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**UNIVERSITY OF MARYLAND SCHOOLS OF DENTISTRY AND MEDICINE RECEIVE
\$10.7M GRANT TO CONDUCT SYSTEMS BIOLOGY RESEARCH ON CONTROL AND
PREVENTION OF SEXUALLY-TRANSMITTED INFECTIONS**

Research goal is to identify better diagnostic, vaccine and treatment targets for chlamydia and gonorrhea

BALTIMORE, MD, July 29, 2014 — The University of Maryland Schools of Dentistry (UM SOD) and Medicine (UM SOM) jointly announced today that they have received a five-year \$10.7 million grant award from the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (Grant #2U19A1084044-06) to study the causes, prevention and treatment of sexually-transmitted diseases (STDs). The grant, which renews a previous \$12 million five-year NIAID-funded research program, represents a new direction for the research by studying chlamydial and gonorrheal diseases as the outcome of complex interactions between the host genetics, the urogenital polymicrobial microbiome, and the pathogen’s unique genetics. By applying modern “omics” technology, the study aims at identifying novel molecular “biomarkers” of susceptibility to sexually transmitted infections (STIs), ensuing disease severity, and conversely protection from STIs and STDs. Biomarkers can be measured in the body (or its products) as a means to predict and potentially influence pathways related to disease. They may reveal mechanisms of infection or disease that can be exploited as therapeutic or diagnostic targets.

The long-term goal of the research is to develop strategies and the means to reduce the incidence of STIs and STDs worldwide – particularly chlamydia (caused by *Chlamydia trachomatis*) and gonorrhea (caused by *Neisseria gonorrhoeae*, also known as the gonococcus). Chlamydial genital infections are the most common bacterial infectious disease in America, with 2.8 million cases estimated annually. Gonorrhea is estimated at 820,000 infections in America each year. These infections together cause most of the 750,000 cases of pelvic inflammatory disease seen each year

in the United States. Pelvic inflammatory disease, in turn, is a leading cause of female infertility and life-threatening conditions in women such as ectopic pregnancy.

“This grant is particularly significant because it is the first time that a comprehensive systems biology (or ‘multi-omics’) approach will be utilized to conduct STD research with the ultimate goal of developing knowledge to prognose, diagnose, prevent and treat sexually transmitted infection and disease,” said Jacques Ravel, PhD, Professor of Microbiology and Immunology and Associate Director for Genomics at the Institute for Genome Sciences (IGS) at the UM SOM, who is the co-principal investigator on the study. “By looking at how human genetics and the microbiome affect and influence infections in humans, we can gain a much better understanding of how to protect against these types of infection, which is critical for improving public health.”

“We believe that this project will generate new essential knowledge into the mechanisms of sexually transmitted infection and disease as they occur, both in the human host and within the microbes that cause chlamydia and gonorrhea,” says co-principal investigator Patrik Bavoil, PhD, Professor and Chair of the Department of Microbial Pathogenesis at the UM SOD. “We will be identifying human and microbial biomarkers that will tell us who is most susceptible to infection, who is most susceptible to severe disease, even in the absence of symptoms,” adds Dr. Bavoil, who is also an adjunct professor in the Department of Microbiology and Immunology at the UM SOM. “These biomarkers could also provide us with new targets for new ways to prevent and treat STIs and STDs long before these microbes have a chance to endanger a woman’s reproductive health.”

The new grant establishes one of five nationwide Cooperative Research Centers on Sexually Transmitted Infection (CRC-STI), which will be jointly led by the UM SOM and UM SOD, to implement three projects:

Project 1 will explore the role of human genetic variance in dictating the outcome of the ‘dialogue’ between the pathogen, the microbiota and the host in both experimental infections and patient samples. The underlying hypothesis of this project is that host genetics plays an important role in determining susceptibility to STIs and ensuing disease severity. This project will be led by Drs. Raphael Valdivia and Dennis Ko, both at Duke University.

Project 2, which will be co-directed by Drs. Bavoil and Garry Myers, PhD, Associate Professor at the University of Technology in Sydney, Australia, aims to identify antibody and miRNA-based biomarkers of chlamydia infection, chlamydia/gonorrhea co-infection and pelvic inflammatory disease with a specific focus on the translational potential of these biomarkers in clinical and public health.

