It is a pleasure and a privilege to welcome you to the Medical College of Georgia’s annual research magazine, *MCG Tomorrow*. The stories highlighted on these pages represent only a small part of the biomedical research that MCG scientists and their research teams do every day as part of their search for medical breakthroughs that are predictive, preventative and personalized.

The theme of this year’s magazine, Bench to Bedside: Better Health Through Discovery, acknowledges the progress being made by the university’s Discovery Institutes, the translational science initiative now entering its third year. Aligned along MCG’s research strengths, the Discovery Institutes place researchers, physicians and other health professionals on the same team to more quickly turn laboratory discoveries into clinical applications.

It is thrilling to know that these multidisciplinary teams are making substantial improvements to the longevity and quality of life for Georgians, not just today, but for many years to come.

Thank you for taking the time to read about and support MCG’s research. I think you will be impressed with our progress and more optimistic about the future of health care in Georgia.

Dr. Robert K. Yu, a professor in MCG’s Institute of Molecular Medicine and Genetics, searches for novel strategies in disease diagnosis and therapies by researching the underlying mechanisms of a variety of neurodegenerative disorders, including autoimmune demyelinating neuropathies, multiple sclerosis, mucopolysaccharidoses and sensorineural hearing loss.
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From Bench to Bedside: BETTER HEALTH THROUGH DISCOVERY

MCG concentrates its research efforts into seven areas of focus:
- brain & behavior
- cancer
- cardiovascular disease
- child health
- diabetes/obesity
- infection/inflammation
- vision
FACTUAL FINDINGS:
From 2001 to 2009, research dollars at MCG more than doubled: from $33 million to $84 million; 28 stimulus grants were secured totaling $8.1 million through the American Recovery and Reinvestment Act of 2009. Most impressive is the fact that our basic science faculty is second in the nation among peer institutions for per-capita research funding.

**Sponsored Research Funding**

- **FY 2006**: $18.6M (NIH), $45.2M (Other)
- **FY 2007**: $21.8M (NIH), $43.5M (Other)
- **FY 2008**: $29.5M (NIH), $44.3M (Other)
- **FY 2009**: $26.3M (NIH), $57.5M (Other)
- **FY 2010**: $23.9M (NIH), $63.0M (Other)

**Total Awards ($)**

- **Cancer**: FY 2009 $15.0M, FY 2010 $15.8M
- **Cardiovascular Diseases**: FY 2009 $14.1M, FY 2010 $16.8M
- **Diabetes**: FY 2009 $15.0M, FY 2010 $16.8M
- **Infection/Inflammation**: FY 2009 $17.3M, FY 2010 $25.6M
- **Brain & Behavior**: FY 2009 $15.0M, FY 2010 $29.1M

**Active Awards (#)**

- **Cancer**: FY 2009 66, FY 2010 60
- **Cardiovascular Diseases**: FY 2009 99, FY 2010 95
- **Diabetes**: FY 2009 162, FY 2010 178
- **Infection/Inflammation**: FY 2009 15, FY 2010 128
- **Brain & Behavior**: FY 2009 16, FY 2010 30

**Number of Awards Received**

- FY 2006: 600
- FY 2007: 600
- FY 2008: 643
- FY 2009: 643
- FY 2010: 666

**Number of Submissions**

- FY 2006: 903
- FY 2007: 928
- FY 2008: 928
- FY 2009: 1,038
- FY 2010: 933

**Sponsored Awards by Agency**

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Meet Our People

**Ricardo Azziz, M.D.**
MCG President

**Frank A. Treiber, Ph.D.**
Vice President for Research Development; Regents Professor of Pediatrics

**Betty J. Aldridge**
Senior Associate Vice President for Research Administration

**Anthony L. Mulloy, Ph.D., D.O.**
Senior Associate Vice President for Clinical Research Affairs

**John D. Catravas, Ph.D.**
Acting Director, Cancer Research Center

**David Hess, M.D., Co-Director**
Joseph Z. Tsien, Ph.D., Co-Director

**Gregory Harshfield, Ph.D., Co-Director**
Martha Tingen, M.S.N., Ph.D., Co-Director
Bernard L. Maria, M.D., Co-Director;
Chairman of the Department of Pediatrics

**Gaston Kapuku, M.D., Co-Director**
Stephen M. Black, Ph.D., Co-Director

**Yanbin Dong, M.D., Co-Director**
David W. Stepp, Ph.D., Co-Director

**Andrew W. Mellor, Ph.D., Co-Director**
David H. Munn, M.D., Co-Director

**Julian J. Nussbaum, M.D., Co-Director**
Sylvia B. Smith, Ph.D., Co-Director

**FACTUAL FINDINGS:**
The Discovery Institutes were established in 2008 to expedite the translational science process of moving the discovery out of the laboratory and into applications to benefit patients.

Each institute is co-directed by a basic scientist and a clinician. Through a partnership with MCG’s affiliated 478-bed teaching hospital, these researchers have access to one of the Southeast’s largest patient populations for clinical trials.
Imagine that novice turning into pro wrestling bad boy Tommy “Outlaw” James, who dons a black trenchcoat and cowboy hat before stepping into the ring to pound – and be pounded by – men outweighing him by as much as 100 pounds.

Imagine him running 10 miles three days a week, then hitting the gym the other four to stay ahead – and alive – in the contact sport of professional wrestling.

Now imagine the day in January 2009 when the Outlaw found himself unable to get up from his own living room floor.

Remote stroke diagnosis, experimental drug save former pro wrestler from the big takedown

Imagine professional wrestling great Gene Anderson tossing a 6-foot-2-inch, nearly 300-pound man like a sack of potatoes over the top of a wrestling ring for innocently inquiring about how he learned to take an eight-foot fall onto the concrete floor.
Tommy, 47, readily admits he hasn't seen the inside of a gym since he retired from wrestling as a “senior” at the ripe old age of 40. He had developed diabetes a couple of years later and had some heart problems too but, despite it all, still smoked.

“I don’t take care of myself,” he flatly acknowledges. Fishing and golf became favorite sports and the long days working in the family’s drywall business kept him moving until that January day.

**Stopped in his tracks**

Tommy had been putting up drywall in a Holiday Inn not far from the home he shares with wife Sally on a quiet cove on Lake Hartwell in Lavonia, Ga.

He stopped to pick up a pizza on the way home. The couple were eating and watching television when he got up to refill his iced tea. Sally heard his favorite plastic cup hit the ground and saw ice skate across the kitchen floor. She laughed, stayed put and hollered to him about cleaning up his mess.

No response.

He was still uncharacteristically quiet and leaning on the counter when she reached the kitchen.

“I put my arm around her because that always calms her down,” Tommy said. They were walking back into the living room when Tommy, still quiet, took a nose dive into the entertainment center and then the floor.

“My right side just collapsed on me,” he said.

He struggled to get up, but Sally pulled a wrestling move of her own to keep him down. “I told him, ‘If you don’t say something, I am calling 911.’”

Tommy thought he had been talking to her. But now he was quiet even inside his own head: He wanted her to call for an ambulance. Paramedics quickly suspected stroke and took the couple to Cobb Memorial Hospital, a 71-bed facility in nearby Royston, Ga.

