comparative Effectiveness
- Predictive Modeling
- Behavior Change

According to David Ledbetter, Ph.D. chairman of Geisinger's External Scientific Advisory Board, and co-chair of the Research Task Force, "...initial areas of focus will include projects in genomics, bioinformatics and other scientific approaches utilizing imaging and nanotechnology."

"Financial support for Geisinger's personalized healthcare program will be based on a robust philanthropic initiative, coupled with grants and a number of entrepreneurial projects," added Bruce Hamory, M.D., co-chair, Geisinger's Research Task Force.



## Dr. Steele Interview

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will enable us to recruit and retain the brightest and best clinicians, students, and residents. It's the perfect circle of progress to ensure that those we are all ultimately here to serve – our patients – reap the benefits of outstanding health care now and well into the future.

**Q. What do you see as the most critical elements of the new research strategic plan? How do you see the plan supporting clinical goals?**

A. At Geisinger we are fortunate to have an outstanding foundation of clinical leaders in many areas of practice. Moving forward, one key strategic goal is to complement our existing strengths by developing a critical mass of clinical leaders who have already achieved success in pursuing clinical applied research, for example, in areas such as clinical reengineering, health services research, and clinical and translational research.

This is important strategically because we want to build on the buzz we've created through our innovations over the past 10 years. We will continue this momentum by establishing a research environment that makes Geisinger a must-visit venue for younger practitioners and demonstrating that this is the best place for them to launch careers as clinical and research leaders. We aren't quite there yet, but we're making progress – and now is the time to act.

We also need to have an endowment for research capacity expansion, which will help us sustain our research mission over the long haul no matter what happens in the outside world. Research never pays for itself, and clinical

margins are nowhere near enough in the current environment to subsidize either the educational aspect or the research aspect of our operations. Working to establish a dedicated, permanent endowment for this purpose should be at the top of our strategic planning wish list.

**Q. Why do you believe Geisinger is uniquely positioned to develop a personalized healthcare program?**

A. Geisinger has an amazingly stable population and serves a huge group of folks who are first- second- and even third generation Geisinger families who have always received their healthcare here. If we do something that fundamentally changes how we treat patients with diabetes, hypertension, or heart disease - or even if we simply perform an acute care service – we can follow effect not just for 30 days or 6 months but, for 30 years. What better way to deliver personalized health care than capitalizing on that type of continuity?

The other huge advantage we have is a very large patient population whose health care information is stored in MyCode™, a system-wide biobank with more than 23,000 DNA samples, proportionately more samples than from any other biobanking facility nationwide. Samples include disease specific and population cohorts, linkable to the electronic health record. This allows clinical phenotypes to be matched to genomic and other research data and to be mined for disease risk factors.

The unique longitudinal, long-term evaluation we can do at the individual patient level via their electronic health records gives us an advantage over other health systems which are very

fluid in terms of patients seen, and often still dependent on paper records.

**Q. Since Geisinger is not an academic center, many folks wonder what is the payback for research? Is it worth the investment?**

A. Geisinger is every bit as much of an academic center as the University of Chicago or the Harvard hospitals. But our mission is different. Our mission is innovation. We do more clinical innovation than the typical academic venue. The fact that we can link what Buzz Stewart does in the Center for Health Research to what Peter Berger does at the Center for Clinical Studies, and finally to what Dave Carey and our basic scientists do at the Sigfried and Janet Weis Center for Research, is a very specific kind of research and development focus - one that links every single thing we investigate and has a direct connection to how we reengineer care to improve patient outcomes. We're every bit as academic in the knowledge discovery sense, just different in the application of that knowledge.

Finally, we are very proud of the progressive development of Geisinger's research realm over the last 10 years. If you look at the grant portfolio now - whether peer-reviewed or industry-sponsored - we are close to accomplishing our original goal. Now it's time to expand our reach and our horizons in research – and that expansion will be a powerful factor in our ability to continue to recruit the best and brightest.

## Inter-institutional collaborations key to today's research

Achieving meaningful advances in many technology-intensive research disciplines, such as genetics, proteomics, and molecular biology, is often dependent on a robust commitment of resources. By leveraging its internal capabilities, Geisinger has established a number of mutually beneficial partnerships with major research and academic institutions that allow researchers to pursue questions specific to their core areas of interest without recreating the resources already available elsewhere.

