Building evolution-proof drugs

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A new generation of drugs could help combat the growing number of bacterial diseases that are becoming resistant to antibiotics, a study reveals.

Diseases that are currently curable could become life-threatening if they evolve resistance to existing treatments.

Antibiotics work by killing the bacteria, or stopping their growth, so any bacteria that are resistant to the drug will thrive, giving them an advantage over non-resistant ones. This advantage means the resistant bacteria are more likely to spread and become dangerous.

So researchers from the University of Edinburgh and University of Nottingham have been studying anti-virulence drugs, which work in a different way to antibiotics.

Anti-virulence drugs don't harm the bacterium itself; instead they target the part of the cell that makes people ill. If they still allow the bacteria to grow, these newer drugs won't allow resistant strains an advantage over non-resistant ones.

'Most pathogens have many virulence factors, factors that harm their hosts, but they all will have different functions, it's about picking the right factor as a target for the anti-virulence drugs,' explains PhD student Richard Allen of the University of Edinburgh, who led the research. 'If you don't affect growth then resistant strains won't be at an advantage.'

The ability of anti-virulence drugs to target certain parts of a bacterium, preventing the evolution of resistant strains, has led to claims these revolutionary drugs could be evolution-proof.

Allen and his colleagues carried out a review, published in *Nature Reviews Microbiology*, of work into anti-virulence drugs over the past five years, to assess whether or not these drugs are as evolution-proof as some claim.

'We need to understand exactly how virulence affects the fitness of a pathogen before we develop the drugs and with that knowledge we can target drugs towards virulence in a way that does not give resistant strains an advantage,' says Allen.

Anti-virulence drugs are not currently being used, and Allen suspects they are at least 20 years away from being commercially available. But reviews like this will help developers to build versions of these drugs which are the most likely to prevent the spread of resistant bacteria.

'It's important to think about these issues early so we can focus on the anti-virulence drugs which are less likely to develop resistance,' Allen concludes.