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Genomics Jump-Start
Stepping in to Help
News Briefs

pulse

News from the Duke Heart Center | Duke University Medical Center

Genomics Jump-Start

Largest Ever Database Seeks New Clues in Heart Disease

by Jeni Lyttle

Cardiovascular disease stems from countless combinations of many ingredients—some genetic, some related to lifestyle and the environment—and its hidden recipe can be as diverse as the people who suffer from it.

In an effort to better understand the inner workings of heart disease—and ultimately, to develop patient-specific prevention and treatment strategies—the Duke Cardiomics Network (DCN) will collect clinical and genetic data from a half-million cardiac catheterization patients over the next five years.

Led by Duke's Kristin Newby, MD, and Kevin Schulman, MD, MBA, the DCN is a wholly owned, non-profit subsidiary of Duke University. The largest data collection project of its kind, it was sparked by Duke faculty, but brought to fruition by medical students. It is also unusual in that it enlists the help of physicians at cardiac catheterization laboratories across the country and invites them to be active participants—by serving on a governing scientific board and authoring research studies using the database.

A Concept Ahead of Its Time

The group of six third-year medical students—four MD/MBA candidates, one MD/MPH candidate, and one MD/PhD candidate—researched hundreds of issues before settling on a collaborative network rather than a commercial Duke-based venture. They developed institutional review board materials and a web site, www.dukecardiomics.org and information for participating investigators. They attended meetings of the American Heart Association and the American College of Cardiology to test the concept among practicing physicians. Finally, they had to prove the concept to the key Duke players who would fund it—Rob Califf, MD, director of the Duke Clinical Research

Institute (DCRI); Huntington Willard, PhD, director of the Duke Institute for Genome Sciences and Policy (IGSP); Pascal Goldschmidt, MD, chair of the Department of Medicine; and R. Sanders “Sandy” Williams, MD, dean of Duke's School of Medicine.

According to Willard, the DCN may one day have commercial potential, but it is at least five years ahead of its time. However, it represents a tremendous investment in research on the genomics of cardiovascular disease.

According to Califf, collaboration is the most expedient means of translating research findings to improved patient care.

“No one institution is capable of assimilating-within this short time



continued inside



Third-year Duke medical students John Kim, Yogin Patel, and Krishna Udayakumer review statistics.

frame—the massive number of samples needed to account for the many variables that come into play

in cardiovascular disease,” says Califf. “By partnering with physician alumni and other cardiologists across the country, we hope to quickly build a critical mass of data that people can begin mining to pinpoint the important genes, proteins, and metabolites in heart disease and its associated clinical events.”

Putting Genomic Medicine into Practice


The goal is to eventually be able to identify—through a simple blood draw—those individuals at risk for

heart disease and the most appropriate therapeutic approach to delay, prevent, and/or treat one of the world’s leading causes of death and disability.

The DCN is one of many ways Duke is embracing the application of genome science to the practice of medicine. For example, Duke researchers have developed a method for classifying the aggressiveness of breast tumors based on their genetic composition. Others have identified genetic components in autism, Alzheimer’s and Parkinson’s diseases, as well as genetic factors that can determine which patients will respond to certain drugs.

Because genomic medicine allows physicians to look at the physiological building blocks and patterns behind disease, it enables them to proactively pursue the most effective, patient-specific interventions earlier in the disease process than through other methods. According to Newby, cardiac catheterization offers an excellent starting point.

“We will collect clinical and genetic information on patients at cardiac catheterization, so we’ll have a good description of these patients, their disease and its treatment, and their lifestyle and clinical history,” she says. “Not only that, we will know what their arteries look like and be able to track how they fare over time. We’ll also be able to determine the protein and metabolite composition of their blood along with their genetic profile—and all these factors are invaluable in making important links.”

To learn more about the Duke Cardiomics Network, call (919) 668-8805 or visit www.dukecardiomics.org. 

Dear Friends,

With this issue of *Pulse*, we are pleased to say thank you to the more than 340 individuals who have supported the Duke Heart Center this past year. Your support is vital to our mission of advancing the field of cardiology internationally, providing the best care for our patients, and educating the cardiology leaders of tomorrow.

