FOR IMMEDIATE RELEASE: June 13, 2012
Contact: Karen Robinson (karobinson@som.umaryand.edu)
(410) 706-7590
Sarah Pick (spick@som.umaryland.edu)
(410) 706-0866

UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE PLAYS MAJOR ROLE IN FIRST MAPPING OF MICROBES ON AND IN HUMAN BODY

Series of Coordinated Scientific Papers Published in Nature, PLoS Analyze Human Microbiome Project Data Based at University of Maryland Institute for Genome Sciences

Baltimore, Md. – June 13, 2012. Research scientists at the University of Maryland School of Medicine's Institute for Genome Sciences have played a leading role in mapping for the first time the microbes that live on and in the healthy human body. Trillions of these tiny microorganisms, known as the human microbiome, live inside and outside the human body, sometimes causing illness but usually existing in harmony with their hosts. The Human Microbiome Project (HMP), a $153 million National Institutes of Health-sponsored program that launched in 2007, enlisted a national consortium of researchers, including Institute for Genome Sciences faculty, to sequence the genomes of these microbes in order to learn more about them and how they interact with the human genome. Institute for Genome Sciences research scientists and their colleagues are now reporting their findings in a sprawling series of coordinated scientific reports published on June 14, 2012, in Nature and several journals of the Public Library of Science (PLoS).

The University of Maryland's Institute for Genome Sciences is the home for the Human Microbiome Project Data Analysis and Coordination Center, an elaborate core database system that stores all of the information collected by the consortium, a group of 200-some researchers from 80 institutions nationwide. Owen White, Ph.D., professor and associate director of the Institute for Genome Sciences, was chosen by the National Human Genome Research Institute (NHGRI), part of the NIH, to spearhead the Data Analysis and Coordination Center. The center is a database system that analyzes, organizes and disseminates the genomic information gathered at various sites as part of the Human Microbiome Project. The Data Analysis and Coordination Center makes the information gathered as part of the project available for free to U.S. investigators, making possible the series of papers that were just published.

“We have played a strong leadership and management role in this project,” Dr. White, a bioinformatics expert, says of himself and three fellow Institute for Genome Sciences faculty who worked on the project: Brandi Cantarel, Ph.D., a research associate, Michelle Giglio, Ph.D., assistant professor and associate director for analysis of the IGS Informatics Resource Center, and Anup Mahurkar, M.B.A., executive director of bioinformatics software engineering at the institute. “It was thrilling to be a part of this project,” Dr. White adds. “The sheer volume of data made possible by next-generation sequencing technology simply hasn’t been done before. Work of this kind is being used to investigate the human microbiome and its relationship to diseases like obesity, celiacs and even autism. Based on what we’re learning about the microbiome, it’s beginning to seem possible that relatively simple intervention strategies could really change the quality of life for a lot of people. It is all very exciting.”

The goal of the project was to define the normal, healthy human microbiome in order to provide a point of comparison for the study of the microbiome and its role in disease. The consortium’s researchers sampled 242 healthy U.S. volunteers (129 male, 113 female), collecting tissues from 15 body sites in men and 18 body sites in women (including three vaginal sites). Researchers collected up to three samples from each volunteer at sites such as the mouth, nose, skin (two behind each ear and each inner elbow), and lower intestine (stool); each body site can be inhabited by organisms as different as those in the Amazon Rainforest and the Sahara Desert.

Historically, doctors studied microorganisms in their patients by isolating pathogens and growing them in culture. This painstaking process frequently identifies only a few microbial species, as they are hard to grow in the lab. In HMP, researchers purified all human and microbial DNA in each of more than 5,000 samples and ran them through DNA sequencing machines. Using bioinformatic tools, researchers could sort through all 3.5 terabytes of genomic data and identify specific signals found only in bacteria – the variable genes of bacterial ribosomal RNA called 16S rRNA – that can be used to identify microbial species. Focusing on this microbial signature allowed HMP researchers to subtract the human genome sequences and analyze only the bacterial DNA. In addition, metagenomic sequencing, or the sequencing all the genes in a microbial community,

allowed the researchers to also study the metabolic capabilities coded in the genes of these microbial communities.