While each partnership is unique, all depend on intellectual synergy between Geisinger researchers and partner researchers. Formal institutional partners include the Translational Genomics Research Institute (TGen) and the NYU Langone School of Medicine. In addition, Geisinger researchers routinely collaborate with researchers at University of Maryland, University of Pennsylvania, Yale, Mt. Sinai, Coriell Institute, The Johns Hopkins University and the HMO Research Network (HMORN), among others.

"Research collaborations are based on mutual trust and cannot be forced," explained Judith Argon, chief administrative officer, research.

For example, T Gen, a non-profit Phoenix-based biomedical research institute with deep genomic proteomic and bioinformatics expertise, emphasizes a translational research process intended to quickly turn laboratory discoveries into new drugs and other treatments. TGen and Geisinger's collaboration began with an obesity project and is now looking at genetic variations that predispose individuals to disease, congestive heart failure, abdominal aortic aneurysms and the potential side effects of prescription drugs.

"Merging Geisinger's wealth of clinical information with our genomic and proteomic experience should provide researchers a richer framework for exploring the genetic origins of disease,

and hopefully to improve treatment and outcomes," said Jeffrey Trent, TGen's President and Research Director.

Geisinger and NYU are developing a joint research and training program focused on the science of healthcare delivery, behavioral health, comparative effectiveness research, and genomics. Involving 18 co-investigators from both institutions and nine jointly funded pilot projects that are expected to result in submission of R01 applications to NIH and span molecular and genetic studies of obesity and addiction, comparative effectiveness of treatments, molecular and population studies of community-acquired anti-body resistant bacteria, and the joint development of new approaches to health services research.

One seed grant is for Geisinger and NYU researchers to expand comparative effectiveness research in orthopaedics at the two institutions. Geisinger and NYU are administering electronic questionnaires to their very divergent populations with osteoarthritis (OA) and results will allow physicians to track patient-reported outcomes, which are critical in developing evidence-based protocols in OA management. "Through the NYU collaboration, we will be able to enhance our understanding of how best to care for patients with osteoarthritis as well as to improve our assessment technology and our ability to engage patients in their care," noted Walter Stewart, Ph.D, director, Geisinger's Center for Health Research.

In addition, there can be advantages to collaboration independent of the demand on resources. "Our patient population is not especially diverse, which is a strength as well as a weakness. When we work with a center like Temple University, which largely serves an inner-city population, there are advantages for each institution," Ms. Argon observed.

## Progressive Chronic Kidney Disease is Focus for Rob Perkins, MD

Rob Perkins, M.D., was winding down a decade-long stint in the military that included time in Baghdad as an assistant chief of an intensive care unit (his wife also served in Iraq).



**Rob Perkins, M.D.**

The question before him now was, what next?

"What really attracted me to Geisinger was the chance to have dedicated research time. I would be able to focus on clinically oriented research that would be quickly translatable into real-world patient care. Geisinger really promotes that idea, which is very rare."

Dr. Perkins' primary research interest is progressive chronic kidney disease, one of the chronic recurrent diseases that are of special interest to Geisinger's research efforts. Dr. Perkins currently is reviewing the entire cohort of Geisinger patients and isolating those with progressive chronic kidney disease, trying to identify risk factors and, ultimately, establish a prospective cohort to be followed by the nephrology department. "Geisinger is the only health system I know where a clinical investigator can do research like this."

With two-thirds of his time dedicated to research and the rest to patient care, Dr. Perkins personifies the clinician investigator's dual role. "It is very important that I spend time as a clinician, particularly because just about every research idea I have has come out of my experience as a clinician."

## Translational Research to Aid Clinical Practice

Geisinger's research strategy is to advance personalized healthcare through a system-wide focus on translational research to accelerate findings for the betterment of patient health. Key to accomplishing this goal is developing cohesive groups of clinical investigators and researchers, who share a common goal and interest.

### *Bedside to Bench to Bedside*

Geisinger has a long tradition of enabling interaction and collaboration between scientists and clinician researchers to improve patient care.

