

MCOR is making progress

From basic research discoveries to development of clinical programs, we are making progress in building a multidisciplinary team of researchers, health care providers, and community advocates who will help the Mississippi Center for Obesity Research (MCOR) achieve its ultimate goal: to improve lives through research, discovery, innovation, and translation of discoveries to prevention and better treatment of obesity, diabetes and related disorders.

This newsletter highlights some of the MCOR's progress for the past year. Additional information can be found in the 50-plus publications (see web link at: <http://www.umc.edu/mcor/>) describing the research findings of MCOR scientists who also made at least 30 presentations of their work at national and international meetings.

Obesity and its associated diseases have rapidly become the greatest challenge to our health care system. Current estimates indicate that Mississippi is spending at least \$925 million on health care costs directly related to obesity and this number is expected to rise to \$3.9 billion by 2018 if current trends continue. Despite the enormous health and economic consequences of obesity, we do not fully understand the biological and environmental factors that have contributed to this rapid increase in obesity and there are few treatment options available.

People often ask me why we need more research. Isn't the solution to the problem simple - eat less and exercise more? Although dieting and exercise are often successful in producing weight loss for a few months, most people regain the excess weight in less than a year. Many people assume that the reason is a lack of willpower. However, we have learned through research that hormonal and nervous mechanism of the body resist the weight loss by slowing down metabolic rate and causing extreme hunger. Even after a year of weight loss the body continues to produce increased levels of the "hunger hormone" ghrelin and decreased levels of the satiety hormone leptin. These observations challenge conventional thinking about obesity, weight loss and willpower but also provide insights that may lead to novel therapies.

Unfortunately, there are currently no safe and effective drugs to treat obesity. MCOR researchers are working with pharmaceutical companies as well as with researchers at the School of Pharmacy at the University of Mississippi to develop better drug therapies for obesity and diabetes. Bariatric surgery is also an option for patients who have severe obesity and the **UMMC Bariatric Surgery Program**, under the leadership of **Dr. Kenneth Vick**, resumed in November, 2013, providing a surgical means of weight loss.

A major goal of the MCOR is to develop "wellness" programs aimed at obesity prevention. UMMC health care professionals are working to

develop wellness programs for our employees and for communities throughout Mississippi. A great example of this effort is the **Community Health Advocates Program**, a joint effort of the **Healthy Linkages and Southern Remedy** programs at UMMC (see brief description in this newsletter).

The MCOR programs are currently funded mainly from extramural sources, including gifts from generous donors and grants from the National Institutes of Health (NIH). This past year the MCOR received a \$500,000 gift (\$100,000 annually for 5 years) from **AFLAC**, the insurance giant, to support building a team of basic, clinical and population scientists specializing in obesity, diabetes and related research. **Joe and Kathy Sanderson** provided a \$2 million gift to establish an endowed chair in the MCOR; this generous gift will enable us to recruit a distinguished researcher to help lead the MCOR. The National Institute of General Medical Sciences of the NIH awarded us a \$11.4 million research grant (over 5 years) to establish a Center of Biomedical Research Excellence that will provide funding for research core facilities, research projects, equipment, and training of the next generation of researchers who will help translate discoveries into novel therapies for obesity and related cardiovascular, kidney and metabolic diseases.

Looking back at the accomplishments in 2013, we have many people to thank for their strong support. We are fortunate to have an outstanding group of researchers at UMMC and many dedicated health care professionals and support staff who are working hard to improve the lives of Mississippians. This newsletter provides just a few highlights that I hope you enjoy reading. Thanks for your support.



John E. Hall, Ph.D.
Arthur C. Guyton Professor and Chair
Director, Mississippi Center for Obesity Research



Dr. John Hall

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Revitalized bariatric surgery program already notching **success stories**



Elizabeth Beasley with Dr. Kenneth Vick

Elizabeth Beasley has so much energy she can't lie still for a nap, and not that she wants to.

She's shed 80 pounds since Dec. 9, when she became the first patient to undergo a weight-loss procedure in UMMC's just-revived bariatric surgery program. Beasley, operations director of the University Physicians Grants Ferry Clinic, has happily embraced a lifestyle change in which her health trumps the eventual number of pounds she'll lose.

"I didn't do this to get skinny," said Beasley, 40, a Ridgeland resident who now exercises at least once daily. "I did this to live life. I have more energy now than I remember having in my 20s. I'm not diabetic anymore. I'm not on high blood pressure meds anymore."