Like most small hospitals, Cobb Memorial doesn’t have a stroke specialist in house but, via web-based examination, its physicians have 24-7 access to stroke specialists such as Dr. David Hess, chairman of the Department of Neurology at the Medical College of Georgia.

When Hess saw Tommy’s computerized tomography scan, he knew that bleeding in the brain – responsible for about 12 percent of strokes – wasn’t the problem. That made Tommy eligible for the clot-busting drug tPA, which stands for tissue plasminogen activator. The clinical exam appeared to confirm Hess’ suspicions: weakness on Tommy’s right side and the inability to speak suggested a clot in his left middle cerebral artery, the most common stroke site.

“He could understand a little bit but could not say a word,” Hess recalled.

Tommy was getting high marks on the National Institutes of Health scoring system, suggesting a big stroke and a bad prognosis. Hess worked with the physician in Royston to ensure Tommy got tPA, the only FDA-approved stroke medicine, within the three-hour treatment window.

Despite 14 years of proof that tPA can make a real difference in stroke recovery, most American stroke patients are not diagnosed quickly enough to receive it. Physicians must make treatment decisions based on the patient’s symptoms and a CT scan.

“It requires a lot of clinical judgment,” Hess said.

The need for rapid access to stroke care is what led MCG researchers to hatch the idea for the web-based diagnosis, and in 2000, REACH was born.

REACH — Remote Evaluation for Acute Ischemic Stroke — has been in use since 2003. The system has a portable station at the remote site that is accessible by a stroke specialist from any computer with Internet access. Hospital staff reach the on-call member of MCG’s stroke team by calling...
PUTTING DISCOVERY INTO PRACTICE:

Dr. Jerry Buccafusco, a Regents Professor of Pharmacology and Toxicology until his death in 2010, developed novel Alzheimer's therapies and biomarkers for early detection of the disease.

Putting discovery into practice:

a 24-hour Emergency Communications Center. The system is now in use at 16 hospitals in Georgia and 100 others across the nation. Hess expects to have an international presence soon.

A study published in Stroke in October 2003 showed virtually identical outcomes of patients seen via REACH and those seen by physicians in person. A 2005 study in the same publication showed that with REACH, rural patients like Tommy can be treated as rapidly as patients at bigger city hospitals with in-house stroke teams.

Reducing the risk

The risk of using tPA is brain bleed – about 6 percent of patients experience hemorrhages that can worsen stroke's impact.

Still, Tommy and Sally opted to receive tPA in Royston. Tommy's mother, who years earlier received no acute stroke treatment, spent many months in rehabilitation and never fully recovered. He was fortunate to get a quick diagnosis.

"My mother's stroke came on real slow," he said. "Me, I was lucky: bam, I fell out."

Tommy was fortunate in another way, too. He was offered the opportunity to receive another drug that Hess, and others on the stroke research team, believe is a good adjunct therapy for tPA.

It's an old intravenous antibiotic: minocycline. The drug is no longer used in the United States for its bacteria-fighting ability, but Hess is helping lead an NIH-funded, early-phase clinical trial studying the drug in 60 stroke patients in Georgia, Kentucky and Oregon.

His studies with colleague Dr. Susan C. Fagan, professor of pharmacy at the University of Georgia and assistant dean for the MCG program of the University of Georgia College of Pharmacy, have shown the drug works multiple ways to reduce stroke damage. It appears to inhibit white blood cells and enzymes activated by stroke that, at least acutely, can destroy brain tissue and blood vessels.

"When they get activated, they get angry and produce materials that damage the brain," Hess said. "The inflammatory cascade is bad and good. Early on it's bad, later on it may actually do some good things," such as releasing growth factors and promoting the growth of new blood vessels.

Minocycline has other stroke benefits. It blocks matrix metallo-proteinases, also released during stroke, that destroy the basement membrane of blood vessels, resulting in dangerous bleeding. This bleed-stopping ability is one of many reasons MCG scientists think minocycline is a good partner for tPA.

"We think it will reduce tPA hemorrhages," Hess said.

He hopes the NIH will fund a large, 1,600-patient trial as a final step before seeking a Food and Drug Administration ruling on minocycline as a stroke therapy.

The antibiotic also helps block apoptosis, or cell suicide, an observation originally made by MCG cell biologist Zheng Dong, in addition to the expected benefit of reducing pneumonias and infection. Years of clinical experience with the drug as an antibiotic have shown it is safe in people and additional animal and human trials have shown it's still safe at higher levels; about twice the antibiotic dose is given for stroke treatment.

Gaining access

A 2010 study, published in Stroke by MCG's Dr. Jeffrey A. Switzer, showed that telestroke networks such as REACH can help rural residents access novel stroke therapies such as minocycline.

When the Jameses were offered minocycline as an experimental procedure, they said yes.

"I said, ‘Fine, do it,’" said Sally, who signed a consent form before seeing Tommy off for a quick helicopter ride to Augusta.
Dr. David Hess, chairman of MCG’s Department of Neurology, calls tPA – the drug that aided in Tommy James’ stellar recovery – a “good but imperfect drug.”

Patients must get their first dose within six hours of symptom onset then receive incrementally larger doses for three days. By 3 a.m. Tommy was determined to go to the bathroom on his own. By 8 a.m., he was essentially back to normal and a follow up MRI confirmed the vestiges of a very tiny stroke.

In fact, the MCG team had trouble keeping Tommy still once he found his legs – and voice – again.

“We are trying to minimize the pathway that causes bleeding and to find something that might work more directly to cleave the clot,” the vascular biologist said. Her target is fibrin, the glue that binds cells, cholesterol, fat, calcium and other substances into a clot.

TPA cuts fibrin indirectly by activating the precursor of an enzyme called plasmin, which does the actual work. The problem with this process is that the body activates inhibitors to block plasmin when it senses high levels of the clot buster are in circulation. This likely helps account for the fact that only about half of patients who get tPA actually get significant clot-busting and blood-flow restoration.

To find the optimal combination of an efficient cutter that can avoid near-instantaneous elimination by the body’s natural inhibitors, she is studying the structure of plasmin, which structurally resembles a train. The engine is called a protease, a catalyst for breaking down proteins. Behind it are five boxcars called kringles, protein domains that actually do the work by binding to fibrin.

The “mini-plasmins” Sazonova is developing will one day be tested on mice genetically engineered to simulate human stroke that were developed by MCG postdoctoral fellow Dr. Nasrul Hoda to more precisely study tPA and its undesirable side effects, such as bleeding.

She believes there are drugs that can block this bleeding better than minocycline, and she is hopeful there may be a drug that can stop a stroke entirely.

In the meantime, to improve the efficacy of tPA, she is analyzing the plasma of stroke patients who get tPA and healthy volunteers to determine if those who get the best results have consistent biomarkers. The goal is to develop a bedside test to ensure those who would benefit the most from tPA actually get it.

“They really need to get the word out about this telemedicine. It saved me, I tell you. It’s a shame that only 3 percent of the population gets the opportunity to get the results I had.” —Tommy James

“I’ve been thinking about the possibility of using telemedicine for a couple of years now,” Tommy said. “I think we really need to get the word out about this. It saved me, I tell you. It’s a shame that only 3 percent of the population gets the opportunity to get the results I had. That’s a shame, man.”