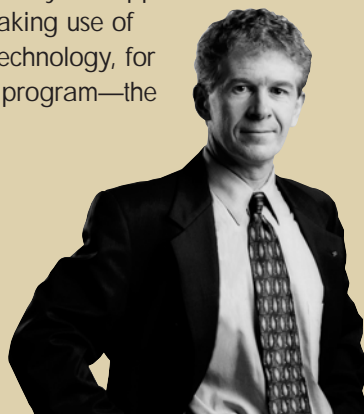
As we celebrate American Heart Month, we are delighted to tell you about Duke’s work in the emerging science of genomic medicine. Genomics has tremendous potential to transform the way we treat—and, increasingly, prevent—heart disease. The Duke Cardiomics Network is giving participating investigators across the country a big head start in gathering the data they need to learn more about genetic risk factors, discover new drug targets, and design treatments tailored to individual patients.

And it is especially heartening to share news of the Patient Care Fund established by our colleagues in the Cardiac Rehabilitation Program. It is good to know that many of our patients are reaching out to help provide these life-sustaining services to others whose insurance fails to cover it. We are a family at the Duke Heart Center, and we do our best to ensure all our patients receive the care that will put them on the road to better health.

Again, a heart-felt thank you to all of you. Without your support, many of our most valuable efforts—our groundbreaking use of robotics, minimally invasive surgery, MRI and CT technology, for example, or our cardiovascular residency training program—the country’s largest—would not be realities.

Best wishes for a healthy and happy 2004.

Sincerely,
Tom Ryan, MD
Director, Duke Heart Center



Stepping in to Help

Patients and Staff Establish Fund to Cover What Most Insurance Doesn't

by Jeni Lyttle



Exercise physiologist Karen Craig, MA, leads patients Alex Kovacs and Anna Currie in their cardiac rehab workouts.

Imagine surviving a potentially life-threatening cardiac event—a heart attack, perhaps, or maybe coronary bypass surgery—only to discover that you can't afford the rehabilitation necessary to get your heart on the road to recovery.

This is the situation many heart patients—even those with health insurance—face today. A newly established Cardiac Rehabilitation Program fund will help.

A Long-Term Approach to Health

The 26-year-old Cardiac Rehabilitation Program—located within the Duke Center for Living's Health and Fitness Center—is a component of the internationally acclaimed Duke Heart Center.

With a multidisciplinary staff that serves nearly 300 patients annually, the Cardiac Rehabilitation Program takes an individualized, holistic approach to helping patients manage heart disease over the long term by emphasizing education, nutrition, exercise, and psychosocial

issues like stress management. Evening sessions, as well as special programs for diabetics—who are at nearly twice the risk for developing heart disease as non-diabetics—are also offered.

“Our goal is to help patients get on with their lives after they leave the hospital,” says program director and exercise physiologist Karen Craig, MA. “We provide comprehensive tools for them to get a jump start on living more heart-healthy lives.”

A Standard of Care Often Out of Reach

There is no question that patients who complete cardiac rehab fare better than those who don't. It's been well documented through clinical outcomes research, according to Bill Kraus, MD, medical director of Duke's Cardiac Rehab Program.

“Cardiac rehabilitation really should be considered the standard of care after a patient is diagnosed with heart disease, and it's the next logical step after interventions like bypass surgery or angioplasty, for example, or for people with heart disease who aren't candidates for certain interventions,” says Kraus.

However, the types and amount of rehabilitative care heart patients receive is often limited by their insurance coverage.

Although coverage varies greatly, most plans don't cover—or cover at a prohibitive cost to the patient—the cost of cardiac rehabilitation for people suffering from congestive heart failure or those who've had an angioplasty or a heart transplant. Medicare covers cardiac rehab only when patients have one of three diagnoses—heart attack, bypass surgery, or stable angina—and Medicaid doesn't cover it at all.

Even for patients whose insurance does cover some cardiac rehab costs, the \$15-30 per session co-payments

can add up; a “typical” rehabilitating heart patient, Craig says, is advised to participate in cardiovascular strength and flexibility exercises three times a week for two or three months.

Helping Patients Help Themselves

Over the past several years, staff at the Duke Cardiac Rehab Program began to realize that more and more of their patients were foregoing life-prolonging care because they couldn't afford it.

“We thought, “There must be something we can do to help these people,”” says Craig, “so we decided to start this fund”—which kicked off with a 2002 fund-raiser dinner attended largely by grateful patients and current and former staff members. Since then, the fund has been fed solely by contributions from patients who have the means to pay for their rehab care out of pocket.

When the fund has grown enough to start generating interest income, patients will be able to apply for assistance. Program staff will select recipients based on demonstrated need and their potential to benefit from cardiac rehab care.

