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UMB Heads \$12.2 Million Study of Chlamydia, Leading Bacteria Public Health Issue

Perhaps the most comprehensive, multi-institutional study yet of the sexually transmitted bacteria chlamydia is under way at the University of Maryland, Baltimore (UMB).

A new \$12.2 million, grant from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, will allow a team of scientists to perform molecular genomics analyses of the disease-causing powers of chlamydia on a scale never attempted before, according to NIH officials.

The team will apply precise genome mapping of changes that happen to the bacteria as it interacts within their natural environment with other microbes in the body. The multidisciplinary expertise of the team brings a unique approach to the study, and it is anticipated that the results will greatly advance scientific understanding of chlamydia, a major cause of infertility in women.

Microbiologist Patrik Bavoil, PhD, associate professor at the Dental School at UMB, who has expertise in the virulence of sexually transmitted diseases (STDs), and researcher Jacques Ravel, PhD, associate professor at the University of Maryland School of Medicine's Institute for Genome Sciences, an expert in microbial genomics, will lead the five-year project.

The scientific team includes experts in clinical human STD studies and others in biostatistical and bioinformatics data analysis. The multidisciplinary team will use state-of-the art genomic

technologies to characterize the relationship between chlamydial infections and the vaginal microbiome, as well as to investigate genomic diversity for this highly relevant public health issue.

According to the Centers for Disease Control and Prevention, chlamydia is the most commonly reported infectious disease in the U.S. The disease can be cured with antibiotics, but as many as 40 percent of women with untreated chlamydia develop pelvic inflammatory disease (PID), and one in five women with PID becomes infertile.

In recent years, chlamydia passed gonorrhea as the leading sexually transmitted bacterial pathogen in the U.S. According to the Centers for Disease Control and Prevention, there were 1,030,911 chlamydial infections reported in 2006, and it is believed to be greatly under-reported. Many people with chlamydia are not aware of their infections and don't seek testing.

The bacterium is difficult to culture in the laboratory, adding additional challenges to previous research on prevention and vaccines. Previously, chlamydia researchers have studied so-called "reference strains" that are adapted for laboratory studies. "Laboratory strains don't behave the way chlamydia does in its natural environment," explains Bavoil.

"We have assembled a multidisciplinary team that integrates ecological, genomics, clinical, and molecular analyses to study chlamydial infections," says Ravel. "As a team, we have the expertise and breadth to use a combination of newly developed bioinformatics and genomic tools to better understand the molecular mechanisms, which drive both chlamydial infections and the host microbiota in the reproductive tract." Ravel is a well-recognized researcher of the microbes associated with the human body, particularly the vagina.

"The bacteria in the microbiota serve as a first line of defense against infection," he adds. "We will develop a better understanding of how chlamydia can establish an infection in spite of that protection."

The study will involve swab samples collected from hundreds of infected women and men under the direction of Ligia Peralta, MD, associate professor of pediatrics and chief of the School of Medicine's Division of Adolescent and Young Adult Medicine at UMB. The researchers also will look for elements in the microbiota, the natural collection of microorganisms in healthy individuals, which may provide some disease protection for some women. A parallel modeling study will involve sexual transmission of chlamydia in guinea pigs under the direction of Roger Rank, PhD, professor, University of Arkansas for Medical Sciences.

Bavoil will characterize the different types of "chlamydia in the study to r help the team learn how to find, trace, and diagnose the bacteria better, and eventually develop a vaccine. "Basically, you have to know the enemy before you can fight it," he says.

The \$12.2 million grant also covers four other laboratories supporting the core work at UMB with guinea pig studies, mathematical modeling and the emergence of antibiotic resistance in chlamydia, to understand the link between chlamydia and other STDs, as well as health outcomes, such as pelvic inflammatory disease. The other laboratories involved are the Uniformed Services University of Health Sciences in Rockville, Md.; the University of New South Wales in Sydney, Australia; the Arkansas Children's Hospital Research Institute in Little Rock, Ark.; and the University of Idaho in Moscow, Idaho.

The researchers are optimistic they will discover new knowledge of chlamydia in its natural environment because they say that previous research funding on chlamydia has rarely addressed such fundamental questions. The studies of the bacteria have been dominated previously by epidemiological research. Such research, says Ravel, has often assumed that every woman's vaginal environment is the same, and has not considered differences in the microbiota environment that could be conducive to protection from sexually transmitted disease.

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