Researchers modify harmless bacteria to kill harmful bacteria

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(PhysOrg.com) -- Researchers in Singapore have modified the DNA of one type of bacterium, *Escherichia coli*, to first sense the presence of another bacterium, *Pseudomonas aeruginosa*, and then to explode, releasing a special kind of toxin that will kill it. Chueh Loo Poh and Matthew Wook Chang of Nanyang Technological University in Singapore, describe their research in *Molecular Systems Biology.*

P.aeruginosa is a common microbe that is responsible for difficult to treat infections in people, particularly those with comprised immune systems. It generally colonizes the gastrointestinal tract or the respiratory system and is believed to be responsible for up to ten percent of all hospital acquired infections. The general approach to treating it is massive amounts of antibiotics which don't always work and also tend to kill off good bacteria in the process.

To get around this problem Poh and Chang modified the DNA of *E. coli* in such a way as to allow it to be able to detect LasR, a molecule used by P.aeruginosa bacteria to communicate with one another. When the LasR is detected, the *E. coli* begins producing a toxin called pyocin until it's full, at which point it explodes releasing the pyocin which kills *P.aeruginosa* by eating holes in its exterior, allowing its innards to pour out.

This approach is the first time that bacteria have been used to kill other bacteria and is a step up in the ongoing battle against infectious diseases. It's one that is of critical importance due to the dearth of new anti-

bacterial drugs; only two new ones have come on the market in the last ten years and the old ones are becoming increasingly ineffective as new strains of bacteria have evolved that are resistant to them.

The research team says that in the lab, the modified *E. coli* were able to kill up to 99% of the *P.aeruginosa* when they were in standalone mode. Perhaps more importantly, they were also able to kill off nearly 90% of them when they were banded together in large communities called biofilms, which are notoriously difficult to treat with conventional methods.

The one major obstacle to using such engineered *E. coli* as a stealth agent, at least at this stage, is its inability to actually hunt for its victim, rather than sit by passively waiting for the right bacterium to pass by before exploding itself. The hope is that other bacteria with sensing abilities could be used instead of *E. coli*; ones that could actually track down the specific target, perhaps allowing for a kill rate of 100%.

The next step in the testing of the new treatment will be introducing the modified *E. coli* into mice to see if it will work as well in a live animal, and also of course, to see what side effects might occur.

More information: Engineering microbes to sense and eradicate Pseudomonas aeruginosa, a human pathogen, *Molecular Systems Biology* **7** Article number: 521 doi:10.1038/msb.2011.55

Abstract
Synthetic biology aims to systematically design and construct novel biological systems that address energy, environment, and health issues. Herein, we describe the development of a synthetic genetic system, which comprises quorum sensing, killing, and lysing devices, that enables Escherichia coli to sense and kill a pathogenic Pseudomonas aeruginosa strain through the production and release of pyocin. The

sensing, killing, and lysing devices were characterized to elucidate their detection, antimicrobial and pyocin release functionalities, which subsequently aided in the construction of the final system and the verification of its designed behavior. We demonstrated that our engineered E. coli sensed and killed planktonic P. aeruginosa, evidenced by 99% reduction in the viable cells. Moreover, we showed that our engineered E. coli inhibited the formation of P. aeruginosa biofilm by close to 90%, leading to much sparser and thinner biofilm matrices. These results suggest that E. coli carrying our synthetic genetic system may provide a novel synthetic biology-driven antimicrobial strategy that could potentially be applied to fighting P. aeruginosa and other infectious pathogens.