Geisinger's integration of research with clinical practice spans the entire care continuum from ethics and informatics to biobanking and the electronic health record (EHR). Critical to achieving the ultimate goal of creating value-based solutions to clinical problems, Geisinger actively seeks collaborations and partnerships with academic, research, and industrial organizations outside of the

health system to provide knowledge and resources. These shared resources help avoid expensive duplication of equipment and services.

"Our ability to begin at the basic science level, move through population-based research and testing and translate discoveries to clinical trials in real patients puts Geisinger among a handful of distinguished research centers nationwide," noted Peter Berger, M.D., director, Geisinger Center for Clinical Studies.

"Geisinger clinicians focus on their patients' problems and then engage basic scientists who seek to address the problem, the solution for which is then brought back to the clinic for trial," explained Christopher Still, D.O., director of the Obesity Institute.

"Take fatty liver disease, for example," noted Dr. Still. "We went to basic scientists at the Geisinger Clinic Genomics Core and complained that there was no good way to test for it except

by liver biopsy," Dr. Still continued. "So the clinicians worked with the scientists to develop a blood test that detects individuals who are at risk for developing fibrosis, which is directly related to their fatty liver disease.

"At Geisinger, clinician investigators help close the circle," he added.

Geisinger's exemplary electronic health record (EHR) system, which has been held up nationally as a model to emulate, plays a vital role in ensuring the synergy between clinical practice and research. "We have a huge database," Dr. Still noted, "with over 700 patient variables that are captured and followed longitudinally. We work with the biostatistics team daily so that we can scrutinize our patient population. The EHR truly is a great clinical tool."

Today, Geisinger has established a reputation for its forward-thinking integration of research and clinical care to improve the health of patients.

## Research Plan

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innovations, such as detailed electronic health records (EHRs) and genomic research, into "value-based solutions to clinical problems."

"Currently, many of our therapies, although based on scientific evidence, are not tailored to the unique traits of individuals. We know that not everyone responds to even our most effective therapies. The plan develops a foundation on which to build a multifaceted approach to personalized health research," Dr. Torretti explained.

### *Emphasis on five clinical areas*

The task force's plan calls for a prioritization of research resources to emphasize five clinical areas in which Geisinger has an opportunity to make meaningful advances:

- oncology;
- cardiology and vascular diseases;

- neurologic and neurodegenerative diseases;
- obesity and metabolic syndromes;
- chronic recurrent illnesses, such as headache, back pain, and asthma.

Geisinger has strong research programs in these areas, including the accumulation of important clinical databases based on EHRs that are greatly facilitating the ability of researchers to address key clinical questions. While studies in other clinical areas will continue, these areas represent priorities for recruitment and programmatic development. Clinical champions in each area will encourage a culture of research within the broader clinical context and promote the development of tools and resources to support the research as well as partnerships with national research centers with capabilities complementing those at Geisinger.

As the research programs of the first five targeted areas mature, additional priority area will be added.

### *Plan provides detailed pathways to goals*

In addition, the plan articulates underlying concepts and principles that will drive Geisinger's research approach and philosophy as well as very detailed and specific pathways to reach the goals. For example, the plan calls for a 50 percent increase over the next 10 years in the number of full-time investigators, along with an increase in the number of researchers who divide their time between research and clinical activities. What's more, the document defines and describes the steps needed to sustain the sense of mission among researchers, who require an atmosphere of collaboration and support to excel.

## Staff Publications

These publications (from January thru May 2010) feature Geisinger employees as authors. Publications jointly authored by a Geisinger employee and employee(s) of other institutions feature an asterisk after the Geisinger employee's name. When a Geisinger employee is the sole author, no marking exists.

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65. Tromp G, Kuivaniemi H, Hinterseher I, Carey DJ. Novel genetic mechanisms for aortic aneurysms. *Curr Atheroscler Rep.* (2010) May 6. [Epub ahead of print] PMID:20446064

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69. Wang J, Peng Q, Lin Q, Childress C, Carey D, Yang W, Calcium activates Nedd4 E3 ligases by releasing the C2

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## Recent External Awards

This list includes new awards and competitive renewals from external agencies and Geisinger's Clinical Research Fund from February 2010 to June 2010. To protect sponsors' confidential information, dollar amounts for clinical trials and industry-sponsored agreements and some clinical listings are omitted. If an award is inadvertently overlooked, please forward the information to Shawna Seger (smseger@geisinger.edu) for inclusion in the next issue.

