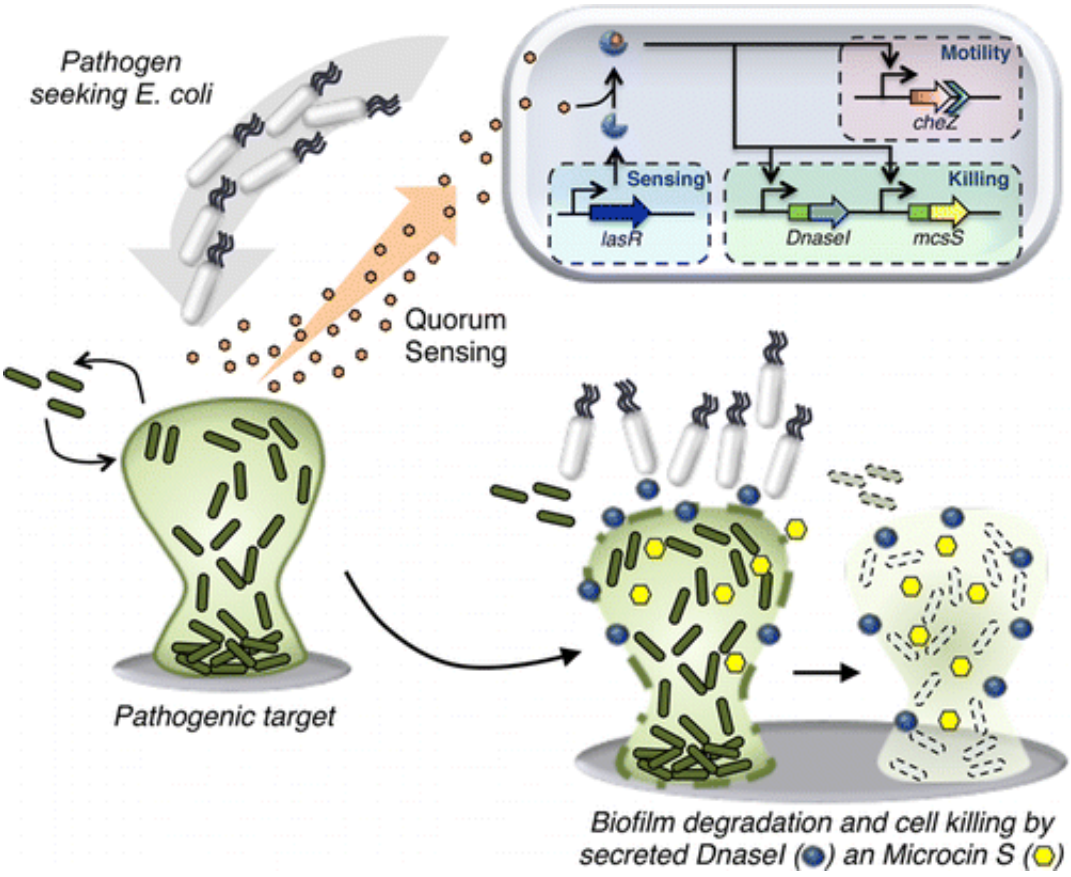
Recruiting E. coli to combat hard-to-treat bacterial infections

October 2 2013



The notorious bacteria *E. coli* is best known for making people sick, but scientists have reprogrammed the microbe—which also comes in harmless varieties—to make it seek out and fight other disease-causing

pathogens. The researchers' report appears in the journal *ACS Synthetic Biology* and describes development of this new type of *E. coli* that can even kill off slimy groups of bacteria called biofilms that are responsible for many hard-to-treat infections, such as those that take hold in the lungs, the bladder and on implanted medical devices.

Matthew Wook Chang and colleagues explain that biofilm infections are difficult to treat because the bacteria hide away under a protective barrier of sugars, DNA and proteins. That shield makes them very resistant to conventional therapies. In addition, overuse of antibiotics in medicine and agriculture also have made some bacteria, such as MRSA, shrug off most known treatments, making at least 2 million Americans sick every year. This growing public health threat has motivated scientists to look for new antibiotics and alternative treatments to beat infections. In the past, researchers made bacteria that fight off other microbes, but they had limitations. Chang's team addressed those limitations by making a new kind of bacterial "gun-for-hire" that can sense an infection, swim toward it and kill off the disease-causing microbes.

They reprogrammed *E. coli* to sense *Pseudomonas aeruginosa*—a bacteria that can form biofilms and causes hospital-acquired infections in the lungs and the gut. The new *E. coli* then swims directly toward *P. aeruginosa* and launches an attack with an antimicrobial peptide and an enzyme that breaks down biofilms. Though the researchers successfully tested their engineered microbe on *P. aeruginosa*, they say that their engineering strategy could be used to combat other pathogens as well.

More information: Reprogramming Microbes to Be Pathogen-Seeking Killers, ACS Synth. Biol., Article ASAP. DOI: 10.1021/sb400077j

Abstract

Recent examples of new genetic circuits that enable cells to acquire biosynthetic capabilities, such as specific pathogen killing, present an attractive therapeutic application of synthetic biology. Herein, we demonstrate a novel genetic circuit that reprograms Escherichia coli to specifically recognize, migrate toward, and eradicate both dispersed and biofilm-encased pathogenic Pseudomonas aeruginosa cells. The reprogrammed E. coli degraded the mature biofilm matrix and killed the latent cells encapsulated within by expressing and secreting the antimicrobial peptide microcin S and the nuclease DNaseI upon the detection of quorum sensing molecules naturally secreted by P. aeruginosa. Furthermore, the reprogrammed E. coli exhibited directed motility toward the pathogen through regulated expression of CheZ in response to the quorum sensing molecules. By integrating the pathogen-directed motility with the dual antimicrobial activity in E. coli, we achieved signifincantly improved killing activity against planktonic and mature biofilm cells due to target localization, thus creating an active pathogen seeking killer E. coli.

Provided by American Chemical Society