Mycobacterium abscessus double-reporter strains: new tools to fight mycobacterial infections

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Nontuberculous mycobacteria (NTM) are responsible for increased pulmonary infections in immunocompromised individuals and patients with underlying pulmonary diseases like cystic fibrosis. The treatment is a very long multidrug regimen associated with severe side effects and increased antibiotic resistance, which urges the discovery of new anti-NTM drugs. However, there is a significant discrepancy between in vitro antibiotic susceptibility and clinical effectiveness. Therefore, new antimycobacterial compounds must be tested in in vitro setups able to simulate the in vivo complexity of infection as accurately as possible. In this context, we are developing new strains of *Mycobacterium abscessus*, which simultaneously express the gene for a fluorescent protein, mScarlet, and the gene for the light-generating enzyme, luciferase. The fluorescent signal can be used as a marker of bacterial load, and the bioluminescent signal to monitor bacterial metabolism. We characterized these new double-reporter strains by comparing their growth profile with the non-transformed strain and by evaluating their susceptibility to antibiotics already used in the clinic to treat *M. abscessus* infections. We also assessed their ability to form biofilms to infect host cells, such as murine macrophages and human organoid-derived alveolar cells, and validated them for in vivo infection using bioluminescence imaging technology. The results show that these new double-reporter strains can be an essential tool to aid in the discovery of new drugs against mycobacterial infections.

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