Of course, the final test of the therapy occurred when he got back to Lavonia. The self-described “numbers guy” wondered whether his mind was still sharp enough to run a 20-man family drywall business.

As sure as he hit the ground when Gene Anderson tossed him, Tommy fell right back into his life.

“Except for the economy, life is good,” he said. “My life has always been good.”

And his doctor?

“Dr. Hess is a cool fellow.”

Building a better clot buster

Dr. Irina Sazonova wants to make a great drug, and she’s searching for clues by studying the body’s natural clot-busting mechanism.

Better health through discovery

PUTTING DISCOVERY INTO PRACTICE:

Dr. Joe Z. Tsien identified a protein critical to brain cell communication that enabled him to selectively erase memories in laboratory animals.
Rosa Barbour knew something wasn’t right when she felt the lump in her breast last November.

“It was the Monday before Thanksgiving last year,” she recalled. “Breast cancer was the first thing that came to mind.”

The grandmother from Thomson, Ga., who had been cancer-free for 68 years soon found out from physicians at the Medical College of Georgia that she not only had a stage III breast cancer, but had a particularly aggressive form that disproportionately affects black women.

Barbour’s cancer is known as triple-negative breast cancer because it does not express the genes for the three receptors targeted by standard breast cancer treatments: estrogen, progesterone and HER2/neu. This makes it more aggressive and harder to treat, and it is more frequently diagnosed in black and Hispanic women.
“It’s the one type of breast cancer where we don’t have good treatments,” said Dr. Thomas A. Samuel, an MCG hematologist/oncologist who specializes in breast cancer. “The antibody- and hormonal-based drugs will not work for triple-negative patients.”

Currently, the only treatment option is chemotherapy, a regimen of drugs that kill cells that divide rapidly, such as cancer cells.

Barbour undergoes pre-surgical chemotherapy at the MCGHealth Cancer Center to shrink what was once a walnut-sized tumor.

“It’s down tremendously,” she said. “Now, you can hardly feel it.”

The drawback to chemotherapy is that the drugs also harm normal cells that grow rapidly, resulting in hallmark side effects such as hair loss, inflammation of the digestive tract and suppression of the immune system.

Much like the way standard breast cancer drugs were developed using mostly white women, Samuel and MCG cancer researchers are hoping a molecular look at the mostly black women diagnosed with triple-negative breast cancer will yield a more effective treatment for the disease.

continued
“We’re looking for something better than chemo,” Samuel said.
A study he co-authored that was recently published in Clinical Breast Cancer showed black breast cancer patients had significantly poorer overall survival rates than white patients based on a review of 1990-2005 data from the MCG Tumor Registry. The study showed that white women were more likely to receive hormonal therapy, but showed virtually no differences in treatments regarding radiation, surgery or chemotherapy.

“African-American women get breast cancer less often than white women, but get it in a much more aggressive way and die more often,” said Dr. John K. Cowell, associate director for basic science at the MCG Cancer Research Center. “We want to know why these disparities exist. The underlying fundamental is genetic.”

Cowell, who studies how cancer starts and spreads, has applied for a National Institutes of Health grant to examine indicators in tumors of black women related to genes and to gene expression caused by mechanisms other than DNA. He is using the same biostatic information used in the Clinical Breast Cancer study as well as samples statewide through the Georgia Cancer Coalition.

If researchers can identify a receptor unique to triple-negative cancer, a drug could potentially be made to target it, similar to the way the antibody-based drug Herceptin was created after HER2/neu protein was identified in the late 1980s as a root cause of an aggressive type of breast cancer.

Until then, physicians are left to treat triple-negative patients as best they can. Barbour is optimistic about her outcome, and she’s hopeful a better treatment will be found someday for the disease that hit her fast and hard.

“I was well so long, I didn’t think there was any sickness in me,” she said.
Breast Cancer at a Glance

Overview: Disease in which malignant cells form in the tissues of the breast, most commonly in the inner lining of milk ducts (ductal carcinoma) or the lobules that supply the ducts with milk (lobular carcinoma). The disease affects both sexes but is rare in men.

Classification: The four stages of breast cancer are based on the size of the tumor, whether it has spread (or metastasized) to the lymph nodes and other parts of the body, such as bones, lungs, brain or liver. A Stage I tumor is smaller than 2 centimeters and has not spread to the lymph nodes; Stage IV is cancer that has spread to other organs.

Incidence: 194,280 new cases of breast cancer (99 percent women) in the U.S. in 2009

Mortality: 40,610 deaths (98.9 percent women) in the U.S. in 2009; is the No. 1 cause of cancer death in Hispanic women and is the second most common cause of cancer death (after skin cancer) in white, black and Asian women.

Risk factors:
- Old age
- Not having children, or having children late in life
- Caucasian
- Menstruation at an early age
- Having been treated with radiation therapy to the chest
- Having a mother or sister with breast cancer
- Taking hormones or oral contraceptives
- Alcohol consumption
- Being physically inactive or overweight
- Having mutations in your BRCA1 and BRCA2 genes

Treatment: Therapies vary by the stage and type of breast cancer and can involve a combination of surgery, chemotherapy, radiation therapy and drugs that block the hormone and protein receptors that promote tumor growth.
Study casts light on sudden cardiac death

Fibrillation Illumination

BY CHRISTINE HURLEY DERISO

CARDIOVASCULAR DISCOVERY INSTITUTE
Many heart conditions are relatively straightforward. Heart attacks, for instance, generally result when blocked or narrowed vessels impede blood flow to the heart, starving the organ of oxygen. But another heart condition can be much more cryptic. Fibrillation is a type of abnormal heart rhythm that causes heart chambers to quiver rather than contract when the heart’s electrical signals become rapid and chaotic. Fibrillation in the heart’s upper chambers—atrial fibrillation—is seldom fatal. Fibrillation in the lower chambers, on the other hand—ventricular fibrillation—almost always causes instant death unless the victim has immediate access to cardiopulmonary resuscitation or a defibrillator, which electrically shocks the heart back into its normal rhythm.

“Without fast intervention, death occurs within minutes of the episode.”
—Dr. Robert Sorrentino

The heart is notoriously fickle, but in more ways than you might imagine.

“Without fast intervention, death occurs within minutes of the episode,” said Dr. Robert Sorrentino, director of arrhythmia services at MCGHealth and interim chief of cardiology in the Medical College of Georgia School of Medicine.

Implantable cardioverter defibrillators “are the best way to prevent cardiac arrest in certain groups of patients who are at high risk,” Sorrentino said, noting that risk factors include previous heart attacks and genetic predisposition. “The devices, which are inserted into the chest area, act as a built-in emergency room. Just like a team of heart specialists would, the ICD consistently monitors the heart’s rhythm...”
How to Perform CPR

Cardiac arrest occurs when the heart stops pumping blood. Cardiopulmonary resuscitation combines rescue breathing and chest compressions to support a small amount of blood flow to the heart and brain, ideally buying time until normal heart function is restored.

