MCOR MISSISSIPPI CENTER FOR OBESITY RESEARCH

OBESITY RESEARCH NEWS

AT THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER

Vol. 1 Issue 1 | SPRING 2013

Introduction and overview letter from Dr. John Hall

A stack of 30-plus obesity-related studies, articles and book chapters that UMMC faculty published just since the launch of the Mississippi Center for Obesity Research (MCOR) less than two years ago indicates one thing:

We're on the move.

In addition to our published research output, faculty members from schools and departments across the University of Mississippi Medical Center campus have made at least two dozen oral and research poster presentations at professional association meetings in the past couple years.

We've also raised nearly $3 million and have commitments for another $350,000. We finished construction on a whole floor of prime-quality laboratory space dedicated to MCOR. And we organized the hugely successful Global Obesity Summit 2010.

The Global Obesity Summit, held in November 2010, attracted more than 560 scientists, researchers, business leaders and health policy makers representing 28 U.S. states and 15 countries. This gathering demonstrated the commitment at many levels to addressing obesity in our state and nation.

We were honored to welcome notable national speakers to Mississippi, including Kathleen Sebelius, secretary of the U.S. Department of Health and Human Services, Dr. Kenneth Cooper, founder and chairman of the Dallas-based Cooper Clinic and Karen Miller-Kovatch, chief scientific officer of Weight Watchers International.

Their contributions sharpen our understanding of the problem and focus our collective energies on the missions of reducing obesity and improving the health of Mississippians.

Building our obesity center

This year we're conducting an international search for a director of MCOR. We're identifying candidates who are both highly accomplished obesity researchers and proven leaders ready to build a world-class center.

Construction of the center's core physical infrastructure, the fifth-floor of the Arthur C. Guyton Research Center, is complete. The space includes first-class laboratories, equipment rooms and offices. This cutting-edge facility will help us recruit and retain investigators for MCOR.

We've also begun building a team of accomplished researchers for the center's core membership. By including researchers from a variety of departments and backgrounds – including anatomists, biochemists, physiologists, pharmacologists and physicians – our multidisciplinary team will approach the problems of obesity and related diseases from many angles.

Dr. Jussara do Carmo, assistant professor of physiology, left, and Dr. John Hall, professor and chair of physiology, discuss genetic differences in mice that result in weight gain.

As well, we're training graduate students and post-doctoral fellows. They are the next generation of researchers.

But whether in the world of science, education, policy or prevention, our work has just begun. The impact obesity makes on our health, the prosperity of our state and our future generations has never been greater.

We ask your help in making MCOR a first-class center for research, clinical care and prevention. For more information, contact UMMC's research development business administrator, Rachel Jones at (601) 815-5000 or MCOR@umc.edu.

Thank you for your continued interest and support.

Sincerely,

John E. Hall, Ph.D,

UMMC Associate Vice Chancellor for Research

MPB explores Mississippi's **BIG** Problem

Dr. Rick deShazo interviews Dita McCarthy in a Bay St. Louis farm market she started while MPB videographer Jeremy Burson shoots the scene for the Mississippi's Big Problem documentary series about obesity.

To explore and further educate Mississippians about obesity, the Medical Center and Mississippi Public Broadcasting paired up to produce television documentary series, Mississippi's Big Problem.

The four-segment series detail the state's obesity crisis, the effects of obesity on the body and the economics effects of obesity on the state.

Produced under Mississippi Public Broadcasting's Southern Remedy program and hosted by UMMC Professor of Medicine Dr. Rick deShazo, Mississippi's Big Problem episodes debuted on MPB-TV in 2011 but are available anytime online.

Jenny Wilburn, executive producer of Southern Remedy, said the final episode gets to the root of a dichotomy. Mississippi receives federal money directed toward obesity. However, low productivity and high health-care costs plague the state, due in part to obesity.

