SYNTHETIC BIOLOGY

Licensing bacteria to kill

The introduction of synthetic genetic systems into bacteria holds much promise for the production of drugs and biofuels and for the bioremediation of contaminated environments. With the design and testing of an engineered *Escherichia coli* strain that specifically targets *Pseudomonas aeruginosa*, Saeidi *et al.* now show that bacteria can also be engineered for novel antimicrobial approaches.

P. aeruginosa is a pathogen of the respiratory and gastrointestinal tracts, and infections can be fatal to immune-compromised individuals. Owing to its efficient drug efflux systems, *P. aeruginosa* is intrinsically resistant to many antibiotics. To circumvent potential drug resistance, Saeidi *et al.* designed and constructed an *E. coli* strain that can sense the presence of *P. aeruginosa* and release an antimicrobial peptide in response. LasR, a transcription factor that binds to the *P. aeruginosa* quorum sensing acyl-homoserine lactone 3OC₁₂-HSL and activates transcription from *luxR* promoters, was introduced into *E. coli* to enable sensing of *P. aeruginosa*. For the killing component, a *luxR* promoter

was placed upstream of the gene encoding pyocin S5, a bacteriocin that is produced by some strains of *P. aeruginosa* and exhibits strong bactericidal activity against clinical isolates of *P. aeruginosa* (but not *E. coli*). To ensure the release of the toxin, the gene encoding the lysis protein for colicin E7, also under the control of a *luxR* promoter, was introduced. Above a certain threshold concentration, this protein can perforate the *E. coli* membrane, leading to release of the accumulated pyocin S5.

To test the efficacy of this engineered *E. coli* strain, the authors exposed it to 3OC₁₂-HSL, either obtained commercially or in the form of a filtered supernatant from

a *P. aeruginosa* culture, and then collected filtered supernatant from the *E. coli* culture. When this was added to *P. aeruginosa* growing on agar, a strong growth inhibition was observed. Similarly, in co-culture experiments, the authors observed that pyocin S5-producing *E. coli* inhibited the growth of *P. aeruginosa* by >99%. Finally, to examine the potential of the engineered bacterium to inhibit growth in a more clinically relevant setting, the

authors used a static biofilm inhibition assay. They found that the presence of the engineered *E. coli* strain inhibited biofilm formation by nearly 90%.

Antimicrobial resistance and the diminishing drug discovery pipeline are worrying problems. Now, engineered genetic devices such as those described here have the potential to enable us to provide resident members of the human microbiota or probiotic bacterial strains with the tools to fight pathogens on our behalf.

Andrew Jermy

“Pyocin S5-producing *E. coli* inhibited the growth of *P. aeruginosa* by > 99%.”

ORIGINAL RESEARCH PAPER Saeidi, N. *et al.* Engineering microbes to sense and eradicate *Pseudomonas aeruginosa*, a human pathogen. *Mol. Syst. Biol.* **7**, 521 (2011)