Here’s a crash course in CPR:

1. Call.
   If the victim is unresponsive, call 911 and return to the victim. In most locations, the emergency dispatcher can provide CPR instructions.

2. Blow.
   Tilt the head back and listen for breathing. If the victim isn’t breathing normally, pinch his nose and cover his mouth with yours and blow until you see the chest rise. Give two breaths, each lasting one second.

3. Pump.
   If the victim is still not breathing normally, coughing or moving, begin chest compressions. Push down on the chest one and a half to two inches between the nipples 30 times at a rate faster than once a second. Continue until help arrives.

Sources: www.americanheart.org; www.mcghealth.org

and automatically delivers a short, high-energy shock when you develop a dangerous rhythm.”

But ventricular fibrillation can also strike people with no known risk factors at all. This is the group being targeted by Dr. Autumn Schumacher, assistant professor in the Department of Physiological and Technological Nursing.

‘It Just Happens’

“Ventricular fibrillation happens in people with known risk factors, but the condition also affects another group: people who seem absolutely fine and it just happens,” Schumacher said.

Since joining the faculty four years ago, she has used sophisticated imaging tools to try to better understand the process in hopes of preventing it.

“Ventricular fibrillation is symptomless before it strikes,” she said. “We don’t know it happens until it happens.”

But her research—which was presented at the annual International Society for Computerized Electrocardiology last spring—is providing important new information.

Schumacher’s research initially focused on the role of adrenalin in ventricular fibrillation, but now she is increasingly interested in the role of age.

She and her colleagues, including Dr. Nathan Yanasak, director of MCG’s Core Imaging Facility for Small Animals, are studying many factors, including age and gender, to try to determine what sets the process in motion.

“As we age, the heart enlarges a bit,” Schumacher said. “We don’t know why. But I suspect the enlargement is related to the risk of ventricular fibrillation increasing with age.”

Yet ventricular fibrillation affects only a relatively small percentage of the elderly. What makes the difference? “I think there’s more to it than age alone,” Schumacher said.

“A Deadly Collision Course

In the rats, she uses magnetic resonance imaging; with the rabbits, she uses voltage-sensitive fluorescent imaging—both means of analyzing the heart’s tissue in extraordinary detail. MRI illuminates tissue abnormalities such as inflammation; fluorescent imaging uses high-speed cameras to photograph the heart’s electrical activity at 1,000 frames per second. Those images show ventricular fibrillation forming distinct patterns—“spiral waves that often collide with each other and spin off more spiral waves,” Schumacher said. “Hopefully, the MRI will show some abnormalities that could influence these spiral wave patterns in the elder heart.”

She and her colleagues, including Dr. Nathan Yanasak, director of MCG’s Core Imaging Facility for Small Animals, are studying many factors, including age and gender, to try to determine what sets the process in motion.

“Ventricular fibrillation is symptomless before it strikes.”
–DR. AUTUMN SCHUMACHER

Dr. Raymond P. Ahlquist, a former chairman of the Department of Pharmacology, published research in 1948 laying the groundwork for beta-blocking drugs.

PUTTING DISCOVERY INTO PRACTICE:

Dr. Robert G. Ellison Sr., chief of the Section of Cardiothoracic Surgery from 1947-87, performed Georgia’s first open-heart operation using bypass in 1956.
The Role of Inflammation

She suspects that inflammation plays a major role.

“In tissue, low-level inflammation may occur with age,” Schumacher said. “Several studies have verified inflammation in aging arteries, and we’re seeing increasing evidence that it is in tissue as well. I’m trying to find noninvasive ways to detect this subtle chronic inflammation in the elderly.”

If her studies ascertain that inflammation increases the risk of ventricular fibrillation, she hopes that treatment such as anti-inflammatory medication or lifestyle modifications can address the problem long before the heart’s electrical activity revolts in response to a process that is years in the making.

“If we can say to someone, ‘Yes, you feel fine, and your blood pressure is fine, but we see these tiny changes that will affect you 20 years from now,’ people may change their lifestyle.”

In addition to better understanding ventricular fibrillation, Schumacher’s studies are casting intriguing light on the subject of aging in general.

“We don’t understand the aging process in the heart very well,” she acknowledged. “Some folks live to age 90 and beyond and do just fine. How come? Research is increasingly showing that it’s not just genes and not just lifestyle. There is a bit of luck involved, but something else is going on.”

As her research progresses, she’s getting closer and closer to finding out what that something is.

Ventricular Fibrillation at a Glance

Risk Factors:
- Heart attack
- Heart failure
- Heart surgery
- Coronary artery disease
- Family history of heart disease
- Congenital heart disorders
- Advancing age
- Diabetes
- High cholesterol
- High blood pressure
- Smoking
- Substance abuse
- Excess weight
- High-fat diet
- Sedentary lifestyle
- Stress
- Certain medications, including some decongestants and diet and herbal supplements

Prevention:
- Drink plenty of water
- Eat a heart-healthy diet
- Eliminate unnecessary stress
- Exercise regularly, particularly aerobic exercise
- Maintain a healthy weight
- Quit smoking
- Avoid excess alcohol or other drugs
- Inform your physician of any symptoms that may signal heart problems
Researchers use culturally tailored program to reduce asthma costs

If it weren’t for a car accident with his father at age 5, Eric Hannah might not have even known he had asthma.

“Eric was the only one in the accident without a scratch on him, but he was having some trouble breathing,” said Eric’s mother, Lucia.

Doctors at their small-town hospital in Jefferson County, Ga., diagnosed him that day with bronchitis and asthma. Though the Hannahs noticed that their son was often short of breath, they attributed it to his activity level.

“Eric was up and never stopped from the time his daddy got up in the morning at 5:30,” she said of her now 17-year-old son. “He was always running around doing something, always playing. We just thought he was short of breath because he was so active.”

But he wasn’t.

In fact, Eric was experiencing asthma attacks – a feeling he describes as his chest caving in, making him...
feel dizzy and suffocated. Over the next six years, until he was 11, Eric experienced frequent attacks – sometimes twice a month.

“I spent many nights in and out of emergency rooms,” Hannah said. “We tackled it as a family though. If I was working, my husband was with him. When my 14-year-old daughter got out of school, she was with Eric at the hospital.”

Things became more difficult to manage when Hannah’s husband died almost eight years ago.

But then, when Eric was 11, a breakthrough occurred.

He and his doctor, Shelly Griffin, found the right combination of medicine to treat his disease. Eric is on a combination of an albuterol inhaler and Advair, a steroid. They say it’s prevented him from having all but one asthma attack in the last five years. Eric also takes Concerta, a stimulant, for attention deficit hyperactivity disorder.

“Once he got a hold of the right medicines, he took off,” Hannah said.

“He didn’t let his asthma slow him down anymore.”

For Eric, who is still as active as ever (he’s even participating in Jefferson County High School’s football camp this summer), it’s a harder pill to swallow.

“I do pretty good when I take my medicine, but I haven’t been able to do that lately,” he said. “I’ve just been going as hard as I can, waiting, hoping I get back on track with my medicine soon.”