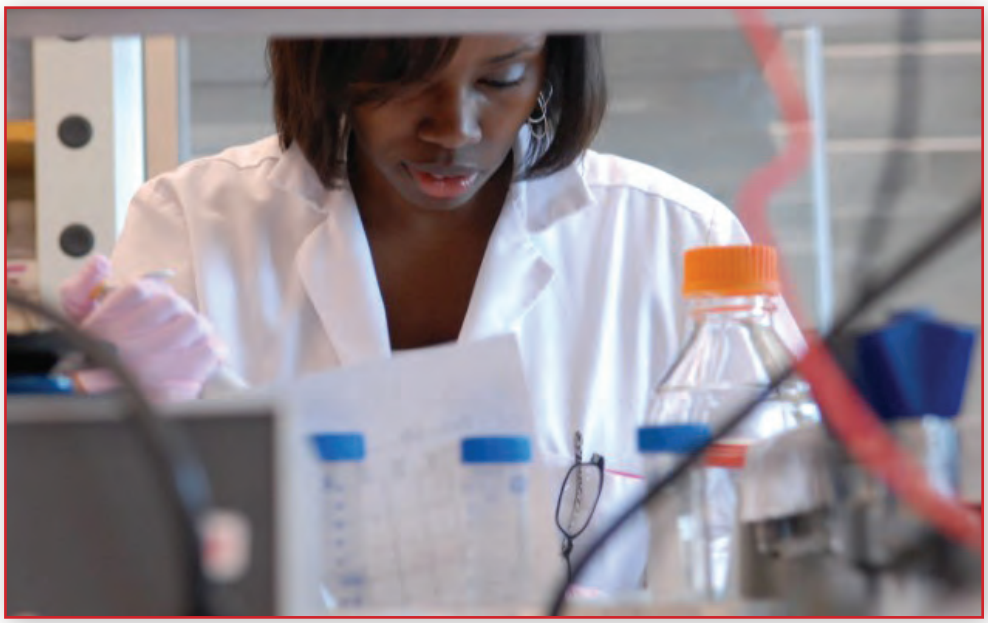
As an educational series, Mississippi's Big Problem strives to help people understand the grave nature of obesity. Obesity and related co-morbidities including hypertension, heart disease, cancer and diabetes devastate the state's population. Through awareness and education, the show can equip people to make better individual and collective decisions.

To view the episodes, visit www.mpbonline.org/southernremedy/ and scroll down to the Television Episodes section. On his Southern Remedy radio show, which airs Wednesdays at 9 a.m., deShazo and guests discuss medical topics and take listener questions.

Northington wins **weight-loss** competition

Dr. LaDonna Northington, professor of nursing, won a friendly biggest loser-style competition this summer among School of Nursing faculty. Northington was announced winner during a celebration this month by program organizer Josie Bidwell. In all, 16 participants lost a total of 144 pounds in eight weeks.

With $2M gift
Sanderson family endows **obesity research chair**



The Mississippi Center for Obesity Research at UMMC received a $2 million gift from Joe and Cathy Sanderson of Sanderson Farms.

The gift has endowed a chair for a distinguished researcher. Dr. John Hall, associate vice chancellor for research, said the money from the Sanderson family will be very beneficial.

"An endowed chair will be a major advantage in helping us to attract a leading obesity researcher to become the center director," said Hall, who also chairs a search committee to fill the researcher position.

Mississippi leads the nation in the percentage of obese adults and children. While some public-education efforts exist, no aggressive coordinated strategy addresses all the issues surrounding obesity, including prevention and treatment. Also, the state lacks a center devoted to scientific and medical research of obesity. MCOR will strive to serve those needs, Hall said.

The center will be located on the fifth floor of the Arthur C. Guyton research building at the UMMC campus. Though MCOR's offices and labs are established, many other needs remain. The center requires funding for staffing of senior and junior researchers and lab techs as well as equipment.

"It is the first large gift from the community of Mississippi and therefore demonstrates to others in Mississippi the importance of the center in addressing the impact of obesity on the health and economy of Mississippi," Hall said.

Joe Sanderson, CEO and Sanderson Farms board of directors chairman, said he and his wife, Kathy, were impressed by the idea of the obesity center. They wanted to help.

"When (University of Mississippi Chancellor) Dr. Dan Jones talked to us about what they wanted to do as far as creating a chair for research, teaching and outreach for obesity we thought that was a good thing for Mississippi. We were aware of the problem that Mississippi faces with obesity and we thought the center would be impactful and helpful for the people of Mississippi," Sanderson said.

The center delves into more than just research on obesity. MCOR also aims to improve Mississippi's economy. Obesity affects people's lives, but also affects the workplaces as well. Obesity – linked with hypertension, diabetes, and other diseases – increases the cost of health insurance for employees and employers.

Duane O'Neill, president and CEO of the Greater Jackson Chamber Partnership, said obesity lowers quality of life and hurts the economy. An unhealthy work force can lower a business' productivity and, in a regional sense, make recruiting new businesses more difficult.

"The workers are not as productive if they are fighting the effects of obesity. It's important to small and large businesses to understand this problem. Mississippi is still leading the nation in obesity and we don't want to be there. We are the walking laboratory and this (UMMC) seems to be the place to do the study," O'Neill said.