The bariatric surgery program, a collaboration with the UMMC-based Mississippi Center for Obesity Research, is fast meeting its new goals of completing 50 procedures this year while impacting the understanding and treatment of obesity. The program briefly went on hiatus so that physicians could develop other resources for Mississippi's obese population, but now is fully operational, with Dr. Kenneth Vick, associate professor of surgery, leading the rejuvenation.

Bariatric surgery offers the morbidly obese the option of weight loss that's more rapid than with conventional diets, and it can save the lives of patients who suffer from obesity-related diseases such as type 2 diabetes, high blood pressure and heart disease. Life

expectancy and the quality of life are dramatically improved, and other related conditions such as acid reflux and sleep apnea can disappear altogether.

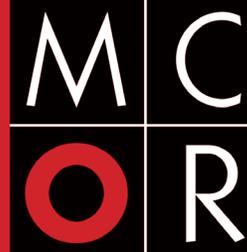
Adam Dungey, administrator of weight management services for the bariatric program, and the bariatric medical team that includes bariatric nurse practitioner Jennifer Godbold, registered nurse coordinator Darla Byrd and dietitian Paul Robertson, are evaluating candidates for the surgery. Since December, Dungey said, 12 people have had procedures. "We have another 15 people who are either scheduled, or in a work-up now, to have the surgery over the next six to eight weeks," Dungey said.

Those selected will have a gastric sleeve, the less invasive and lower-risk laparoscopic surgery Beasley had, or either gastric bypass or gastric banding. All are performed on the stomach and/or intestines.

In Beasley's case, she weighed 284 when she arrived at the University Hospital Short Stay Unit. She was released in just two days, had a two-week recovery at home, "and was bored to death and felt great the whole time," Beasley remembered.

"We are seeing very similar results like Elizabeth's with other patients," Dungey said. "One had surgery in February and is down 50 pounds. We are offering them accountability and support, with lifelong follow-up."

The surgery requires a lifestyle change in diet and exercise, and often results in changes in the way the digestive system processes food. Patients must take care



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RESEARCH

New funding from Aflac, NIH to boost MCOR missions

A recent gift by insurance giant Aflac and a federal research grant package will help the Mississippi Center for Obesity Research turn the state's status of most obese to its advantage.

A \$500,000 gift from Aflac and an \$11.4 million National Institutes of Health research grant package will fund new hires, research projects and new equipment, and will help move laboratory findings into clinics to treat patients and clinical observations into labs for detailed analysis.

Now at three years young, and with Dr. John E. Hall, professor and chair of physiology and biophysics, recently installed as its director, MCOR has donned its tracksuit and laced its running shoes.

"The gift from Aflac and our recent NIH award both recognize the health crisis that obesity poses to the U.S. and particularly in Mississippi, and reinforces our ability and obligation to address the crisis on multiple fronts," Hall said.

The Aflac funding, \$100,000 annually for five years, will be used mainly to recruit new faculty, he said.

The center heretofore used hardcore laboratory studies to drill into the fundamentals of what makes obesity happen on molecular, cellular and bodily system levels.

But Hall seeks a broader role for MCOR. In the coming five years, he wants to build a team of basic, clinical, and population scientists specializing in obesity, diabetes and related research.

A multidisciplinary team can translate laboratory results into clinical uses that improve the health of patients or, likewise, take clinical observations and population-study findings into research labs for more detailed analysis.



The Mississippi Center for Obesity Research membership is a multidisciplinary team of scientists – including physiologists, neuroscientists, pharmacologists and biostatisticians – and physicians from cardiology, nephrology, endocrinology and rheumatology specialties.

From rear, left to right are, Dr. Kenneth Butler, Dr. Stanley Smith, Dr. Herman Taylor, Dr. Michael Lehman, Dr. Richard Roman, Dr. Michael Griswold, Dr. James Wilson, Dr. Jane Reckelhoff, Dr. Elise Gomez-Sanchez, Dr. Barbara Alexander, Dr. Joey Granger, Christine Purser, Dr. Zibiao Guo, Dr. Heather Drummond, Dr. Alexandre da Silva, Dr. Thomas Lohmeier, Dr. Jan Williams, Dr. Albert Dreisbach, Dr. David Stec, Dr. Luis Juncos, Dr. Jussara do Carmo, Dr. Celso Gomez-Sanchez and Dr. John Hall.