A Dangerous Game

It’s a dangerous game he’s playing, according to Medical College of Georgia researchers.

Black males like Eric have a death rate from asthma that is six times greater than their white counterparts, according to Dr. Dennis Ownby, chief of the MCG School of Medicine Division of Allergy and Immunology. And asthma rates are as bad in rural areas as they are in inner cities.

“The prevalence is probably the same in rural areas,” he said. “But teens from
those areas already face a number of other problems that can complicate their disease – poor housing quality, air pollution, more trouble getting to doctors and smaller, less-equipped hospitals.”

Forgetting to take medications or carry rescue inhalers only exacerbates the problem, as does exposure to tobacco – either from smoking or second-hand smoke. Ownby said previous studies have shown smoking is more prevalent in rural areas than cities.

He and other researchers think that Puff City, a culturally tailored intervention program with lectures and materials aimed at three key areas – reduction of tobacco exposure, adherence to medication and attack readiness – could help at-risk teens better manage their asthma.

Over the next three years, with $2.1 million in funding from the National Heart Lung and Blood Institute, Ownby and Dr. Martha Tingen, a nurse researcher at the Georgia Prevention Institute, will work with 300 ninth- to 11th-graders with asthma from Burke, Jefferson and McDuffie counties. Half the teens will be exposed to traditional educational asthma Web sites; the other half will use Puff City’s entertaining and culturally relevant asthma information.

If it proves to be successful with rural Georgia teens, Puff City could be one way to lessen the burden of a disease that is the third most expensive to Georgia taxpayers.

“We are hoping that this is a program that can be easily disseminated worldwide at a relatively low cost,” Tingen said.

**A Community Approach to Research**

Puff City is just one example of community-based pediatric research, defined by the National Institutes of Health as “scientific inquiry conducted in communities in which community members, persons affected by condition or issue under study and other key stakeholders in the community’s health have the opportunity to be full participants in each phase of the work.”

In addition to playing football, Eric also plays the tuba in his high school band.
Community-based research is just one guiding principle of the new MCG Child Health Discovery Institute, a sort of marriage of the newly constructed two-bed clinical trials unit on the fifth floor of the Children’s Medical Center and the existing strengths of the Georgia Prevention Institute – one of the nation’s premier pediatric disease prevention centers. The institute is one of seven based on the translational science initiative created in 2008 by the MCG School of Medicine.

The institute builds on a lasting legacy of groundbreaking pediatric research that’s carried MCG throughout the last 100 years. “This will enhance our ability to practice research in the context of patient care and education,” said Dr. Bernard Maria, chairman of the Department of Pediatrics and Ellington Charles Hawes Chair in Pediatrics at the MCG School of Medicine.

The institute is led by Maria, Tingen and Dr. Gregory Harshfield, director of the Georgia Prevention Institute. “This arm of the institute will be a productive collaboration between the institute and our community,” said Tingen. “We will observe and respond to health issues that present in the unique populations and environments of our local, regional and statewide communities and then develop and implement effective health promotion, prevention and treatment programs. This also includes aiming to develop collaborations with the community pediatricians.”

The idea is based on engaging the community as stakeholders in research and discovery, something that’s important to the Hanshahns too.

“I thought that with all the time that we’ve spent at doctors’ offices and hospitals, Eric’s story deserved to be told,” Hannah said of her reasons for getting involved with the Puff City grant.

The overall goal, Tingen said, is to improve children’s health by strengthening community involvement among health care practitioners, schools, churches, neighborhoods and industry.

A four-pronged approach

But community-based research is just one “arm” of the Child Health Discovery Institute.

Based around the notion that “children are not just small adults,” the institute operates under four core areas – child- and family-centered research, community-based research, compounds for kids and pediatric scholars, Maria said.

“What we were missing was the concept of practicing research,” he said. “It was like our patients were Evel Knievel and we were asking them jump over the Grand Canyon, where one side was research and the other side was clinical practice. There was no bridge.”

The idea is that the institute will be the “home” of all extramurally-funded pediatric research. It can be a confusing landscape, so the first core area, child- and family-centered research, will focus on helping children and their families navigate it. Plans include hiring a floating pediatric research registered nurse navigator and establishing a pediatric inpatient clinical research unit, where clinical activities are “centered.”

“We see it as sort of a concierge service, a liaison between research discovery and practice for our patients,” Maria said.

Another core area, compounds for kids, will focus on offering the most novel therapeutics available to pediatric patients. It’s an area close to Maria’s heart.

His own research focuses on a novel compound, hyaluronan oligomers, patented by his research partner, Dr. Bryan Toole, that blocks the ability of cancer cells to grow and spread as it reduces their resistance to radiation and chemotherapy.

“We will focus on the development of new drugs in new labs and offering those to our patients,” Maria said.

The fourth core area, pediatric scholars, focuses on the development and training of future pediatric clinicians and scientists. As part of that, the institute is offering more than 20 medical students the chance to train with clinicians and researchers over the summer in hopes of sparking their interest in research.

“That is where it all comes together, research, practice and education,” Maria said. “It is important to prepare ourselves for the future and we must do that by educating future clinicians and scientists. Everyone talks about the aging population, but there will still be children needing long, healthy lives. We need to train pediatricians to think about not just what kind of care they give their patients, but how their patients can provide opportunities for clinical research.”

Better health through discovery
Giggling and squealing, she tries to make it from one end to the other without getting tagged by one of her friends. She succeeds and throws her arms up in triumph.

“Yes!” she screams.

The 10-year-old glances down at her wristwatch and excitedly runs to show her teacher.

“Good job,” says Amber Smith, a research assistant at the Medical College of Georgia’s Georgia Prevention Institute.

The watch tracks Ciera’s pulse. Whoever in the group has the highest heart rate receives a prize.

“It’s so fun to win a prize,” says Ciera, a fourth grader at Meadowbrook Elementary School in Augusta. “I love playing the exercise games because they keep me moving so my heart rate gets higher.”
Tag is one of several games she and a group of 8-11-year-old elementary school children play weekdays after school as part of a study led by Dr. Catherine Davis, a clinical health psychologist in the Georgia Prevention Institute. The study involves 50 mostly obese children, half of whom participate in an aerobic exercise program while the other half participate in sedentary activities.

The exercises are just one part of MCG’s research to reduce diabetes and cardiovascular disease in children. While other MCG scientists are trying to unlock the mysteries of the disease at a molecular level, researchers such as Davis are studying the impact of behavioral intervention on keeping at-risk children from developing diseases as adults.

She’s also testing physiological measures related to diabetes risk, including liver disease and stiff arteries, both typically found in adults.

The study’s exercise group participates in activities and games such as jumping rope and shooting hoops. The recreation group focuses on sedentary activities, including board games, painting self portraits and building miniature houses.

“I heard about the study during registration at Ciera’s school,” says her mother, Shavonne Fuller. “I didn’t have that chance when I was younger, so I signed her up. It means a lot to me that she’s learning to live a healthy life.”

“It means a lot to me that she’s learning to live a healthy life.”

