Reply to Jones and Niederweis

To the Editor—We thank Jones and Niederweis for sharing their views [1] about our article [2]. Apart from bacterial enumeration in the organs of guinea pigs infected with the mbtE mutant or the parental strain of Mycobacterium tuberculosis, we performed Ziehl-Neelsen staining...
of the lung tissues 4 weeks and 10 weeks after infection to directly ascertain the presence of bacteria (Figure 6C [2]). We were able to easily detect the bacilli in Ziehl-Neelsen-stained lung tissues in the case of infection with M. tuberculosis. However, despite extensive screening of tissue sections obtained from all 6 animals infected with the mbtE mutant, we did not observe a single bacterium in the lungs at either time point studied. The absence of bacilli, specifically in the case of infection with the mbtE mutant (as shown by both bacterial enumeration and Ziehl-Neelsen staining of the tissues), is obviously associated with the mutation in mbtE, resulting in the inability of the pathogen to synthesize mycobactins, consequently limiting its replication. The pathology at 4 weeks, observed in the case of infection with the mutant, was the result of limited replication that the pathogen underwent during the early period after infection (before dying due to the unavailability of mycobactins). The pathology at this time point, despite the death of bacteria, could be observed, as tuberculous lesions require more time for resolution. Indeed, no explanation is required for the absence of pathology at 10 weeks: if there were no bacilli even at 4 weeks, the absence of pathology at 10 weeks is only an expected observation.

With regard to the concern expressed by Jones and Niederweis about plating on the supplemented medium, we conclude that the influence of disruption of mycobactin biosynthesis on M. tuberculosis is bactericidal and not bacteriostatic. This work was supported by a research grant from the Department of Bio-technology, Ministry of Science and Technology, Government of India.

**Potential conflicts of interest.** All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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