<b>George Argyropoulos, PhD</b> Genetic Variants in the CACNA1G Gene Confer Susceptibility for Developing Obstructive Sleep Apnea Administrative Committee for Research \$100,000	<b>Helen Kuivaniemi, MD/ Gerard Tromp, PhD</b> Preeclampsia as a Disease of Genetic Interaction Between Mother and Fetus Administrative Committee for Research \$99,992	<b>Diane Smelser, PhD</b> Gene-Environment Interaction in Childhood Obesity Administrative Committee for Research \$79,823
<b>Peter Berger, MD</b> A Gynecologic Surgery Bio-Banking Effort Administrative Committee for Research \$21,384	<b>Al Neuner</b> Geisinger Cogeneration Plant Commonwealth of Pennsylvania \$2,250,000	<b>Robert Smith, MD</b> Drug Induced Liver Injury Thomas Jefferson University \$49,440
<b>Catherine Berlot, PhD</b> Molecular and Cellular Analysis of G Protein Function National Institute of Health \$1,368,672	<b>Evan Norfolk, MD</b> Prevalence of Proteinuria and Accuracy of a Single Untimed Morning Urine Sample for Estimation of Proteinuria in Obese: Patients Referred to a Management Clinic-A Cross Sectional Study Administrative Committee for Research \$14,635	<b>Marius Sudol, MD</b> DUSPS and a Panel of 11 Genes as Molecular Markers of Tumors that Harbor Activated SRC Oncogene PA Breast Cancer Coalition's Breast and Cervical Research Initiative \$50,000
<b>David Carey, PhD</b> Genetic Factors Associated with Aneurysms Pennsylvania Dept of Health \$104,117	<b>Robert Perkins, MD</b> Characteristics, Prevalence, Risk Factors and Outcomes of Highly Progressive CKD: A Retrospective Cohort Study Administrative Committee for Research \$14,042	<b>Nikolas Tapinos, PhD</b> Role of an Alternatively Spliced Nuclear Variant of ERBB3 in the Nervous System National Institutes for Health \$1,765,315
<b>Glenn Gerhard, MD</b> Mid-Atlantic Nutrition Obesity Research Center NORC-Subcontract \$152,348	<b>Robert Perkins, MD</b> Characteristics, Prevalence, Risk Factors and Outcomes of Highly Progressive CKD: A Retrospective Cohort Study Administrative Committee for Research \$14,042	<b>James Walker, MD</b> Keystone Beacon Community: Proposal for a Rural Community-Wide Medical Home Department of Health and Human Services \$16,069,110 Improving Rural Healthcare Transitions through Health Information Exchange National Institutes of Health \$ 2,296,926
<b>Edward Gorak, M.D.</b> W2010-0103 "A Substudy to Assess the Effect of Treatment With Bendamustine in Combination With Rituximab on QT Interval in Patients With Advanced Indolent Non Hodgkin's Lymphoma (NHL) or Mantle Cell Lymphoma (MCL) Within Study C18083/3064/NL/MN (3070)" Cephalon, Inc. \$35,700	<b>Thanjuvar Ravikumar, MD</b> Geisinger Clinical Cancer Center Program National Institutes of Health \$1,731,280	
	<b>Thomas Scott, DO</b> 2009-0184 "DESERT: Drug Eluting Stent Registry of Thrombosis" MedStar Research Institute, Inc. \$15,625	

## Staff Publications

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- domain-mediated auto-mediated auto-inhibition. *J Biol Chem.* 2010 Feb 19 [Epub ahead of print]
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72. Zbierajewski-Eischeid SJ, Loeb SJ. Recognizing myocardial infarction in women. *Nursing.* 2010;40(Suppl):1-7.
73. Zhang S, Chen H, Gerhard GS. Heme synthesis increases artemisinin-induced radical formation and cytotoxicity that can be suppressed by superoxide scavengers. *Chem Biol Interact.* Epub ahead of print, March 31, 2010