—SHAVONNE FULLER
PUTTING DISCOVERY INTO PRACTICE:

Dr. Virgil P. Sydenstricker, chairman of the Department of Medicine from 1922-57, developed a system of blood transfusion with stored citrated blood that laid the foundation for today’s blood banks. He also documented the first case of sickle cell disease. He added immeasurably to the scientific community’s understanding of nutrition and vitamins, discovering, among other things, niacin as a cure for pellagra.

because I haven’t been setting a good example. I want her to do well in life, and this program is helping.”

Davis began her research with $2.7 million in grants from the National Institute of Diabetes and Digestive and Kidney Diseases that showed regular exercise reduces anger expression and diabetes risk in overweight children.

“That’s really the motivator of all my research,” says Davis, principal investigator on the study. “In trying to prevent type 2 diabetes in kids, exercise was a very appealing behavioral intervention because unlike a restricted diet, it’s clearly a safe and appropriate thing for them to be doing.”

One of the problems is that children seem to be less physically active.

“Nobody’s walking to school or playing outside. Everybody’s got their video game in hand.” – DR. CATHERINE DAVIS

“Nobody’s walking to school or playing outside. Everybody’s got their video game in hand. Therefore, we have more fat kids than we ever did before – it’s a childhood obesity epidemic we’re experiencing. With that comes an increased risk of diabetes and cardiovascular disease,” she explains.

Type 2 diabetes, once known as an adult disease, is a chronic condition that affects the way the body metabolizes sugar.

“When I first started this career, I had recently heard that children were getting it. When they start getting diseases at such a young age that only adults used to get, it’s like the sky is falling,” Davis says.

She investigated different ways regular exercise benefits children at risk for some adult diseases and is studying how it affects metabolic disorders, such as nonalcoholic fatty liver disease, which affects about 40 percent of obese children.

The disease, which increases the risk of cardiovascular disease and diabetes, may show no signs or symptoms and no complications. But in some people, the fat that accumulates in the liver can cause inflammation and scarring and turn into a more serious form called nonalcoholic steatohepatitis and even liver failure.

“It’s essentially another aspect of the metabolic imbalance these children are experiencing when they’re overweight and inactive and is a signal they’re at very high risk for diabetes,” Davis says.

She has already found that exercise reduces inflammation; visceral fat (a type of fat similar to liver fat that is situated between the organs); body mass index (calculated using weight and height) and insulin levels. The exercise group showed improvement on virtually all of those measures after just 20 to 40 minutes of daily aerobic exercise for 12 weeks. She presented the findings at the American Heart Association’s Nutrition, Physical Activity and Metabolism Conference in March.

The positive results encouraged Davis to examine potential improvements in other measures of cardiovascular disease, such as atherosclerosis, an adult disease in which arterial stiffness results from plaque buildup in the arteries.
Dr. Reda Bassali, associate professor of pediatrics in the MCG School of Medicine and lead author of a study published online in the International Journal of Pediatric Obesity, found that children, ages 7-11, with more fat around their midsections could be at higher risk of developing cardiovascular disease later in life. “What that means is that children with a waist circumference at or above the 90th percentile are at a greater risk of developing the warning signs of cardiovascular disease,” Bassali says. “Our results indicate that routine clinical measurement of the waist may help clinicians identify which obese children are at a greater risk.”

Dr. David Stepp, vascular biologist at the MCG Vascular Biology Center and co-director of the Diabetes & Obesity Discovery Institute, found that deleting or mutating the gene PTP1B puts mice at risk for hypertension by interfering with an endogenous mechanism that should help prevent it. The findings were published in the Sept. 1 issue of the American Heart Association journal Circulation. “In a normal individual gaining weight, PTP1B should increase and they would be protected in theory from hypertension,” says Stepp, the study’s corresponding author. “But if you don’t have a good copy of PTP1B and you become obese, then you are going to have a problem. So in theory this gene can segregate the obese people who will become hypertensive and those who won’t.”

Dr. Martha Tingen, nurse researcher at the Georgia Prevention Institute, found that overweight children ages 7-11 exposed to environmental tobacco smoke (secondhand smoke) had a higher percentage of body fat, larger waists, poorer resistance to distraction and were more likely to screen positive for sleep-disordered breathing than their non-exposed peers. She presented her findings at the Society for Research on Nicotine and Tobacco Conference in April 2009. “Eventually, environmental tobacco smoke may worsen obesity and its adverse outcomes,” Tingen says. “Therefore, comprehensive interventions that target multiple health risk factors are needed.”

Better health through discovery

Davis discovered that children with a greater body mass index, body-fat percentage and less endurance had stiffer central arteries compared to leaner and fitter children. The findings, which were presented at the 31st Annual Society of Behavioral Medicine Meeting in April, indicate that atherosclerosis is related to fatness and fitness at a young age.

“Measurement of it may be informative in studies of childhood cardiovascular risk and its amelioration,” she says.

Davis also is focusing on other liver measures, including fibrosis, and working with Dr. Sudipta Misra, MCG pediatric hepatologist, to use novel ultrasound technology instead of the traditional biopsies to gauge liver stiffness.

“That way, we’re not hurting the child,” Davis says. “A gentle pulse will pass through the liver, and the echo will determine if the liver is stiff (indicating disease) or nice and soft.”

Davis hopes her research will encourage children to exercise and stay active and help keep these illnesses, once considered adult diseases, from impacting children.

For Ciera, staying active won’t be a problem.

“I love the exercises we’ve learned and do them every day after my auntie and I finish walking,” she says. “We do the stretches I learned, too. They make me feel longer.”

Standing on her tip-toes with her arms stretched above her head, palms to the sky and fingers locked, Ciera mimics another stretch she’ll take home to teach her aunt.
Inflammation, the body’s biological response to infection, irritation and injury, can be your best friend if you suffer a burn, get a splinter or are bitten by an insect. The telltale warmth, redness and swelling indicate the body is fighting whatever is harming it.

However, if the fight goes on after the battle is won, inflammation becomes your worst enemy.

The inappropriate triggering of the inflammatory response damages cells, tissue and entire organs. Dr. Joseph Hobbs, chairman of the Medical College of Georgia Department of Family Medicine, said chronic inflammation is behind many of the illnesses physicians treat on a regular basis.

“We are learning more and more that chronic inflammation is a precursor to many disease processes,” he said. “It can occur in the basement membranes of arteries and affect the function of different organs. If it is allowed to stay present for a long time, the damage is irreversible.”
Chronic inflammation is the hallmark of autoimmune diseases such as lupus. It is also linked to degenerative diseases such as atherosclerosis, diabetes, rheumatoid arthritis and, increasingly, is being identified as a key player in asthma and cancer.

Currently, there are two primary methods to keep chronic inflammation in check. One is steroids, primarily corticosteroids, which block multiple targets that trigger allergic and inflammatory responses. The other is non-steroidal anti-inflammatories, a class of drugs known as NSAIDs that block cyclooxygenases, the enzymes responsible for the formation of prostaglandins and other chemicals involved in inflammation.

Both have drawbacks. “None of our current anti-inflammatories are site-specific,” Hobbs said. “Every cell gets exposed to them and we have to use greater concentrations to get the desired impact.”

