In Vitro-Selected Linezolid-Resistant *Mycobacterium tuberculosis* Mutants

Development of resistance against linezolid, an alternative drug for the therapy of multidrug-resistant tuberculosis (2), was assessed to be rare (5). We aimed to generate linezolid-resistant *Mycobacterium tuberculosis* strains from 10 different, fully susceptible *M. tuberculosis* parental strains. Ten linezolid-resistant colonies could be isolated from six different parental strains. The frequency of the in vitro appearance of linezolid-resistant mutants was $2 \times 10^{-8}$ to $5 \times 10^{-9}$. Previous investigations with a genetically engineered *Mycobacterium smegmatis* derivative that harbored only one of the original two copies of the *rrn* operon revealed a similar rate of $4.5 \times 10^{-9}$ (6).

MIC value determination gave identical results performed with both Bectec 460 TB system and Bectec MGIT 960 (Becton Dickinson Diagnostic Systems, Sparks, MD). MIC values of the linezolid-resistant strains varied from 4 to 32 (Becton Dickinson, Sparks, MD). MIC with both Bactec 460 TB system and Bactec MGIT 960 (6).

Resistant was assessed to be rare (5). We aimed to generate linezolid-resistant *M. tuberculosis* strains from 10 different parental strains. The isolated *M. tuberculosis* mutants can be divided into two classes corresponding to in vitro-generated linezolid-resistant *M. smegmatis* clones (6). In that study, one class showed wild-type growth characteristics in cultures, lower MIC values of 4 to 8 μg/ml, and no mutation in the 23S rRNA, pointing to a nonribosomal mechanism of resistance (6). Mutants of the other class had alterations in domain V of 23S rRNA, high MIC values of $\geq 64$ μg/ml, and a decreased growth rate in culture. In contrary to the study by Sander et al., who found exclusively G2447T mutations in *M. smegmatis*, different mutations were found in *M. tuberculosis* and other bacterial species (1, 3, 4). Whereas the G2576T mutation is well known and often described as the predominant mutation in various other gram-positive bacteria, such as *Enterococcus faecalis* and *Staphylococcus aureus* (3, 4, 7), to our knowledge the G2061T mutation found in four *M. tuberculosis* strains is described here for the first time.

We thank, K. Ott, F. Schaefer, and I. Radzio, Forschungszentrum Borstel, Germany, for excellent technical assistance.

**REFERENCES**


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