“Patients who come to our program tend to be the ones who are most interested in positively impacting their own outcomes and investing in their own care,” Kraus says. “It's important to help those people who want to come, but don't have the means.”

To learn more about Duke's Cardiac Rehabilitation Program or to find out how you can help support the patient assistance fund, contact Karen Craig at craig004@mc.duke.edu or (919) 660-6724, or visit www.dukefitness.org—and click on *Programs*, then *Rehabilitation*, then *Cardiac Rehab*. 

Pulse NEWS Briefs

Nitric Oxide Marker Indicates Risk

Duke researchers have shown a relationship between changes in nitrate, a biochemical marker of nitric oxide production, and physiological changes in arteries' reaction to stress.

The discovery could lead to a non-invasive method of determining who is at risk for developing cardiovascular disease—and because up to half of those who develop heart disease do not have typical risk factors, such a simple diagnostic is significant. In addition, the study has shown that exercise improves the marker in patients at risk for developing cardiovascular disease.

The systemic production of nitric oxide, a chemical that plays a key role in controlling artery constriction

and relaxation, was linked with changes in the endothelial lining of arteries after being stressed.

Nitric oxide also protects against cardiovascular disease by inhibiting blood platelet clumping, preventing smooth muscle proliferation within arteries, and inhibiting the immune response.

Conversely, risk factors like diabetes, hypertension, mental stress, and smoking can reduce nitric oxide's protective properties. Patients with these factors are thought to produce

more oxygen free radicals—highly reactive chemicals that are the potentially destructive by-products of the disease process—which impair the body's ability to respond appropriately to nitric oxide.

Can This Heart Muscle Be Saved?

Duke researchers have used cardiac magnetic resonance imaging (MRI) to demonstrate that heart muscle thinned by a heart attack can be “saved” by revascularizing (restoring blood flow to) the affected region.

When a portion of heart muscle is deprived of blood flow, as it is during a heart attack, those muscle cells are deprived of needed oxygen and nutrients. As the muscle cells in the walls of the heart die, they are replaced by collagen, which makes the walls thinner and less effective in pumping.

In the past, physicians often have deemed thinned heart tissue as unsalvageable—and have therefore not pursued revascularization therapy with coronary bypass surgery or angioplasty. But Duke researchers say that because cardiac MRI enables them to visualize the beating heart with such precision, they can better judge when damaged heart muscle may still be viable with appropriate treatment.

Although the study was based on a small sample of heart patients seen at Duke and Chicago's Northwestern

University, “most cardiologists are beginning to recognize that MRI is becoming the gold standard for viability testing, because with its extremely high spatial resolution, it can detect details not seen before,” says Duke cardiologist Dipan Shah, MD. “The ability to differentiate between living and dead cells makes MRI a more direct measure of tissue viability than any other method.”

Raymond Kim, MD, co-director of the Duke Cardiovascular Magnetic Resonance Center, reports that researchers not only found thinned areas that could be saved by revascularization, they “learned some new concepts that will allow us to predict which of the thinned areas could be saved.”

“It appears to depend on the ratio of viable cells to scar tissue in the thinned area and not just the absolute amount of viable cells,” Kim says. “This is important since most other viability tests measure only the amount of viable tissue and not the amount of scar. Thus, thinned areas will generally be interpreted as dead because the amount of viable tissue is small by definition.”

Kim says larger studies are needed to see how often patients with thinned muscle actually have salvageable tissue—and what impact revascularization can have on that tissue. “But we have already proven that we can detect alive-but-injured tissue and bring it back with revascularization,” he adds.

Duke team members also included Robert Judd, PhD; Michael Elliott, MD; Igor Klem, MD; Louise Thomson, MD; and Michele Parker.



Jason Allen, PhD, conducts a study of the brachial artery in the arm.



Pulse NEWS Briefs

Repair and Rejuvenation—Some Have More Capacity Than Others

The mechanisms by which some people's bodies repair arterial damage, or atherosclerosis, better than others may help explain the relationship between aging and the disease process in general.



Pascal Goldschmidt, MD

Duke cardiologist and Department of Medicine chair Pascal Goldschmidt, MD, cites as examples those individuals who smoke all their lives, but do not get cardiovascular disease, or those who have eaten unhealthy diets, but still reach old age with clear arteries.

Goldschmidt and cardiologist Eric Peterson, MD, of the Duke Clinical Research Institute, believe so much time has been spent investigating disease risk factors that the other half of the equation—the body's innate ability to protect and repair itself—has been neglected.