Steroids, among other things, suppress the entire immune system by impeding the function of white blood cells, leaving the body susceptible to infections. NSAIDs, which include over-the-counter medicines such as aspirin and ibuprofen, can have an adverse effect on the gastrointestinal tract and kidneys. Several newer forms of NSAIDs, the “COX-2 blockers,” have been withdrawn from the market over fear of causing increased risk for heart attack and stroke.
MCG researchers believe a protein that provides the basis for a powerful type of anti-cancer therapy has potential to become a new class of anti-inflammatory drug.

Their focus: heat shock protein 90, or hsp90, a molecular chaperone essential for the creation, maintenance and destruction of proteins. Scientists have already determined that blocking hsp90 promotes the death of cancer cells, whose mutated, unstable and overactive proteins demand hsp90 even more than normal cells. Now, MCG researchers believe hsp90 inhibitors can also short circuit chronic inflammation.

“This may turn out to be the best anti-inflammatory we have,” said Dr. John Catravas, Director of MCG’s Vascular Biology Center and Acting Director of MCG’s Cancer Research Center. His studies with inflammation in mice have shown that hsp90 inhibitors appear to have few side effects, similar to the way hsp90 inhibitors have shown little adverse reactions in humans when used as an anti-cancer therapy. Also, because hsp90 is stress-activated, the inhibitors have demonstrated the ability to target a specific area, such as a tumor, or in the case of Catravas’ research, a site of chronic inflammation.

“If the inflammation is in the foot, for example, then most of the inhibitor dose will go to the foot because that is where the inflammation is most active,” he said.

A recent $1.47 million, four-year grant from the National Heart, Lung and Blood Institute will enable Catravas’ team to do more studies into hsp90 inhibitors’ role in inflammation control as well as its impact on the cardiovascular complications that typically occur in people with type 2 diabetes and obesity.

A post-mortem comparison of healthy lung tissue from mice (left) to those treated with an inflammatory endotoxin (center) and those treated with the endotoxin and a heat shock protein 90 inhibitor (right) shows far fewer white blood cells (stained brown for visibility), an indication of less severe inflammation in mice treated with the hsp90 inhibitor.

**PUTTING DISCOVERY INTO PRACTICE:**

Dr. Edgar Pund, an MCG faculty member and the university’s second president, and Dr. Robert B. Greenblatt (inset), chairman of the Department of Endocrinology from 1946-72, described the pathogenic cell in granuloma inguinale, a widely endemic venereal disease. Greenblatt’s finding that mycins (a type of antibiotic) could cure the disease was a major contribution to public health.

Dr. Greenblatt also performed studies that laid the groundwork for fertility and birth-control treatments.

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1936: Japanese researchers extract the steroid diosgenin from plants, paving the way for the synthesis of progesterone and corticosteroids such as cortisone.

1944: Lewis Hastings Sarett, an American chemist, prepares the first synthetic cortisone for Merck & Co., allowing for the large-scale production of steroids.

1948: Mayo Clinic physicians report dramatic improvements in arthritis patients who were given daily injections of a corticosteroid, leading the press to trumpet the discovery of a “wonder drug.”

1953: Acetaminophen first marketed in the United States as an aspirin alternative for children and people with ulcers. Two years later, McNeil Laboratories begins selling the drug under the Tylenol brand name.

1961: Ibuprofen (the ingredient behind modern brands Advil and Motrin) is patented and launched as a rheumatoid arthritis drug in Great Britain.
By the time a patient is diagnosed with Goodpasture syndrome, a rare form of kidney disease, it’s usually too late to save the organ. The rapidly progressive autoimmune disease, which attacks the capillaries in the kidney that perform the first step in blood filtration, causes inflammation so severe that kidney failure often occurs within days. Though the condition is rare, an MCG researcher believes its molecular foundation can provide a way to deliver anti-inflammatory drugs deep inside kidneys to treat other, more common, forms of kidney disease.

Dr. Michael P. Madaio, a nephrologist and chairman of the MCG Department of Medicine, plans to re-engineer human antibodies that bind to a collagen molecule unique to the kidneys. The antibodies, which bind to the basement membrane of the kidney’s tiny capillaries, called glomeruli, normally cause disease by recruiting inflammatory cells.

Madaio’s plan is to create human monoclonal antibodies that retain their binding capacity but deliver either anti-inflammatory or anti-fibrotic molecules to suppress disease instead of causing it. He and his team have found these particular antibodies bind to create a tight chain-link fence formation within the lattice of the alpha-3 chain of type IV collagen. This collagen, which is expressed in only a few organs, is normally sequestered or hidden. However, the antibody binding sites are exposed in the kidney during inflammation, which creates a unique target for drugs.

“‘This is a kidney-specific delivery system,” Madaio said. These unique properties could be used to deliver disease-suppressing agents to patients with Goodpasture syndrome, lupus and other diseases that cause kidney inflammation, a condition known as nephritis.

Modified antibodies, such as the kind Madaio created, are known as “minibodies” and are already used as a form of immunotherapy in cancer patients. Madaio’s two-year, renewable National Institutes of Health grant is funding studies of the modified antibody in mice. He said pharmaceutical companies could be interested in pursuing the antibody as a kidney-drug delivery mechanism if animal studies are promising.

Alternatively, this approach could be used as a biomarker to determine a patient’s level of kidney damage. Because the antibody binds to normal collagen, linking it to radiologic imaging materials could potentially show how much viable tissue is in the kidney, helping physicians determine the best course of treatment.

Currently, physicians rely on non-precise indicators such as kidney size and biopsies.

“The way we look at kidneys now is relatively crude, and many investigators are looking for better biomarkers to gauge reversible disease and predict response to therapy,” Madaio said. “This method would integrate nicely with these new approaches.”

Kidney researcher using antibodies to bring drugs to inflammation’s doorstep  

BY DAMON CLINE

A molecular model of the antibody created by Dr. Michael P. Madaio (second from left) and his research team (from left), Maggie McMenamin, Dr. Nino Kvirkvelia and Kapil Chaudhary, shows how its heavy chain (green) and light chain (blue) interact with both major targets in the alpha-3 chain of type IV collagen within the glomerular basement membrane of the kidney, the C2 (red) and C6 (brown) epitopes.
In the South, a toddler’s first snow is monumental, but for Tyler it was something more. He could see the snow. A year earlier, that might never have been possible. At less than 90 days old, doctors told Tyler’s parents their son was blind.

“Tyler is fearless,” his father John said about his adventures in the snow.

The same could be said about the Medical College of Georgia physicians who saved his sight using an experimental procedure.

Sixteen-month old Tyler Cashin just experienced snow for the first time. He bundled up, went sledding with his father and helped his big brother Jake build a snowman in the front yard.
Kelly Cashin was nearly 26 weeks pregnant with twins when she went to her job as an adult oncology nurse at University Hospital on Sunday, Oct. 12, 2008. At a routine check-up the week before, her obstetrician told her that she was on track for a healthy, normal delivery.

“All of a sudden, they started to come,” Kelly recalled. She walked downstairs to labor and delivery. Eleven hours later – and more than three months early – the twins were born. Tyler weighed 2 pounds, 1 ounce and his sister Erin, 1 pound, 14 ounces.