"We also want to develop better treatment programs for obesity, a state-of-the-art bariatric surgery program and a wellness program, which would not only help people lose weight, but also prevent obesity," Hall said.

Outcomes research would collect data on treatments and programs to decipher what methods work best in which situations.

MCOR would develop into a hub to connect researchers, health-care providers, state and local governments, business leaders and community groups to work toward solutions.

The lab work, called basic science research, will continue, too. The \$11.4 million from the National Institutes of Health will fund a plan that includes four projects of junior investigators, three core facilities, pilot grant programs and several training mentorship programs.

Two of the junior faculty-led projects investigate diabetes and other kidney diseases closely associated with obesity. The other two focus on how the nervous system and a particular hormone produced by fat influence the heart, kidneys and blood pressure system.

The NIH grant is an Institutional Development Award (IDeA), specifically for institutions in states with underdeveloped research infrastructures.

For years, Hall has maintained that Mississippi's obesity title makes it a prime location for obesity-related research.

Hall said he has an ambitious plan for MCOR, and like solving the obesity crisis itself it won't happen overnight.

Whether in the world of science, education, policy or prevention, MCOR's workout has just begun. But with momentum from its new resources, Hall said it's already finding its stride.

— Jack Mazurak

Why Does Obesity Cause High Blood Pressure?



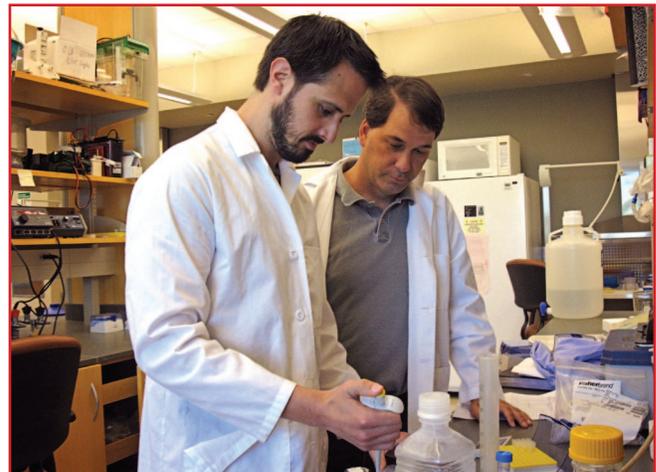
From left, Sydney Moak, Dr. Jussara do Carmo and Kasra Mokhtarpouriani

Dr. Jussara do Carmo, assistant professor of Physiology and Biophysics, and her team are studying the hormone leptin, which is produced by fat cells. Leptin regulates appetite, body weight, glucose, motor activity, and increases blood pressure in obesity. It acts on the brain to activate proopiomelanocortin (POMC) neurons, to promote the release of alpha-melanocyte stimulating hormone which is the endogenous activator of melanocortin-4 receptors (MC4R) in the brain. The importance of the leptin-brain melanocortin system on body weight regulation is evident by the fact that leptin deficiency or MC4R loss-of-function mutations cause morbid obesity in experimental animals as well as in humans. Recently, Dr. do Carmo showed that deletion of leptin receptors only in POMC neurons completely eliminated the effects of leptin to raise blood pressure but did not alter leptin's ability to reduce appetite or to improve glucose usage by the body. These observations indicate that leptin controls appetite by action on non-POMC neurons whereas leptin's cardiovascular actions are dependent on POMC neurons. Dr. do Carmo's group also demonstrated the importance of MC4R in POMC neurons on body weight regulation and blood pressure responses to stress. Her lab is currently investigating the intracellular signaling mechanisms and brain regions that participate in the regulation of body weight and cardiovascular function by the leptin-melanocortin system axis. These studies are expected to provide new insights into fundamental mechanisms controlling body weight and blood pressure with broad implications for the treatment of obesity and obesity-induced hypertension. Dr. do Carmo's research is funded by the Center for Biomedical Research Excellence (COBRE) grant from the National Institutes of General Medical Sciences, National Institutes of Health.

Why are African-Americans more prone to Chronic Kidney Disease?

