

Proteins discovered in gonorrhea may offer new approach to treatment

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This is an electron micrograph image of membrane vesicles isolated from *N*. *gonorrhoeae*. Credit: Oregon State University



Researchers at Oregon State University have discovered novel proteins in, or on the surface of the bacteria that causes gonorrhea, which offer a promising new avenue of attack against a venereal disease that is showing increased resistance to the antibiotics used to treat it.

Only a single, third-generation cephalosporin antibiotic still shows good efficacy against gonorrhea, creating a race against time to find some alternative way to treat this disease that can have serious health effects. It's the second most commonly reported infectious disease in the United States.

Investigations based on these proteins might lead to new ways to combat the disease, including a vaccine, new types of drugs to block the growth of the <u>bacteria</u>, or even restoring the efficacy of some older antibiotics that have lost their usefulness, said Aleksandra Sikora, an assistant professor in the OSU College of Pharmacy.

"This could be a milestone in finding new ways to treat a global problem," Sikora said. "It appears that one or more of these proteins, either within the bacterial cell envelope or on its surface, are essential to its growth and survival. Now we have a new target to aim at."

World health officials have raised alarms that the growing resistance of gonorrhea to antibiotics could cause it to become untreatable. There are more than 60 million cases of this venereal disease treated around the world every year – and 300,000 just in the U.S. – in people who experience clear symptoms. But some of the worst damage is done among millions of other cases that are very mild or asymptomatic.

Such symptomless infections, most common in women, can cause <u>pelvic</u> <u>inflammatory disease</u>, ectopic pregnancy and infertility, as well as increase the transmission of the HIV virus. Gonorrhea can also affect joints and heart valves, and cause blindness in infants infected during



birth.

The new findings were just published in *Molecular and Cellular Proteomics*, by researchers from OSU and the University of Washington. The research has been supported by OSU and the Medical Research Foundation of Oregon.

Using the evolving science of proteomics - which is the large-scale, highthroughput study of proteins and their functions - researchers identified a plethora of proteins that reside in a space in the gonorrhea bacteria, an "envelope" and its small outpouchings, or membrane vesicles.

This cell envelope shields the interior of gonorrhea from the environment and is essential for survival of the microbes, as well as their ability to cause disease. The proteins localized there help acquire nutrients, provide a permeability barrier, suppress the immune response and keep the bacteria fit.

Other proteins on the bacteria surface also help it attach to the host. The membrane vesicles are spherical structures that contain proteins and DNA, and are involved in antibiotic resistance, microbe communication and delivery of factors important for infection.

Any or all of these proteins may now offer a way to attack the survival and spread of the gonorrhea bacteria, Sikora said. None of them have yet been used for that purpose.

"Some past approaches to create a gonorrhea vaccine failed because they were focused on proteins essential to infection, which were quite unstable," she said. "Because they were changing so constantly they were unsuitable for a vaccine. The proteins we've now identified offer a much more stable and vulnerable target."



Researchers have already quantified their abundance of these cell envelope proteins and are learning their basic function, and in continued studies will screen compounds for activity against some of them.

"With this information, the chance to create either a vaccine or new drug treatments is very promising," Sikora said.

The gonorrhea bacteria, *Neisseria gonorrhoeae*, is a pathogen specific to humans and no other animals. It dates to antiquity and it's uncertain when it first developed. Many epidemics have been reported in world history.

Provided by Oregon State University

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