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In the news

ANTIBIOTICS TAKE A RADICAL APPROACH

A single mechanism — the production of reactive oxygen species — is used by three classes of antibiotics to kill bacteria, report Kohanski, Collins and colleagues in *Cell*. This finding suggests that treatment of bacterial infections could be potentiated by targeting bacterial systems that mediate free-radical damage.

Antibiotics that kill bacteria (bactericidal antibiotics), as opposed to antibiotics that inhibit growth, fall into three classes, depending on what they target: DNA replication and repair; cell-wall synthesis; or protein synthesis. "Prior thinking", explains Collins, "was that cell death arose principally from those interactions and that each [class] acted differently." (*The Scientist*, 6 September 2007.)

Now, Kohanski *et al*. have shown that, in addition to their unique killing pathways, all bactericidal antibiotics induce the generation of free radicals via a shared pathway — they impair the tricarboxylic acid cycle, which decreases NADH levels and, consequently, increases hydroxyl radical formation. Furthermore, inhibition of free-radical generation significantly reduces the efficiency of bactericidal antibiotics, which highlights the importance of this pathway for causing cell death.

Free radicals will, in the words of Kohanski, "damage DNA, proteins, lipids in the membrane, pretty much anything. They're equal opportunity damagers." (*ScienceDaily*, 7 September 2007.) And indeed, the authors witnessed evidence of these types of damage. Defence mechanisms to cope with misfolded proteins and DNA damage were upregulated following treatment with bactericidal antibiotics. Moreover, the authors may have found a way to increase antibiotic efficiency. "We showed that if you can inhibit or block the bacterial defence mechanisms to hydroxyl radical damage," says Collins, "you can potentiate or enhance the lethality of bactericidal antibiotics." (*ScienceDaily*, 7 September 2007.)

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