

Research identifies potential antibiotic alternative to treat infection without resistance

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(Medical Xpress) -- Researchers at the University of Michigan have found a potential alternative to conventional antibiotics that could fight infection with a reduced risk of antibiotic resistance.

By using high-throughput screening of a library of small molecules from the Center for Chemical Genomics at the U-M Life Sciences Institute, the team identified a class of compounds that significantly reduced the spread and severity of group A Streptococcus (GAS) bacteria in mice. Their work suggests that the compounds might have therapeutic value in the treatment of strep and similar infections in humans.

"The widespread occurrence of <u>antibiotic resistance</u> among <u>human</u> <u>pathogens</u> is a major public health problem," said David Ginsburg, a faculty member at LSI, a professor of internal medicine, <u>human genetics</u>, and pediatrics at the U-M Medical School and a Howard Hughes Medical Institute investigator.

Ginsburg led a team that included Scott Larsen, research professor of medicinal chemistry and co-director of the Vahlteich Medicinal Chemistry Core at U-M's College of Pharmacy, and Hongmin Sun, assistant professor of medicine at the University of Missouri School of Medicine. Their research results were published online Feb. 13 in the Proceedings of the National Academy of Sciences.



Work on this project is continuing at U-M and the University of Missouri, including the preparation of new compounds with improved potency and the filing of patents, Larsen said.

Current antibiotics interfere with critical biological processes in the pathogen to kill it or stop its growth. But at the same time, stronger strains of the harmful bacteria can sometimes resist the treatment and flourish.

An alternate approach is to suppress the virulence of the infection but still allow the bacteria to grow, which means there is no strong selection for strains that are resistant to antibiotics. In a similar experiment at Harvard University, an anti-virulence strategy was successful in protecting mice from cholera.

About 700 million people have symptomatic GAS infections around the world each year, and the infection can be fatal. Most doctors prescribe penicillin. The newly identified compounds could work with conventional antibiotics and result in more effective treatment.

The PNAS article is titled "Inhibitor of streptokinase gene expression improves survival after group A Streptococcus infection in mice."

The study was one of four current LSI projects that are part of the Innovation Partnership, which provides researchers with funding guidance from experienced life-sciences industry experts during the process of bringing drugs from discovery to market.

More information: www.pnas.org/content/early/201 /1201031109.abstract



Provided by University of Michigan

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