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Evolution of drug resistance in *Mycobacterium tuberculosis*

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The continued advance of antibiotic resistance threatens the treatment and control of many infectious diseases. This is exemplified by the largest global outbreak of extensively drug resistant (XDR) tuberculosis (TB) identified at Tugela Ferry, KwaZulu-Natal, South Africa, in 2005. It is unclear whether the emergence of XDR-TB was due to recent inadequacies in TB control or other factors. Using whole genome sequencing on clinical and historical isolates we demonstrate the evolution of drug resistance over a 50 year period and identify a common mutational pathway responsible for multiple episodes of de novo evolution. By combining association and correlated evolution tests with strategies for amplifying signal from rare variants, we were also able to identify new mutations associated with resistance. One of these was a loss-of-function mutation in *ald* (alanine dehydrogenase) which conferred resistance to D-cycloserine and emerged independent of antibiotic selection in the evolution of animal adapted strains of the *M. tuberculosis* complex.

Biography

Alexander Pym is an Investigator at AHRI (African Health Research Institute) in Durban, South Africa. He was trained in Clinical Medicine, Infectious Diseases, Microbiology and Mycobacterial Genetics and has completed his PhD research at the Institute Pasteur, Paris followed by Post-doctoral studies at Stanford University. He has a broad research experience and has published on Esx secretion systems, recombinant TB vaccines and population genetics of *M. tuberculosis*. He subsequently worked in South Africa on clinical drug development of Bedaquiline in MDR-TB patients.

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