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UNIVERSITY OF MARYLAND RESEARCHERS IDENTIFY GUT BACTERIA ASSOCIATED WITH OBESITY AND METABOLIC SYNDROME

Additional research to study impact of medicine, diet and lifestyle changes

Baltimore, MD – Aug. 15, 2012. Researchers at the University of Maryland School of Medicine have identified 26 species of bacteria in the human gut microbiota that appear to be linked to obesity and related metabolic complications. These include insulin resistance, high blood sugar levels, increased blood pressure and high cholesterol, known collectively as "the metabolic syndrome," which significantly increases an individual's risk of developing diabetes, cardiovascular disease and stroke.

The results of the study, which analyzed data from the Old Order Amish in Lancaster County, Pa., are being published online on Aug. 15, 2012, in PLOS ONE, which is published by the Public Library of Science (PLOS). The study was funded by the National Institutes of Health (NIH). (UH2/UH3 DK083982, UO1 GM074518 and P30 DK072488)

"We identified 26 species of bacteria that were correlated with obesity and metabolic syndrome traits such as body mass index (BMI), triglycerides, cholesterol, glucose levels and C-reactive protein, a marker for inflammation," says the senior author, Claire M. Fraser, Ph.D., professor of medicine and microbiology and immunology and director of the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine. "We can't infer cause and effect, but it's an important step forward that we're starting to identify bacteria that are correlated with clinical parameters, which suggests that the gut microbiota could one day be targeted with medication, diet or lifestyle changes."

Dr. Fraser says that additional research, including an interventional study with the Amish, is essential. "We can look at whether these bacteria change over time in a given individual or in response to diet or medication," she says. Dr. Fraser notes that the research team, led by Margaret L. Zupancic, Ph.D., then a postdoctoral fellow at IGS, also found an apparent link between the gut bacteria and inflammation, which is believed to be a factor in obesity and many other chronic diseases. "This is one of the first studies of obesity in humans to make a link between inflammatory processes and specific organisms that are present in the GI tract," Dr. Fraser says, noting that participants with metabolic syndrome who had elevated serum markers associated with inflammation tended to have the lowest levels of good bacteria that have been reported previously to have anti-inflammatory properties.

The study is the result of an ongoing collaboration between Dr. Fraser and Alan R. Shuldiner, M.D., in connection with the NIH's Human Microbiome Project, which seeks to characterize microbial communities in the body. Dr. Shuldiner, associate dean for personalized medicine and director of the Program in Personalized and Genomic Medicine at the University of Maryland School of Medicine, operates an Amish research clinic in Lancaster Pa. Over the past 20 years, he and his research team have conducted more than a dozen studies with the Amish, looking for genes that may cause common diseases, such as diabetes, osteoporosis and cardiovascular disease.

"The Old Order Amish are ideal for such studies because they are a genetically homogenous population descended from a few founder families and have a similar rural lifestyle," Dr. Shuldiner, the John L. Whitehurst Professor of Medicine, says. "We believe the results of this study are relevant to a broader population because the clinical characteristics of obesity and its complications in the Amish are no different from the general Caucasian population," he says.

E. Albert Reece, M.D., Ph.D., M.B.A., vice president for medical affairs at the University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and dean of the University of Maryland School of Medicine, says, "Obesity and its related complications have become a critical public health concern, and the number of people who are now considered obese or overweight has skyrocketed. Dr. Fraser and Dr. Shuldiner are two of our most senior research-scientists and leaders in their respective fields. This study provides valuable insights into the role the bacteria in our bodies may play in obesity and the metabolic syndrome. We may ultimately be able to target the gut microbiome to help prevent or mitigate risk factors for a number of diseases."

The researchers analyzed the bacteria in fecal samples of 310 members of the Old Order Amish community, using a process that enables them to identify a marker gene that serves as a bar code for

each type of bacteria. Participants in the study ranged from lean to overweight to obese; some of the obese participants also had features of the metabolic syndrome. "Our hypothesis was that we would see a different composition in the gut microbiota in lean vs. obese individuals and possibly in individuals who were obese but also had features of the metabolic syndrome."

They discovered that every individual possessed one of three different communities of interacting bacteria, each characterized by a dominant bacterial genus. Neither BMI nor any metabolic syndrome trait was specifically associated with any of these communities. Instead, differing levels of 26 less abundant bacterial species present in all individuals appeared to be linked to obesity and certain features of the metabolic syndrome.

Interestingly, researchers also analyzed people's gut bacteria by their occupation and found that those who had regular contact with livestock, such as farmers and their wives, had bacterial communities dominated by Prevotella, a type of bacteria that is also abundant in the gut microbiota of cattle and sheep. "These findings suggest that environmental exposure may play a role in determining the composition of the gut microbiota in humans," Dr. Fraser says.

About the University of Maryland School of Medicine

Established in 1807, the University of Maryland School of Medicine is the first public medical school in the United States, and the first to institute a residency-training program. The School of Medicine was the founding school of the University of Maryland and today is an integral part of the 11-campus University System of Maryland. On the University of Maryland's Baltimore campus, the School of Medicine serves as the anchor for a large academic health center which aims to provide the best medical education, conduct the most innovative biomedical research and provide the best patient care and community service to Maryland and beyond. <u>www.medschool.umaryland.edu</u>.

About the Institute for Genome Sciences

The Institute for Genome Sciences (IGS) is an international research center within the University of Maryland School of Medicine. Comprised of an interdisciplinary, multidepartment team of investigators, the institute uses the powerful tools of genomics and bioinformatics to understand genome function in health and disease, to study molecular and cellular networks in a variety of model systems, and to generate data and bioinformatics resources of value to the international scientific community. The scientific discoveries that are being made at IGS are helping to unravel the mysteries of biological systems and to improve health care for people around the world. http://www.igs.umaryland.edu/

About the Program in Personalized and Genomic Medicine

The Program in Personalized and Genomic Medicine (PPGM) was established at the University of Maryland School of Medicine in 2011. Its mission is to facilitate discovery in personalized medicine

and genomic and other "omic" areas of study; to accelerate the translation of these new discoveries to improve patient care; and to enhance the training and education of future generations of physicians and scientists through a personalized medicine-driven curriculum. Basic science and clinical scientists at all levels across multiple disciplines in the School of Medicine, together with its partner institution, the University of Maryland Medical Center, work toward achieving the program's mission with the ultimate goal of improving treatment and preempting disease in the citizens of Maryland and beyond through individualized health care. http://medschool.umaryland.edu/genetics/

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