"It is this relationship between the body's ability to keep up with the cumulative damage it suffers over time that could be the key to who gets sick and who stays healthy into old age," Goldschmidt explains. "We believe that the key resides in

the bone marrow, which produces stem cells that can repair damage to the body."

The Duke researchers believe that living organisms, including humans, are born with a finite capacity for stem-cell-mediated repair of damaged tissues—capacity that is perhaps determined by the

genetic makeup of the individual.

"Our newly developing insight into the role of stem cells in the disease process should write new chapters in our understanding of the disease process," Peterson says. "We don't truly understand repair and rejuvenation, yet they

are important factors in determining who is at risk for disease and our ability to treat it."

Duke Health System Walkers Lead the Way

More than 350 walkers representing Duke University Health System participated in the Triangle Metro American Heart Walk in November—the most of any participating health care organization.

The Duke walkers contributed more than \$26,500 to the event's overall goal of \$300,000. The Duke




Center for Living team took the honor as the leading fund-raising team from Duke, raising more than \$3,000. Funds raised go to support advocacy, education, stroke-related initiatives, research, and public awareness campaigns.

\$3.6 Million Genomics Project Aims to Improve Elder Care in Guilford County

A landmark study is bringing the future of medicine to the people of rural Guilford County, N.C.

Funded by a \$3.6 million federal appropriation, the Guilford Genomic Medicine Project—a collaboration among Duke's Center for Human Genetics, the Greensboro, N.C.-based Moses Cone Health System, and the University of North Carolina-Greensboro's Institute for Health, Science, and Society—will target cardiovascular disease and neurodegenerative illnesses like Alzheimer's disease.

One of the primary goals of the project—announced in July 2003—is to educate the community's health care providers and residents about genomics and the impact the field is already making on the practice of medicine. Another goal is to collect and analyze clinical and genetic data from consenting patients in the county.

The data will be used to identify the health care needs of community members—especially those of older adults, including the area's large number of veterans—who are particularly at risk for developing cardiovascular and neurodegenerative illnesses. Population-specific clinical applications will then be developed and implemented in pilot programs throughout the community over the next several years. 

The Duke Heart Center would like to thank all of our friends for their generous support during 2003.

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Caring for Women's Hearts,

Sister to Sister




Allison Drucker (center), president of Duke's Alpha Phi chapter, at October's installation ceremony.

After receiving an honorarium during the official installation ceremony at Durham's Millennium Hotel, Beta Nu identified the Duke Heart Center as its first beneficiary.

"Duke is a leader in heart disease research that is specific to women—and for that reason we felt this gift would best represent the ideals of the Alpha Phi Fraternity and the Alpha Phi Foundation," explains Drucker.

Established in 1956, Alpha Phi Foundation is one of the oldest Greek foundations in the U.S. and Canada. The foundation's cardiac care program, Heart to Heart, grants community organizations funds to educate the public about causes, prevention, and treatment of heart disease. Other Alpha Phi charitable programs provide leadership and educational opportunities for women, encourage and recognize superior scholarship, support women's cardiac health, educate women about the value of philanthropy, and assist members in need.

Alpha Phi Fraternity has 90,000 members around the world and 160 student chapters. For additional information about the organization, please visit the fraternity's website at www.alphaphi.org. 

For the past 130 years, Alpha Phi, an international women's fraternity, has cared for women's hearts by supporting cardiac care programs and other charitable projects.

So when a new student Alpha Phi chapter was installed at Duke in October, a \$1,000 donation to the Duke Heart Center seemed the perfect match.

Alison Drucker, vice president of marketing for Duke's new Beta Nu chapter, got involved with Alpha Phi during her sophomore year at Duke. The Lighthouse Point, Fla., native, now a senior, is pleased that the Beta Nu chapter is flourishing with nearly 40 members.

"It was fulfilling to be able to build a new chapter from the ground up, and it was especially exciting to be initiated this year after two years of hard work," says Drucker.

Pulse is published twice a year by Duke Heart Center Development. Your comments, ideas, and questions are welcome. Please contact us at: Duke Heart Center Development 512 S. Mangum Street Suite 400 Durham, NC 27701-3973 (919) 667-2500 e-mail sallie.ellinwood@duke.edu / Director of Development Sallie Ellinwood / Editor Marty Fisher / Contributing Writers Jeni Lyttle, Emma Martin / Photography: Duke University Photography / Produced by the Office of Creative Services and Publications. Copyright © Duke University Health System, 2004 MCO03565



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