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New weapon in fight against antibiotic resistance discovered

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Scientists at St. Boniface Hospital Albrechtsen Research Centre and the University of Manitoba have developed a drug that combats 2 of the top 10 "priority pathogens" recently defined by the World Health Organization (WHO) as antiobiotic-resistant bacteria requiring new interventions. The drug, dubbed PEG-2S, has received a provisional patent, and its development is highlighted in a study published today in the *Canadian Journal of Physiology and Pharmacology* (CJPP). Without affecting healthy cells, the drug prevents the proliferation of a harmful bacteria that possesses a specific type of energy supply shared by a number of other bacteria.

The paper, entitled "Development of a novel rationally designed antibiotic to inhibit a nontraditional bacterial target", revealed that a variety of bacteria share a unique respiratory sodium pump (NQR) that supplies energy vital to the bacteria's survival. The study showed that the drug in question, PEG-2S, inhibits the function of the NQR pump and the production and growth of Chlamydia trachomatis bacteria. The drug is highly targeted and only impacts bacterial cells with NQR pumps and is not toxic to normal, healthy cells. The list of NQR-possessing bacteria is growing steadily as genomic information becomes available. With more than 20 different pathogenic bacteria containing NQR, the possibility for this drug to avoid multidrug resistance through NQR inhibition represents a potential breakthrough in antibiotic design.

Traditional targets for antibiotics are limited; no new antibiotics have been discovered since 1987. Only 2 antibiotics have received US FDA

approval since 2009.

"New drugs are not being approved because they share the same target to which the bacteria are developing resistance. We have not only defined a new and effective target, we have designed a drug to attack it without affecting normal cells," explains St. Boniface Hospital Executive Director of Research and University of Manitoba professor of physiology and pathophysiology Dr. Grant Pierce. "The first pathogen our research team studied (Chlamydia trachomatis) has confirmed that NQR is a good target, and it is shared by many bacteria in need of a more effective antibiotic."

"The results from our collaboration are tremendously exciting," adds lead author, University of Manitoba Faculty of Science professor Dr. Pavel Dibrov. "We are currently designing PEG-2S variations and hope to tailor PEG-based antimicrobials to each specific NQR-containing pathogenic bacterium."

"Antibiotic and antimicrobial resistance to superbugs is a priority research direction in pharmacology. The quality and findings of this study may be instrumental in our efforts to develop new drugs and technologies that effectively address this global health alarm recently raised by the World Health Organization," say CJPP Editors Dr. Ghassan Bkaily and Dr. Pedro D'Orléans-Juste.

"I applaud the research collaboration that resulted in this new breakthrough," said Dr. Digvir Jayas, Vice-President (Research and International) and Distinguished Professor at the University of Manitoba. "Solving the complex and evolving challenges of antibiotic resistance will put new tools in the hands of caregivers around the globe."

"New antibiotics targeting this priority list of pathogens will help to

reduce deaths due to resistant infections around the world," says Prof Evelina Tacconelli, Head of the Division of Infectious Diseases at the University of Tübingen and a major contributor to the development of the WHO list. "Waiting any longer will cause further public health problems and dramatically impact on patient care."

More information: Pavel Dibrov et al, Development of a novel rationally designed antibiotic to inhibit a nontraditional bacterial target, *Canadian Journal of Physiology and Pharmacology* (2017). DOI: 10.1139/cjpp-2016-0505

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