Drug-resistant tuberculosis (TB) caused by Mycobacterium tuberculosis is a global threat and a major public health problem in several countries (1). In South Africa, circulating M. tuberculosis strains are diverse (2), with three spoligotypes being most common: the Beijing spoligotype predominant in Western Cape, and the Euro-American LAM4 and S spoligotypes predominant in Gauteng and KwaZulu-Natal (KZN) provinces (3). The Euro-American S spoligotype (ST34) is prevalent in TB patients within KZN and Gauteng provinces (4).

We describe the draft genome sequences of two extensively drug-resistant (XDR) TB clinical strains of M. tuberculosis belonging to the Euro-American S lineage. The RSA 114 strain showed single-nucleotide polymorphisms predicted to have drug efflux activity. We also detected nonsynonymous changes in rpoB (S450L, I491F), katG (S315T), and gyrA (D94G), previously implicated in drug resistance. Interestingly, RSA114, which lacked known resistance-conferring gyrA mutations, had 14, 7, and 4 nonsynonymous changes in genes encoding efflux pumps (EPs), phthiocerol dimycocerosates (PDIMs) and type VII secretion systems (ESXs), respectively. Drug resistance in M. tuberculosis can be acquired through mutations in EPs that increase their activity to expel a broad spectrum of antibiotics (15), and overexpression of drug resistance genes, such as DNA gyrase mutations, were found to increase drug resistance (16). In RSA114, we identified mutations within the EP-encoding genes Rv0987, Rv2039c, and Rv0402c that are predicted to increase the efflux activity of ESX export enzymes involved in the synthesis of PDIM proteins, which can act as virulence factors (17), and are overexpressed in XDR TB strains, suggesting a contribution to this XDR-level drug resistance (18). Future functional studies are needed to determine the impact of these mutations on drug resistance.

Nucleotide sequence accession numbers. The whole-genome sequences for RSA114 and RSA184 have been deposited at NCBI GenBank under the accession numbers JKJF01000000 and JKQQ01000000, respectively.

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writing of the manuscript; and in the decision to submit the manuscript for publication.

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**REFERENCES**