Dr. Albert Dreisbach, associate professor of medicine, is trying to determine why African-Americans have a higher prevalence of kidney disease and are four times more likely to progress to kidney dialysis than Caucasians. The major focus of his research is on the role of urinary and blood lipids (eicosanoids) in the development and progression of chronic kidney disease in African-Americans. Dreisbach and staff have shown a link with these substances and kidney filtration and high protein levels in the urine, an early marker of kidney disease. They are also looking at genes that affect these substances using data from the **Jackson Heart Study**, the largest African-American study population in the country, and a study of patients recruited from the Jackson metro area. This study may lead to the development of medications to treat chronic kidney disease in the future and prevent it from progressing to dialysis. Dr. Dreisbach's research is funded by the Center for Biomedical Research Excellence (COBRE) grant from the National Institutes of General Medical Sciences, National Institutes of Health.

Can Carbon Monoxide (CO) Releasing Drugs Prevent Obesity?



From left, Dr. Peter Hosick and Dr. David Stec

A team of researchers led by **Dr. David Stec**, associate professor of physiology and biophysics, recently identified a potentially new class of anti-obesity drugs which release small amounts of carbon monoxide (CO) to prevent obesity and the development of type II diabetes in mice fed a high fat diet. CO is an odorless, tasteless gas which can be lethal if inhaled at high amounts but it is also produced naturally in the body where it has several functions. Dr. Stec's research team developed drugs that release small amounts of CO and when mice were treated with these drugs they developed less obesity and milder type II diabetes despite eating the same amount of high fat food as mice which received an inactive drug. Treatment with the CO donor drug caused weight loss by increasing the metabolism of the mice that received the drug. The changes in metabolism were associated with a conversion of the fat tissues of the mice to dramatically increase

their ability to burn fat instead of storing it. The studies were performed by Dr. Peter Hosick, a post-doctoral fellow in Dr. Stec's lab, and recently published in the International Journal of Obesity. The research team is performing further studies to determine if they can reverse established obesity and diabetes by treatment with the CO donor drugs. They are also working with researchers in the department of medicinal chemistry at Ole Miss to further develop the CO releasing drugs so that they could eventually be used in obese human patients. Dr. Stec's research is funded by a grant from the National Heart, Lung, and Blood Institute.

Can Some Fat Be Good For You If It Is Stored In The Right Places?



From left, Dr. Tarek Aba-Elhamid, Dr. Vishnu Garla and Dr. Angela Subauste

The research of Dr. Angela Subauste, assistant professor of medicine, suggests that not all fat is bad and that subcutaneous adipose tissue may serve a protective role in obese individuals. Patients predisposed to the development of type 2 diabetes and heart disease have a more limited capacity of storing fat in subcutaneous adipose tissue which leads to fat storage in other tissues such as the liver, heart and kidneys where it has toxic effects. In collaboration with the Jackson Heart Study she is studying the adipose tissue of obese but healthy individuals and is comparing it to that of unhealthy obese participants. The goal is to determine why the adipose tissue of the unhealthy obese group is unable to store fats appropriately. Dr. Subauste's research is funded by a grant from the National Institutes of Health.

How Do Fat Cells Communicate With The Brain To Regulate Glucose?

Dr. Alexandre A. da Silva, assistant professor of physiology and biophysics at UMMC, is trying to understand how the brain regulates glucose levels in the body. Dr. da Silva and colleagues have shown that leptin, a hormone produced by fat cells in proportion to the degree of adiposity, acts in the brain to produce a very powerful antidiabetic effect. They demonstrated that this effect is so powerful that it can normalize glucose levels even in animals that do not produce insulin, a major regulator of glucose levels. The team has also observed that the commonly accepted mechanisms that have previously been used to explain how the brain regulates peripheral glucose levels do not

appear to mediate the antidiabetic actions of leptin. The main goal of Dr. da Silva's laboratory is to understand how the brain communicates with peripheral tissues to improve glucose metabolism and reduce liver glucose production in response to leptin. The team is also investigating the brain areas that are most important in mediating this effect and the intracellular signaling pathways that are activated by leptin and contribute to its antidiabetic actions. For instance, they have already shown that intact brain melanocortin-4 receptors are required for leptin to exert its effects on peripheral glucose levels. The team is hopeful that once these questions are answered it will be possible to develop novel and improved strategies to treat diabetes and insulin resistance. Dr. da Silva's research is funded by the Center for Biomedical Research Excellence (COBRE) grant from the National Institutes of General Medical Sciences, National Institutes of Health.

Effects Of Obesity On Brain Blood Vessels.



