New gonorrhea treatment targets enzyme needed for respiration

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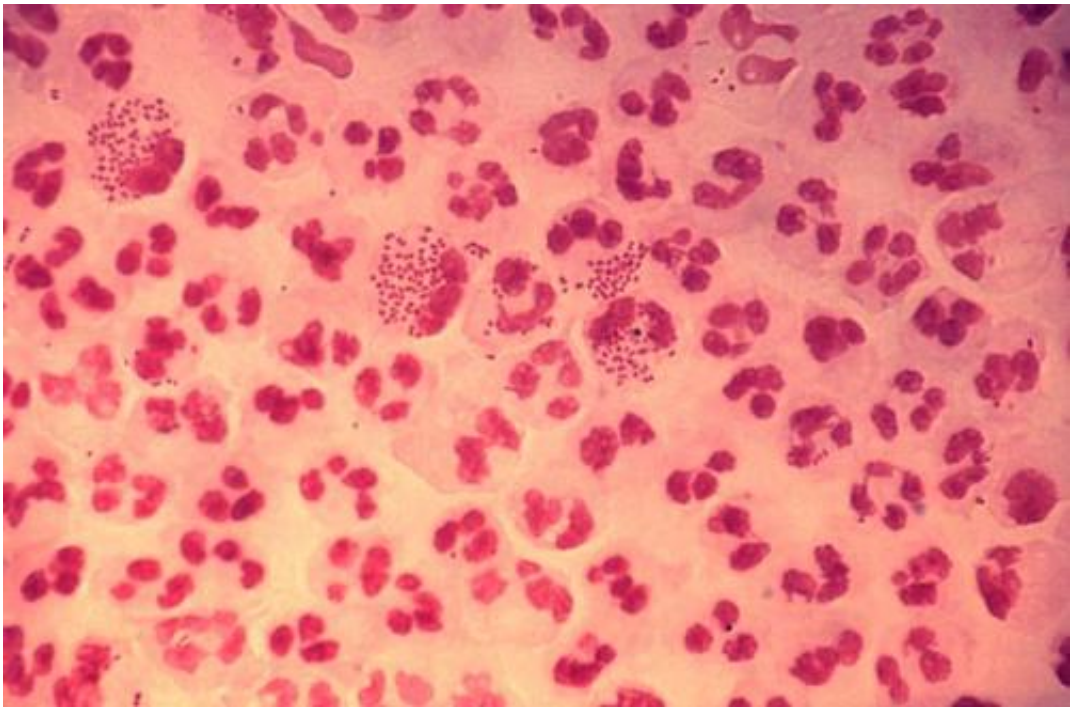

Credit: CDC

Researchers have identified a possible new treatment for gonorrhea, using a peptide that thwarts the infection-causing bacterium by interfering with an enzyme the microbe needs to respirate.

The findings are especially important since Neisseria gonorrhoeae is considered a "superbug" due to its resistance to all classes of antibiotics

available for treating infections.

Gonorrhea, a sexually transmitted disease whose numbers grow by 78 million new cases worldwide each year, is highly damaging to reproductive and neonatal health if untreated or improperly treated.

It can lead to endometritis, pelvic inflammatory disease, ectopic pregnancy, epididymitis and infertility. And babies born to infected mothers are at increased risk of blindness.

"The infections very often are silent," said Oregon State University researcher Aleksandra Sikora. "Up to 50 percent of infected women don't have symptoms, but those asymptomatic cases can still lead to some very severe consequences for the patient's reproductive health, miscarriage or premature delivery."

The need for better antibiotic therapy, and a vaccine, is pressing. N. gonorrhoeae strains resistant to the last effective treatment options have emerged, and failures in treatment are occurring.

Researchers led by Sikora, an associate professor in the OSU College of Pharmacy, have identified a new therapy target, an enzyme known as AniA. The bacteria need the surface-exposed enzyme to respirate without oxygen, or anaerobically, which is their preferred method of respiration in the biofilms of the genitourinary tract.

A biofilm is a group of one or more types of microorganisms that grow on a wet surface, such as dental plaque on teeth.

Sikora and her team identified a peptide - multiple amino acids linked in a chain - that inhibits the AniA enzyme's nitrite reductase activity. That in turn damages the bacteria's ability to grow in the oxygen-poor biofilm environment.

"Bacteria in biofilms display increased resistance to antimicrobials," Sikora said. "The enzyme is only necessary for cell viability when these bacteria grow under anaerobic conditions, including when they grow in the biofilm. Most antibiotics target essential cell functions; this one doesn't. It's only at a certain stage of growth that the bacteria are affected, which means the development of resistance won't be as fast."

Through a technique known as biopanning, OSU scientists and collaborators at the University of Kentucky found 29 unique peptides that bound with the targeted enzyme. One of them, C7-3, was identified as most promising for inhibiting the protein's interaction with nitrite, necessary for anaerobic respiration.

"Imagine this research approach as having a pond with a lot of fish, and you're using the protein as the bait," Sikora said. "The peptides bind with the protein, and you go through multiple rounds to identify the peptides that have the strongest binding ability. You start with a billion peptides and end up with one that strongly inhibits the enzyme and ultimately kills the bacteria."

Findings were recently published in *Antimicrobial Agents and Chemotherapy*, and Sikora has applied for a provisional patent.

More information: Aleksandra E. Sikora et al, Peptide inhibitors targeting the Neisseria gonorrhoeae pivotal anaerobic respiration factor AniA, *Antimicrobial Agents and Chemotherapy* (2017). DOI: 10.1128/AAC.00186-17

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