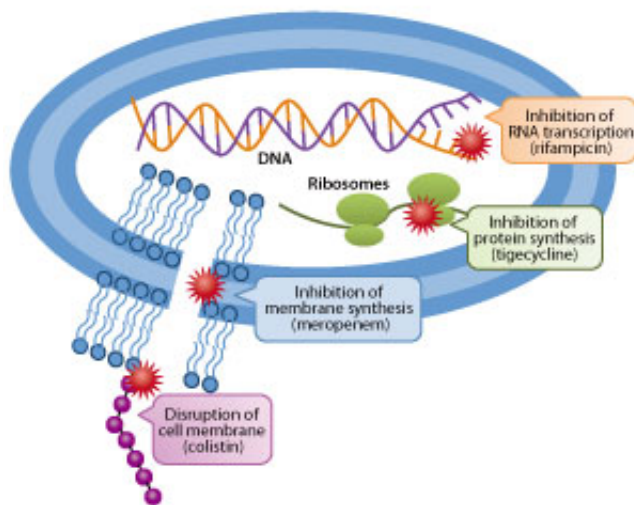


Fighting drug resistance with tailored combinations of antibiotics that kill microbes in different ways

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Using colistin in combination with other antibiotics (rifampicin, tigecycline and meropenem) proved more effective in treating multidrug-resistant bacteria than applying the antibiotics individually. That is because the four antibiotics used had different killing mechanisms against microbes. Credit: Ref 1. Copyright (2016), with permission from Elsevier.

Triple-pronged attacks on microbes that cause life-threatening lung infections are much more effective than individual antibiotics, A*STAR researchers have found. Using cocktails of antibiotics is promising for addressing the rising menace of multidrug-resistant microbes.

Multidrug-resistant bacteria are the plague of the twenty-first century and are predicted to become the leading cause of death by 2050, surpassing even cancer and diabetes, says Desmond Heng Wen Chien of the A*STAR Institute of Chemical and Engineering Sciences. "It is imperative that we act now to stem the rise of antimicrobial resistance and to mitigate its impact with more robust, but safer therapies," he urges.

In particular, superbugs that cause respiratory [lung infections](#) are posing an increasingly ominous threat. They have dire clinical outcomes, with mortality rates reaching as high as 80 per cent for some infections. Furthermore, they have begun to spread from hospitals to the community at large. The last line of defense against such superbugs is the highly toxic antibiotic known as colistin, but there are recent reports of infections that are resistant to even that.

Now, Heng and his co-workers have shown that using three tailored combinations of colistin with two other antibiotics can effectively combat lung infections caused by multidrug-resistant superbugs. They found that all three formulations were highly effective against the multidrug-resistance pathogens in the laboratory. In concocting these combinations, the team drew on initial laboratory screening data and existing clinical data to obtain more effective and robust formulations.

Since the four antibiotics used in these cocktails employ different mechanisms to kill bacteria (see image), their ternary combinations exhibit significant synergistic and additive effects. Their combined effectiveness is much greater than their individual application. The triple-killing mechanism of these ternary combinations, and the potential to rotate the three combinations during therapy, makes it much harder for microbes to develop resistance to them. Using other antibiotics in combination with colistin has the added advantage that it reduces the amount of colistin needed and the toxicity to the patient.

The [antibiotics](#) are easy to self-administer. "Our formulations are designed to be delivered into the deep-lung region by a portable, easy-to-use dry-powder inhaler, which is faster, more direct and more convenient than other modes of treatment," says Heng.

The team intends to conduct in vivo studies in animals and then humans in collaboration with hospital clinicians. The researchers note that the same strategy could be applied to fight other drug-resistant bacteria.

More information: Sie Huey Lee et al. Tailored Antibiotic Combination Powders for Inhaled Rotational Antibiotic Therapy, *Journal of Pharmaceutical Sciences* (2016). [DOI: 10.1016/j.xphs.2016.02.007](#)

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