From left, Dr. Sean Didion and Leslie Miller

Dr. Sean Didion, associate professor of pharmacology and toxicology, is studying the long-term effects of obesity on the function of blood vessels in the brain. Clinically, obesity is associated with an increased risk of cerebral vascular disease and events such as Alzheimer's disease and stroke. Understanding the mechanisms that contribute to obesity-related impairment of blood vessel function may lead to development of therapies directed at limiting the negative consequences of obesity on the brain circulation. Recently, Dr. Didion's team focused on the specific contribution of fat tissue to the impairment of blood vessel function as fat tissue can release several molecules that can circulate in the blood and then affect tissues elsewhere in the body. In collaboration with Dr. Michael Garrett, associate professor of pharmacology, Dr. Didion's team has identified a novel gene, GPR50, which increases its activity several fold in response to diet-induced obesity in mice. The increased activity of this gene appears to be related to the increased levels of leptin, a hormone that increases when body fat mass increases. Dr. Didion's team is currently working to determine whether GPR50 expression is also increased in fat tissue from obese humans and his team is working to identify the functional role of GPR50 in adipose tissue. Dr. Didion's research is funded by a grant from the National Heart, Lung and Blood Institute of the National Institutes of Health.

Obesity Research News continued

Novel Approaches In Treating Diabetes-Induced Kidney Disease.

Dr. Jan Michael Williams, assistant professor of pharmacology, focuses his research on the pathophysiology of diabetic kidney disease. Diabetes is one of the most common causes of chronic kidney failure and end-stage renal disease (ESRD). The early stages of diabetes are characterized by increases in arterial pressure being transmitted to the kidney which may lead to increases in several vasoactive mediators, including matrix metalloproteases (MMPs) that contribute to the development of diabetic nephropathy. Dr. Williams uses several genetic rodent models of diabetes that display similar characteristics of diabetic kidney disease as seen in human patients. Recently, his laboratory found that MMPs are increased during the development of diabetic nephropathy and inhibitors of this pathway slow the development and may even reverse renal disease. However, whether increases in transmitted pressure to the kidney activate MMPs remains to be determined. His research team believes that MMP inhibitors may hold the potential to prevent the progression of renal disease in millions of patients



From left, Lateia Taylor, Dr. Jan Williams and Kasi McPherson

suffering from both CKD and ESRD. Dr. Williams' recently received funding for his research from the Center of Biomedical Research (COBRE) grant awarded to the MCOR.

Faculty News



Intapad

Dr. Suttira Intapad, instructor in the Department of Physiology and Biophysics, received the Novel Disease Model Award from the American Physiological Society, at the Experimental Biology Meeting in San Diego in April. During the meeting, she presented her study on "A new model of intrauterine growth restriction (IUGR) induced by reduced uterine perfusion in the mouse program hypertension in the IUGR mouse offspring".

Dr. Michael Garrett, associate professor of pharmacology and toxicology, received the Excellence in Research Award in October for his research contributions to the University of Mississippi Medical Center.



Garrett



George

Dr. Eric George, assistant professor in the Department of Physiology and Biophysics, received a Pathway to Independence Award from the National Institutes of Health in April. With the three year grant, he will seek to elucidate the underlying mechanisms which cause the symptoms of preeclampsia, and test new therapeutic approaches for its management.

Dr. Angela Subauste, assistant professor of medicine, received a grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health. With this study, she and her team will investigate the potential role of lipid signals in the generation of adipogenic defect.



Sabauste



Reckelhoff

Dr. Jane Reckelhoff, director of the Women's Health Research Center and professor of physiology and biophysics, received the 2013 Harriet Dustan Award from the Council for High Pressure Research of the American Heart Association. This award recognizes female investigators who have made outstanding contributions in the field of hypertension.

Dr. John Hall, director of the Mississippi Center for Obesity Research and professor and chair of physiology and biophysics at UMMC, received the 2013 Distinguished Alumni Award and was inducted into the College of Education, Health, and Human Services Hall of Fame at Kent State University.



Hall

Hill delivers Hearin Distinguished Lecture focusing on Obesity

Dr. James O. Hill, Anschutz Professor of Health and Wellness, professor of pediatrics and medicine and executive director of the Anschutz Health and Wellness Center at the University of Colorado School of Medicine presented the Robert M. Hearin Distinguished Lecture on Thursday, October 17 at the University of Mississippi Medical Center, sponsored by the Mississippi Center for Obesity Research (MCOR), Office of Research and the Department of Physiology & Biophysics. His lecture focused on "Promoting Wellness from the Leanest to the Fattest States in the U.S."

