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Development of animal models and a new vaccine strategy for MDR TB

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Drug-resistant strains of *Mycobacterium tuberculosis* may account for 10% of the 8 million new cases of tuberculosis that occur annually. Recent outbreaks of extensively drug resistant tuberculosis in South Africa represent a very serious public health threat. The emergence of XDR-TB is also an uncomfortable reminder of the limited efficacy of current TB vaccine, BCG. The development of an efficacious new TB vaccine is a crucial and required component of future tuberculosis control. In order to understand the basis for the prominence of KZN strains causing MDR and XDR-TB, we will develop an animal model to study virulence and immunity of these strains, and the effects of drug resistance on virulence. A vaccine candidate that has been modified to secrete less superoxide dismutase will be evaluated for protection against KZN strain challenge in mice following vaccination. Finally, we propose to compare the two vaccine candidates in both BCG and TB backgrounds to establish the importance of presence or absence of broad antigens on immunogenicity of TB vaccines. The long term goal of this study is to engineer safe and more effective live TB vaccines that will contribute to the global control of tuberculosis and also reduce the emergence of drug resistant strains.