They were admitted to University’s neonatal intensive care unit, where Tyler stayed for three months. Erin was transferred to MCG’s NICU a week later for treatment of a perforated intestine.

The twins developed retinopathy of prematurity, an eye disorder characterized by abnormal blood vessels growing in the retina. The potentially blinding disorder primarily affects infants born before 31 weeks of gestation and weighing less than 2 ¾ pounds.

While Erin’s condition was mild and never needed treatment, Tyler’s condition reached the point at
Vision Research at a Glance

- National Eye Institute Director Paul Sieving was the keynote speaker at the Vision Discovery Institute’s second annual scientific retreat in March. The retreat featured research updates from many of the institute’s clinicians and scientists. The institute also hosts a monthly speaker and seminar series throughout the year.

- Electrophysiologist Alan Saul, biologist Jeffrey Mumm and ophthalmologist David Bogorad are investigating whether natural retina stimulation might reveal more about retinal function than the traditional, less comfortable electrophysiological testing used now. They are developing novel testing methods in humans and animal models.

- Occupational therapists Kathy Bradley and Sharon Cosper and electrophysiologist Zhiyong Yang are developing a statistical model to predict a person’s ability to visually search the environment and examining whether low-vision patients could benefit from experiences with visual scanning within controlled natural scenes. The study addresses low-vision patients’ ability to perform in relevant daily living situations.

- Department of Ophthalmology Chairman Julian Nussbaum, Department of Biochemistry and Molecular Biology Chairman Vadivel Ganapathy and ophthalmology resident Emory Patterson are determining the prevalence of a specific HFE gene mutation in patients with age-related macular degeneration. The mutation causes increased iron levels, which have been shown to increase inflammation, a possible cause of the disease.

which his vision would not improve on its own, and he underwent laser eye surgery shortly before he was discharged from University.

He was home for only days before he began aspirating his food and was taken to the MCG Children’s Medical Center. It was a blessing in disguise.

“We brought a blind baby home and did not know it; nobody did,” Kelly said of Tyler’s initial homecoming.

In retrospect, she recalled him being despondent and not opening his eyes at home, but it was Dr. Stephanie Goei, pediatric ophthalmologist at MCG, who first noticed that he was blind. She consulted with her husband Dr. Julian Nussbaum, chairman of the Department of Ophthalmology, and the prognosis was grim. Tyler was diagnosed with Rush disease, a type of retinopathy of prematurity that almost certainly causes permanent blindness.
to Bedside

“If Dr. Nussbaum didn’t stay on the cutting edge of research, we would have been talking to a counselor about how to live with a blind child instead of getting him into surgery the next day.” —JOHN CASHIN

“These babies are given a chance at sight at maybe two places in the world,” Nussbaum said. He told the Cashins that Tyler needed to go to William Beaumont Hospital in Detroit, which is leading a multi-center clinical trial investigating the use of Avastin, a cancer drug used primarily to treat solid tumors in the gastrointestinal tract, as treatment for retinopathy of prematurity.

There is a narrow window of opportunity to inject the drug into the eyes before irreversible blindness occurs, and time was running out. The family struggled unsuccessfully with their insurance company to get Tyler to Detroit. Through a compassionate use protocol, Nussbaum performed the same experimental treatment at MCG to give Tyler a fighting chance of retaining some vision.

“In cancer, the compound works by killing off blood vessels that feed tumors,” Nussbaum said. The same theory applies with eye diseases such as retinopathy of prematurity, where abnormal blood vessels grow in the eye and threaten to detach the retina.

“If Dr. Nussbaum didn’t stay on the cutting edge of research, we would have been talking to a counselor about how to live with a blind child instead of getting him into surgery the next day,” John said.

Fortunately, Tyler responded miraculously. With the exception of strabismus, or crossed eyes (a condition that will be corrected with a follow-up surgery), he now has essentially normal vision thanks to a drug that has not yet been approved for use in the eye.

Dr. Sylvia Smith, professor of cellular biology and anatomy, said, “This is why we do what we do and why translational vision research must be accelerated.” She and Nussbaum are co-directors of MCG’s Vision Discovery Institute.

A window to the body

Many consider the eyes to be the body’s most important sensory organ, said Smith, noting that the brain gets 85 percent of its sensory information from the visual system.

Nussbaum concurred. “If you ask people which sense they would give up if forced to choose one, vision is the one that people don’t want to lose.”

It’s an opinion that’s rooted by fact. People who are legally blind have higher rates of depression than the general population, and about 75 percent of the working-age blind are not in the work force or are unemployed.

Vision problems do not discriminate by age – from the baby with retinopathy of prematurity to the elderly with macular degeneration. The prevalence of type 2 diabetes is causing a surge of diabetic retinopathy not just in the middle aged, but teenagers as well.

The Vision Discovery Institute focuses on all of these. The majority of the researchers focus on diseases of vasculature, including retinopathy of prematurity, diabetic retinopathy and macular degeneration, while others study glaucoma and herpetic diseases of the eye, and parts of the eye including its neurons, supporting cells and cornea.

“People say the eyes are the window of the soul, but they are really the window to the body,” Nussbaum said. That’s important to a clinician who can monitor a patient’s general health or disease manifestation through the eyes. For example, when a patient develops early cataracts or changes to the retinal vasculature, it may suggest chronic hypertension or high blood cholesterol.

Studying the eyes is advantageous to scientists, as well. “It’s a perfect experimental system,” Smith said. “If you’re using an animal model, you have a control eye and a treated eye.”

Smith and Nussbaum hold the translational aspect of interaction between clinicians and scientists in high regard. “Our hope for the Vision Discovery Institute is that our clinicians will understand the research and know what more can be done, and that our scientists understand the clinical aspects of their lab work,” Smith said.

Putting discovery into practice:

Dr. Louis A. Dugas, a founding MCG faculty member, performed the first surgery in the United States using “mesmerism,” or hypnosis, in 1845.

Dr. Charles Iverson Bryans Jr., a 1943 School of Medicine alumnus, pioneered the use of hypnotherapy to quickly return traumatized soldiers to battle.
We hope you have enjoyed learning about the unique therapies, technologies and scientific research chronicled in this edition of MCG Tomorrow. As you can glean from these pages, the work by clinicians and scientists at the Medical College of Georgia directly translates to better health for Georgia’s growing population.

Those of us in MCG’s development office, who are charged with encouraging university supporters to help fund research, are fortunate to be able to tell potential gift givers that their investment can yield results now – not years, decades or generations down the road.

We are also fortunate to have scientists who are good stewards of the funds entrusted to them, and are extremely productive in their laboratories. In fact, MCG’s basic scientists have the second-highest per-capita research awards among peer institutions in the U.S., and The Scientist magazine named MCG one of the top 15 institutions to perform research based on a nationwide survey.

Of course, all these accolades and recognitions would not be possible without the support of grants and awards from corporations, foundations, alumni and friends like you. We invite you to learn more about the cutting-edge health science research at MCG.

Please contact us to see how we can help you become a partner in MCG’s mission. Together, we can accomplish great things and deliver better health through discovery.
From Bench to Bedside: BETTER HEALTH THROUGH DISCOVERY