Collaboration between MCOR and the Greater Jackson Chamber Partnership showcases the importance of employers encouraging healthy living habits. Sanderson understands that too.

"Sanderson Farms has over 11,000 employees, most of whom are in Mississippi. We are well aware that wellness and good health are very much a part of the work force. The center is one area that will help the state to go forward," he said.

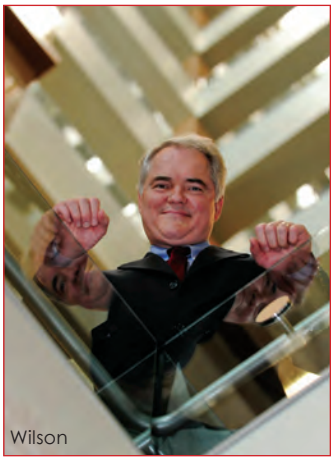
Ultimately the center aims to improve the health of Mississippians through outreach, education, research, prevention and treatment to reduce obesity related death and disease. Donations like the one from the Sanderson family make all of this possible.

"The people of Mississippi are very fortunate to have the Medical Center and what it has become and what it is going to be," Sanderson said. "We believe that as far as research, teaching and providing medical services, the vision that they have for the Medical Center is fantastic. We just hope we can help in a very small way in accomplishing that vision."

— Stephanie Gandy

Obesity Research News

For more information about MCOR research visit: www.umc.edu/mcor/currentresearch


Wilson

Investigators from the Jackson Heart Study have joined a major international effort to find the genetic causes of type 2 diabetes, the most common kind, which typically occurs in overweight or obese adults. The study, known as the T2D-GENES Project, is led locally by **Dr. Jim Wilson**, UMMC professor of physiology and biophysics, who also serves on the project steering committee. Scientists from several continents are working together to determine the genetic sequence of all parts of the genome that code for proteins, known as the coding sequence, in each of 10,000 people recruited from five ethnic groups. Those groups are African Americans, Hispanic Americans, European and European Americans, East Asians made up of Chinese and Koreans, and South Asians, made up of Indians. Half of the participants in each ethnic group have type 2 diabetes and half do not. By comparing the genetic coding sequence in people with and without diabetes, researchers expect to find genetic differences that change the structure and function of key proteins, thus contributing to type 2 diabetes. This is the largest genetic sequencing study targeting the coding sequence. It is also the largest study of coding sequence to focus on a single disease. The scientists expect to find some coding variations that affect the body's ability to produce insulin, and other variations that alter how insulin controls sugar production and transport in the body. In the future, researchers could use new medications to target any of the proteins found to alter these functions, allowing safer and more effective treatment of diabetes.

Dr. Robert Hester, professor of physiology and biophysics at UMMC, and his research team are working to better understand the effects of obesity on cardiovascular function. In particular, his team is investigating the cardiovascular responses after orthopedic trauma in obese subjects. Working with orthopedic surgeons at UMMC, they found that obese subjects that suffer a bone break followed by mild blood loss, common during surgery, show a greater drop in blood pressure than their normal-weight counterparts. The large decrease in blood pressure can damage the cardiovascular system, leading to cardiovascular shock, kidney failure and death. Hester's research group wants to understand the mechanisms that cause or contribute to the blood pressure decrease. Their research has the potential to lead to new treatments for obese patients with orthopedic trauma.


Hester


do Carmo

Dr. Jussara do Carmo, assistant professor of physiology and biophysics, focuses her research on obesity and how it contributes to cardiovascular diseases. She and her team are studying the hormone leptin, which helps regulate appetite, body weight and blood pressure. Fat cells produce leptin, which interacts with receptors in the brain. In a recent study, do Carmo's group deleted leptin receptors in the brain's proopiomelanocortin (POMC) neurons. They found it eliminated the chronic blood pressure effects of leptin but had minimal effects on the appetite and other metabolic functions of leptin. The findings help researchers understand how leptin regulates metabolic and cardiovascular functions differently. They also indicate leptin's control of appetite happens elsewhere than the POMC neurons, contrary to previous thought. She and her colleagues are investigating other areas of the brain that may be involved in mediating leptin's influence on appetite and energy expenditure. They believe unraveling the mechanisms that regulate body weight and blood pressure in obesity may provide new targets for drug and therapy development to better treat obesity-induced hypertension.