Where doctors had previously isolated only a few hundred bacterial species from the body, HMP researchers now calculate that more than 10,000 species occupy the human ecosystem. Moreover, researchers calculate that they have found between 81 and 99 percent of all the genera of microorganisms in healthy adults.

HMP researchers also reported that this plethora of microbes contribute more genes responsible for human survival than humans themselves. Where the human genome carries some 22,000 protein-coding genes that carry out metabolic activities, researchers estimate that the microbiome contributes some 8 million unique protein-coding genes or 360-times more bacterial genes than human genes. In addition, the bacterial genomic contribution is critical for human survival. Genes carried by bacteria in the gastro-intestinal track, for example, allow humans to digest foods and absorb nutrients that otherwise would be unavailable.

Dr. Cantarel used the HMP data to further explore the bacterial communities that allow humans to digest complex plant-based carbohydrates. Scientists already knew that different types of bacterial communities exist in different body sites, but Dr. Cantarel wanted to explore whether these different communities in their various sites of the body still have the potential to perform the same function. She found that they could. “We found that even if you and I have a different majority bacteria in our microbiome, our bacteria have the potential to perform the same functions,” she says. “We’ve never been able to do a study this large to see that result.” Dr. Cantarel also examined different body sites — previously, she had focused only on the bacteria in the stool.

“What we found surprising is that while stool has the largest capability of breaking down these complex carbohydrates, other body sites have a lot of this capacity as well,” she says. “Oral sites and even places like the vagina or the nose have these genes for breaking down complex carbohydrates. Now the question is, how are they getting these complex carbohydrates in the vagina or the nose, and why?”

The question is particularly interesting, she adds, because once the complex carbohydrates are broken down as much as possible, they mediate communication between cells on the cell surface — communication between the host and the microbiome. The access to HMP data made her research possible, Dr. Cantarel says: "This kind of data set is pretty awesome. To get a study with so many samples from so many different body sites on so many different people, samples taken simultaneously — you're not going to find any other study like that," she explains.

The microbiome may also play a role in inflammatory bowel diseases such as Crohn's disease. Researchers at University of Maryland School of Medicine compared the microbiomes of twins with and without Crohn's disease. The results suggest that the microbiome does mediate, at least in part, the effects of genetic and environmental factors on irritable bowel disease. These are among the earliest clinical studies using microbiome data to study their role in specific illnesses. NIH has funded many more microbiome and disease studies using HMP data and techniques, including the role of the gut microbiome in Crohn's disease , ulcerative colitis and esophageal adenocarcinoma; skin microbiome in psoriasis, and atopic dermatitis and immunodeficiency; urogenital microbiome and reproductive and sexual history and circumcision and a number of childhood disorders, including pediatric abdominal pain and intestinal inflammation, and neonatal necrotizing enterocolitis.

In addition to the enormous amount of metagenomic data generated by the HMP, there are numerous additional resources as well. Dr. Giglio comments: "The HMP and DACC have provided the community with around 1,000 new single-isolate complete genomes of reference bacteria that will facilitate the analysis of human microbiome data not just from this project but from any analysis of human bacterial communities." In addition, the HMP has spent considerable effort to standardize laboratory and analysis protocols, not just to keep things consistent across the HMP but to provide a resource for the whole metagenomics community. Dr. Giglio says: "The DACC website contains extensive information on HMP protocols and methods. The HMP and DACC are committed to sharing resources and methods so that metagenomic analysis can be easily accessible to all interested researchers. It is gratifying to be part of an effort that has provided so much data and analysis resources freely to the scientific community."

“Our research scientists at the Institute for Genome Sciences are uniquely positioned for leadership in this research that will unravel the microbiome’s connection to the human genome,” says E. Albert Reece, M.D., Ph.D., M.B.A., vice president for medical affairs of the University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and dean, University of Maryland School of Medicine. “At our multidisciplinary institution, we have basic scientists working alongside clinicians. This collaborative environment makes possible the kinds of translational research that will turn the basic data of the Human Microbiome Project into real treatments for patients and their families.”

####