During his lecture, Dr. Hill offered suggestions drawn from his own experience as executive director of the Anschutz Health and Wellness Center, one of the nation's top obesity treatment and research facilities.

Being the most obese state can work to MCOR's advantage, he said. Hill stated that MCOR needs a robust obesity-treatment program - one that includes integrative medicine and non-traditional methods - as the clinical core component to its basic science research. And Hill advocated partnering with the food industry, detailing how Anschutz created 95,000



From left, Dr. James O. Hill receives the Robert M. Hearin Distinguished lecture plaque from Dr. John Hall.

square-foot building that integrates a research gym for campus employees and study participants, a small grocery store for consumer psychology research, demonstration kitchens and gathering spaces conducive to creating solutions and community involvement.

— Jack Mazurak

Revitalized Bariatric Surgery Continued

not to eat too much or eat the wrong foods, which can cause vomiting and other digestive problems.

Beasley "is a motivator for the Grants Ferry staff, the bariatric staff, and for other patients in the program," Dungey said. "She walks every day at lunch, in addition to once or twice at home, and she has a group of walkers from the Grant's Ferry employees."

"We are obtaining excellent results with our bariatric operations, both in terms of weight and comorbidity reduction," Vick said. "Most of our patients are already beginning to decrease the numbers of medications they are taking for diseases such as type 2 diabetes and high blood pressure."

Significant results are being seen as little as four to six weeks after surgery, Vick said. "Patient satisfaction rates have also been very high, due in large part to the work they put in before and after surgery to make the necessary lifestyle adjustments."

The program also offers non-surgical avenues for weight loss, Dungey said. "There might be a patient who doesn't want to have

surgery but who needs help, or patients who are too large or have too many risks to undergo the surgery. We help them lose weight in a medically supervised program."

Another goal, Vick said, is for the program to win Center of Excellence Accreditation from the Metabolic and Bariatric Quality Improvement Program. "We are also working towards collaborative research efforts with the Mississippi Center for Obesity Research to improve the overall health of Mississippians," he said. "We are continuing our outreach efforts to providers around the state, and word is already getting around. We are seeing an influx of not only new patients, but complex postoperative bariatric surgical patients that might have been lost to follow-up from programs in another state or country."

UMMC's bariatric surgery program "is very competitive in the market," Dungey said. "My staff, the research team, and the OR teams are all very excited about re-offering this specialty service."

— Ruth Cummins



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The University of Mississippi Medical Center Community Health Advocate Program



The goal of the Community Health Advocate Program at UMMC is to identify individuals with undiagnosed hypertension, diabetes and obesity, improve their health literacy, refer them to appropriate medical care and thus reduce health disparities in the state. The CHA program coordinates its activities with UMMC, as well as community and faith-based organizations. This

initiative is a joint effort of UMMC through its Healthy Linkages Program, its affiliation with Southern Remedy Programming at Mississippi Public Broadcasting, and other willing organizations.

The CHA program uses a formal curriculum to provide lay individuals, as well as health care professionals, students and educators the skillset to be successful advocates and health screeners in their communities. The skillset provided includes the ability to take accurate blood pressure, measure blood glucose, calculate body mass index and provide basic dietary counseling in a fashion that respects patient confidentiality and culture.

UMMC leaders of the CHA program are Michael L. Jones, (Office of the Vice Chancellor), Richard deShazo, Deborah Minor (Department of Medicine), and Josie Bidwell and Lisa Haynie (School of Nursing). Thus far, over 1,500 community health advocates have been trained, including medical, nursing, and dental students, students in the School of Health Related Professions, representatives from many churches across the state, teachers, and barbers.

Key partners with UMMC in this effort include:

- The Mississippi Conference of the United Methodist Church
- William Carey University School of Osteopathic Medicine
- The Mississippi Band of Choctaw Indians
- Mississippi Department of Education Office of Career and Technical Education
- Mississippi Delta Health Collaborative (Mississippi State Department of Health Office of Preventive Health)
- Governor Phil Bryant's Health Teens for a Better Mississippi Program
- City of Charleston, Mississippi
- Tougaloo College
- University of Mississippi (Oxford campus)

For further information about the CHA program, please contact Michael Jones at mljones2@umc.edu.