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Tuberculosis drug shows promise against latent bacteria

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A new study has shown that an investigational drug (R207910, currently in clinical trials against multi-drug resistant tuberculosis strains) is quite effective at killing latent bacteria. This revelation suggests that R207910 may lead to improved and shortened treatments for this globally prevalent disease.

Despite numerous treatment advances, tuberculosis (TB) remains a serious disease –fueled by co-infection of HIV patients, the rise of drug-resistant strains, and the ability of *Mycobacterium tuberculosis* to become dormant and linger in the lungs. In fact, one third of the world population is infected, asymptomatically, with latent TB and is at risk of developing active TB disease during their life time.

Anil Koul and colleagues at Johnson & Johnson tested R207910 on dormant *M. tuberculosis* in three different laboratory models of latency. R207910 targets a protein (ATP synthase) essential for making cellular energy (ATP) in actively replicating TB. The researchers reasoned that even dormant bacteria, which are essentially physiologically "turned off", still need to produce small quantities of ATP to survive. As such, a block in ATP synthesis might be an Achilles heel for killing dormant bacteria.

This reasoning proved to be correct and R207190 was able to kill dormant bacteria by greater than 95% whereas current drugs like isoniazid had no effect. Surprisingly, they found that R207910 is slightly more effective in killing dormant bacteria as compared to actively

replicating ones, a unique spin as all known TB drugs are more effective on replicating bugs. Koul and colleagues hope to validate these results clinically, and note that ATP synthase should be looked at as a drug target for other persistent bacterial infections.

Citation: "Diarylquinolines are bactericidal for dormant mycobacteria as a result of disturbed ATP homeostasis" by Anil Koul, Luc Vranckx, Najoua Dendouga, Wendy Balemans, Ilse Van den Wyngaert, Karen Vergauwen, Hinrich Göhlmann, Rudy Willebrords, Alain Poncelet, Jerome Guillemont, Dirk Bald and Koen Andries

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