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ANTIBACTERIAL DRUGS

Tackling tuberculosis

The causative agent of tuberculosis (TB), *Mycobacterium tuberculosis*, has beset humans for thousands of years. Now, a new agent has been identified that might help in the battle against TB, as described in *Science* by Koen Andries and colleagues.

In the 1940s therapies emerged that led to a drastic reduction in TB incidence in the developed world. The success of these drugs created the impression that TB had been conquered, and, partly because of this, research into anti-TB drugs waned — the most recent novel treatment for TB is more than 30 years old.

However, today TB has a worldwide presence: roughly one-third of the world's population, mostly in poor countries, carry latent TB infections. And of these, 2–3 million die annually. HIV epidemics in many countries have led to the emergence of new waves of TB infection, because co-infection with HIV and *M. tuberculosis* makes latent TB more likely to develop into an active condition, often with fatal consequences. Efforts by the World Health Organization to reduce the incidence of TB have met with limited success, and so any further tool in the arsenal against TB would be welcome — particularly one that could combat the increasing problem of resistance to current anti-TB drugs.

Andries *et al.* report just such a development. The researchers have identified a diarylquinoline compound called R207910 that potently inhibits both drug-sensitive and drug-resistant strains of *M. tuberculosis*. Studies of mutant strains indicate that R207910 inhibits a new bacterial target, the bacterial ATP synthase, and R207910 therefore shows a lack of cross-resistance with current anti-TB drugs.

Studies with mice and humans reveal that R207910 is rapidly absorbed, and in mice has a greater bactericidal activity than the commonly used anti-TB drugs isoniazid and rifampin by at least 1 log. Human studies indicate that the drug is safe and tolerable, and at tolerable doses can reach concentrations greater than that which achieves optimal activity in established disease in mice.

One of the biggest problems with TB therapy at the moment is that patients have to take antibiotics for up to 9 months. As many patients feel better before this time, they prematurely stop their treatment, leaving pools of the most drug-resistant *M. tuberculosis* in their lungs. This contributes to the emergence of complete drug resistance in future patients. Because R207910 seems to act more quickly, patients might not need to stay on the drug so long, making it more likely for drug courses to be completed and reducing the likelihood of resistance developing. There is, however, still a long road of clinical development ahead before this drug can reach those who need it.

Daniel Jones

References and links

ORIGINAL RESEARCH PAPER Andries, K. *et al.* A diarylquinoline drug active on the ATP synthase of *Mycobacterium tuberculosis*. *Science* **307**, 223–227 (2005)