Robinson

Dr. Jennifer C. Robinson, associate professor of nursing, researches physical activity and neighborhood context. She often combines multiple methods including socioeconomic modeling and geographic information systems mapping. In a project begun in 2010, Robinson and colleagues are promoting community cancer screenings, biospecimen collection, healthy eating and physical activity. They worked within the Deep South Network for Cancer Control, which has sites two counties in rural Alabama and two counties in rural Mississippi. They have also begun a weight-loss group trial and are fostering research and career development through three pilot programs. The project is also training new investigators in cancer and health disparities research. The Deep South Network for Cancer Control is funding the project.

A team of researchers lead by **Dr. David Stec**, associate professor of physiology and biophysics, recently determined how increases in a protein called heme oxygenase can result in weight loss in mice genetically bred to be obese. Heme oxygenase is an enzyme found naturally in the body that makes carbon

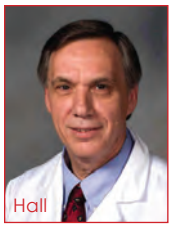

Stec

monoxide and bilirubin. Stec's research team treated obese mice once a week with a specific drug that increased levels of heme oxygenase. The treated mice remained normal weight while a control group not treated became quite obese. Increasing the levels of heme oxygense resulted in weight loss by increasing the metabolism of the mice, thus, the mice lost weight without changing their daily caloric intake. Also, increasing the protein lessened release of harmful factors that promote diabetes and inflammation. Meanwhile the additional heme oxygenase increased the release of factors helpful in fighting inflammation and preventing diabetes. Stec and his team are now working to determine how increases in heme oxygenase ramp up metabolism and change the factors released by fat cells in obesity. The team hopes their findings can lead to development of drugs that would work in a similar way in obese humans.


Russell

Dr. George Russell, associate professor and vice chair of the department of orthopaedic surgery and rehabilitation, along with colleagues Dr. Christine Pierce, Dr. L. Nunley, wrote an article on the financial implications of obesity. They argued that caring for obese patients takes more work and time. They found that was for both operative and non-operative care as well as for injuries and chronic conditions. Yet no system has been proposed to handle reimbursement disparities. The model for health-care reimbursement is changing and the obesity epidemic continues to grow. They recommended discussions take place among all parties to address inequalities in care for obese and morbidly obese patients. The Journal Orthopedic Clinics of North America published the article in its January 2011 issue.

Faculty News


Hall

Dr. John Hall, professor and chair of physiology and biophysics at UMMC, received the Franz Volhard Award for Outstanding Research during the International Society of Hypertension's annual meeting Oct. 3 in Sydney. The award recognizes Hall's research into the intrarenal renin-angiotensin system and pressure-natriuresis in hypertension. During the award ceremony, Hall, who is also UMMC associate vice chancellor for research, gave a lecture profiling his research. The award recognizes recipients' contributions in the field of hypertension or in a related discipline.


do Carmo

Dr. Jussara do Carmo, assistant professor of physiology and biophysics, received the 2012 Harry Goldblatt Award for New Investigators during the American Heart Association High Blood Pressure Research 2012 Scientific Sessions, which was held in Washington D.C. Sept. 19-22. The award recognizes an early career investigator each year and highlights her or his contribution toward understanding blood pressure control, hypertension and related cardiovascular disease. In her research, Dr. do Carmo investigates the effects of the hormone leptin on blood pressure and appetite. The presentation marked the second year a faculty member from the UMMC Department of Physiology and Biophysics has won the award. In 2011, Dr. Alejandro Chade, associate professor of physiology received it.

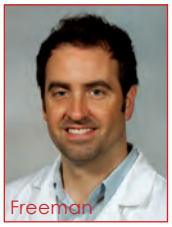

Xiang

Dr. Lusha Xiang, instructor in the Department of Physiology and Biophysics, received a Scientist Development Grant from the American Heart Association in June. With the four-year award Xiang will study how orthopedic trauma impacts pulmonary circulation in obesity and type II diabetes.

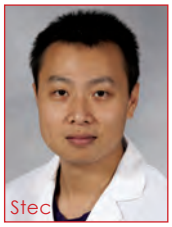

Dubinion

Dr. John Dubinion, instructor in the Department of Physiology and Biophysics, received a New Investigator Award from the Council for High Blood Pressure Research at its meeting in Orlando, Fla. in September. The council is part of the American Heart Association. During the meeting he presented his study on the role of Stat3, a key second messenger protein in leptin signaling. Leptin is a hormone that, in normal-weight individuals, decreases appetite but raises blood pressure. Using genetically modified mice where Stat3 was deleted in a primary target in the brain, Dubinion found the mice became obese and leptin no longer affected blood pressure.

