Researchers develop effective strategy for disrupting bacterial biofilms

June 30 2016

Biofilms are communities of bacteria that adhere to a surface and are nearly impossible to eradicate when they are pathogenic, or disease-causing. Fortunately, a discovery from the laboratories of Lauren Bakaletz, PhD, and Steven Goodman, PhD, in The Research Institute at Nationwide Children's Hospital, provides strong evidence that an innovative therapeutic approach may be effective in the resolution of bacterial biofilm diseases.

"Most, if not all, chronic and recurrent bacterial infections include a biofilm in the disease course," says Dr. Bakaletz, director of the Center for Microbial Pathogenesis in The Research Institute at Nationwide Children's and senior author of the recent study, published in the journal *EBioMedicine*. "Biofilms are sophisticated, towering communities of bacteria that are very resistant to clearance by either our own immune system or the action of antibiotics."

These chronic and recurrent bacterial infections include urinary tract infections, which result in nearly half a million emergency room visits annually, middle ear infections, sinusitis, and chronic wound infections, to name a few.

"Given how common and troublesome biofilm diseases are, we endeavored to develop a novel approach to disrupt these biofilms," continues Dr. Goodman, principal investigator in the Center for Microbial Pathogenesis at The Research Institute and co-author of the study. "This way, traditional antibiotics and/or the body's own natural

immune system could now kill the bacteria released from the biofilm that had caused the infections, thus hopefully providing a cure."

This novel approach involved targeting extracellular DNA (eDNA) and associated DNABII proteins in biofilms, which are common components of biofilms and help maintain the structure of biofilms. Researchers built on their previous work, which demonstrated that an antibody directed against DNABII proteins resulted in the catastrophic collapse of bacterial biofilms.

"One method that we and many of our colleagues who also study biofilms rely upon is to allow the bacteria we are specifically interested in to form a biofilm in a special culture vessel in the lab," says Dr. Bakaletz. "Once that biofilm is mature, we then attempt to disrupt it by targeting specific bacterial proteins within the biofilm."

Using a form of microscopy called confocal scanning light microscopy and COMSTAT analysis software, a program that analyzes image stacks of biofilms, they were able to take a series of images of the biofilm both before and after treatment, according to researchers. This allowed them to determine how effectively they had disrupted the biofilm and released the bacteria that created it.

Of the results, Dr. Bakaletz explains, "We showed that our biofilm disruption technology was highly effective against many different bacteria that cause a variety of human diseases; that it worked synergistically with a traditional antibiotic—tobramycin, which alone was completely ineffective against the biofilm; and further, that it also worked very well in two unique models of human respiratory tract disease."

The monoclonal antibodies used in these studies—a type of protein made in the laboratory that can bind specifically to its DNABII protein

target—are presently being adapted for delivery to human patients in clinical trials, says Dr. Bakaletz.

"We are very excited to develop this technology further, with the hope of making a difference in both human and animal health," adds Dr. Goodman. "We are currently both raising funds and identifying partners that can help us achieve these goals."

More information: Laura A. Novotny et al, Monoclonal antibodies against DNA-binding tips of DNABII proteins disrupt biofilms in vitro and induce bacterial clearance in vivo, *EBioMedicine* (2016). DOI: 10.1016/j.ebiom.2016.06.022

Provided by Nationwide Children's Hospital