Project 3, which will be directed by Dr. Ravel, will employ a systems biology approach to identify biomarkers of the vaginal and penile microbiomes, the genetic variation of the host and pathogens that are associated with increased or decreased risks of infection by chlamydia, gonorrhea or both.

These projects will rely on a strong clinical core, which will establish a STI Network Groups (STING), consisting of multiple networks of sexual partners where at least one of the partners is infected with chlamydia or gonorrhea. The clinical core of the center will involve Drs. Katrina Mark, MD, of the UM SOM Department of Obstetrics, Gynecology and Reproductive Sciences, and Rebecca Brotman, Assistant Professor of UM SOM Department of Epidemiology & Public Health and IGS. Participants in STING will provide clinical specimens, that researchers at the University of Maryland and partner institutions will examine and analyze using cutting-edge genomic, immunologic and genetic techniques, trying to identify novel molecular biomarkers that could help them predict who is at risk for STIs and who is less likely to become infected, based on the subject's own genetics, his/her genital microbiome composition and function, as well as the pathogen's unique genome. The scientists hope to use identified biomarkers to develop new diagnostic and therapeutic approaches for STIs. The projects will be supported by a genomics core led by Dr. Ravel, which will leverage the state-of-the-art capabilities of the Genomics Resource Center and the Informatics Resource Center at the IGS. Additional STI expertise will be provided by biomathematician Dr. David Wilson, of the Kirby Institute, Queensland University of Technology, Sydney, Australia, gonorrhea expert Dr. Alison Criss, University of Virginia, network analysis epidemiologist Dr. David Shoham, Loyola University Chicago and immunologist Dr. Khalil Ghanem, Johns Hopkins University.

The program is based at the University of Maryland, Baltimore, a leading institution in the study of infectious diseases with particular strengths in bacterial pathogenesis, vaccine development, human virology and microbial genomics.

Mark Reynolds, DDS, PhD, MA, Professor and recently named Dean of the University of Maryland School of Dentistry remarked “This grant highlights the ever growing, mutually beneficial, cooperative relationship between the UM SOM and the UM SOD on multiple interdisciplinary research fronts.” He adds “Our school is committed to the concept of global health, and this project on sexually transmitted infections, which are particularly relevant to oral health, is an important focus of our research activities and an essential component of the education portfolio of the modern oral health practitioner.”

“This new NIH NIAID grant is a clear indication of the quality of research and leadership at the UM SOM in studying infectious disease,” said E. Albert Reece, MD, PhD, MBA, vice president for medical affairs at the University of Maryland, and John Z. and Akiko K. Bowers distinguished professor and dean of the University of Maryland School of Medicine. “Our application of large-scale genomics and bioinformatics approaches to investigate the prevention and treatment of STIs truly represents the future of biomedical research.”

About the University of Maryland School of Dentistry

Established in 1840 as the world’s first dental college, the University of Maryland School of Dentistry remains committed to graduating exceptional oral health care professionals. The School strives to promote, maintain and improve the oral and overall health of Maryland residents, while enhancing patient care and contributing to the body of international health research. The School of Dentistry is an integral part of the University of Maryland, Baltimore, a seven-school professional and graduate education institution situated on 61 acres in downtown Baltimore. With its partner schools – Medicine, Law, Pharmacy, Nursing, Graduate and Social Work, we form a vital component of the 11-campus University System of Maryland.

About the University of Maryland School of Medicine

Chartered in 1807, the University of Maryland School of Medicine is the first public medical school in the United States and continues today as an innovative leader in accelerating innovation and discovery in medicine. The School of Medicine is the founding school of the University of Maryland and is an integral part of the 11-campus University System of Maryland. Located on the University of Maryland's Baltimore campus, the School of Medicine works closely with the University of Maryland Medical Center to provide a research-intensive, academic and clinically-based education. With 43 academic departments, centers and institutes and a faculty of more than 1,400 physicians and research scientists and more than \$400 million in extramural funding, the School is regarded as one of the leading biomedical research institutions in the U.S. with top-tier faculty and programs in cancer, brain science, surgery and transplantation, shock trauma and emergency medicine, vaccine development and human genomics, among other centers of excellence. The School is not only concerned with the health of the citizens of Maryland and the nation, but also has a global vision, with research and treatment facilities in more than 30 countries around the world.

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