Faculty News cont.



A $112,000 grant **Dr. Kevin Freeman**, assistant professor in the Department of Psychiatry and Human Behavior, received in May from the National Institute on Drug Abuse will pay for a pilot study on motivation and reward behavior. Using groups of obese and lean rats, Freeman will steadily increase the number of times each rat must press a lever to receive a sugar or drug reward. At some point, the amount of work won't be worth the reward. Freeman said he expects the lean rats will quit first. "The study's aim is to see if obesity is associated with greater sensitivity to food and drug reward," he said. "The hypothesis is that obesity may be instigated and perpetuated by heightened sensitivity to the rewarding effects of palatable foods. Extending these tests with a drug of abuse will test the generality of this effect to non-drug rewards."



Dr. Silu Lu, instructor in the Department of Physiology and Biophysics, was awarded a postdoctoral fellowship in July by the American Heart Association. In his study, he will examine the effect of chronic exercise training on blood vessel function during obesity.

Dr. George V. Russell, associate professor of orthopedic surgery, gave a poster presentation, The Impact of Morbid Obesity on Acetabular Fractures, during the American Academy of Orthopaedic Surgeons 2011 Annual Meeting, Poster Presentation, held February 15-19 in San Diego.

In guest lecture Seeley discusses bariatric surgery

During a guest lecture Oct. 24 presented to the UMMC Department of Physiology and Biophysics, Dr. Randy Seeley, professor and Donald C. Harrison Endowed Chair in Medicine at the University of Cincinnati, discussed lesser-known aspects of bariatric surgery.

Seeley, who is in the Department of Internal Medicine, Division of Endocrinology at the University of Cincinnati, and directs of the Cincinnati Diabetes and Obesity Center, titled his talk "Bariatric Surgery: It's Not What You Think It Is. Identifying Molecular Targets of Surgery."

Seeley's research focuses on the actions of various peripheral hormones in the central nervous system that regulate food intake, body weight and the regulation of circulating fuels. In particular, he has focused upon the numerous hypothalamic and gastrointestinal peptides and their associated receptors that influence both energy intake as well as peripheral metabolic processes.

Seeley holds a Ph.D. in psychology from the University of Pennsylvania. During his doctoral training he specialized in behavioral neuroscience and ingestive behavior. He received the 2003 Lilly Scientific Achievement award from the North American Association for the Study of Obesity given to the individual with the highest level of scientific achievement in obesity research in North America less than 15 years after their terminal degree.

UMMC faculty, staff and students attended the lecture.

Women's health researchers probe **cardiovascular risks** of enhanced testosterone

With weight gain, testosterone levels drop in many men, leading doctors to prescribe supplements of the sex hormone.

Testosterone supplements improve feelings of wellbeing, turn up libido and help prevent osteoporosis. They also help the body gain muscle mass.

But the lack of safety data on those supplements, particularly about cardiovascular effects after chronic exposure, prompted researchers at the UMMC Women's Health Research Center to organize an experiment with rats.

Their study found testosterone helped unlace several detrimental knots of obesity. Leptin, glucose and cholesterol levels all fell in the testosterone treated group of obese rats, as did insulin resistance. But blood pressures shot up.

That came as a surprise, given all the other positive numbers.

"What it suggests is that obese men who have less testosterone would benefit from testosterone supplements but that their blood pressures should be monitored carefully," said Dr. Jane Reckelhoff, distinguished professor of physiology and biophysics and the center's director.

The journal Hypertension published the study online in January and printed it in March. A grant from the National Institutes of Health funded the research.

The alarming increase in Americans' waistlines the past decade means millions of people are in or headed for a condition known as metabolic syndrome.

Characterized by fat in the midsection, poor insulin sensitivity, elevated blood pressure and constant low-level inflammation, metabolic syndrome essentially edges a person toward more serious chronic diseases including diabetes, hypertension and heart disease.

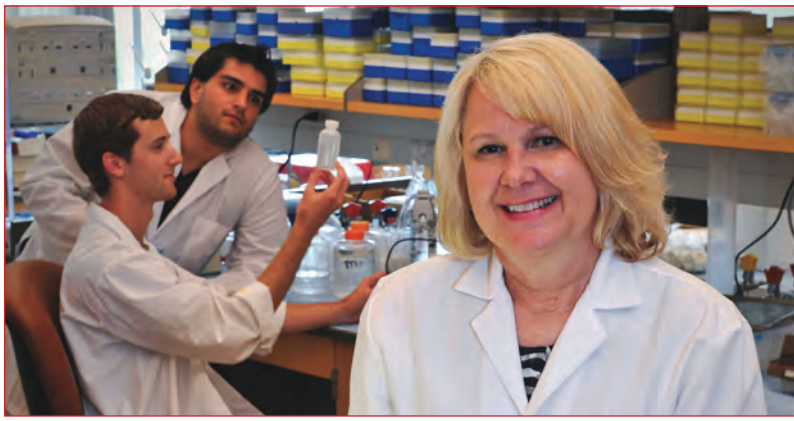
Since men's bodies reduce testosterone output with obesity, which accompanies metabolic syndrome, the researchers wondered if adding supplements would protect against hypertension and cardiovascular disease or speed their progression.

The scientists dosed seven obese male rats and seven lean male rats with testosterone for 10 weeks, time enough to be considered chronic exposure. Two control groups - obese and normal-weight male rats - received no testosterone.

The treated obese rats' weight decreased by 21 percent, insulin resistance improved by 40 percent and their fasted blood-glucose levels were down compared to the untreated obese group. Proteinuria and albuminuria - signs of kidney injury measured in the urine - fell in the treated obese group but increased in the lean test group.

However, blood pressures in the treated obese rats rose on average 10 mm Hg. Meanwhile, blood pressures in the lean rats treated with testosterone didn't change.

In humans, 10 mm Hg can represent enough change to push a person from normal categorization into hypertension.



Dr. Jane Reckelhoff, professor of physiology and biophysics and director of the Women's Health Research Center, investigates sex-based differences in health, including hypertension.

"If men respond to testosterone supplements like rats, they will see positive results like body-fat reductions, increases in lean muscle mass and they'll feel better overall," said Reckelhoff, senior investigator on the study. "But their blood pressures will likely go up and will need to be monitored."

Beyond the obvious liability comparing rats to humans, Reckelhoff said the recent study needs another caveat.

"We increased testosterone levels by tenfold in our rats. That's well past the level you'd see in a normal-weight, middle-aged rat," she said, indicating doctors wouldn't prescribe patients such a high dose of supplements.

Reckelhoff founded the Women's Health Research Center in 2009 to study how gender-based differences - such as sex hormones like testosterone and estrogen - play roles in health and disease.

"Because androgens are illegal in athletics, there are very few studies done in humans on their chronic effects," she said. "The NIH needs to do more safety studies on the long-term effect of testosterone particularly on obese men with regard to their cardiovascular status."

Friedman **focuses on** Leptin in Guyton Lecture

Friedman

Dr. Jeffrey M. Friedman, director of the Starr Center for Human Genetics, professor at The Rockefeller University and investigator at the Howard Hughes Medical Institute, gave the Arthur C. Guyton Distinguished Lecture at UMMC on Sept. 7, 2011.

Friedman, a recognized expert in the genetic aspects of obesity, spoke about how the hormone leptin, which is secreted by fatty tissue, affects body weight and appetite.

He told the crowd of several hundred researchers, students and health-care providers that common refrains about overweight people don't portray the true picture.

"Saying someone is obese because they eat too much simply ignores problem of why they eat too much. There are drivers for appetite," Friedman said.

"Were it any other disease people would immediately accept the conclusion that there is a biological and genetic connection factored in along with other factors such as will and environment. Therefore the important contributions of biology and genetics are underestimated."

Leptin is a key element in the body's negative-feedback loop that creates a biological drive to resist weight changes, both losses and gains, Friedman said.

That helps explain why, within one-to-two years after people lose a substantial amount of weight, diets tend to fail and people return to their previous BMIs.

"When you lose weight by dieting, there's less adipose tissue signaling with leptin. So you get a response from the brain that it's in starvation mode," Friedman said. "Our lab is trying to understand how one molecule - leptin - can control a system as complex as appetite."

UMMC established the lectureship to honor Dr. Arthur C. Guyton, former chairman of the Department of Physiology & Biophysics.

Remembering **Obesity Summit** 2010

Dr. John Hall, standing at podium, addresses guests at the Global Obesity Summit 2010.

Secretary of the U.S. Department of Health and Human Services Kathleen Sebelius, answers questions during a press conference at the Global Obesity Summit held at the Jackson Convention Complex Nov. 9-11, 2010, while Dr. Dan Jones, chancellor of the University of Mississippi looks on.