## Reply to Wallis

To the Editor—Wallis identifies several shortcomings in previous trials that claim a therapeutic role for interferon γ (IFN-γ) in tuberculosis [1]. He also reviews a study that reports increased mortality in the IFN-γ–treated group. With this information, Wallis concludes that IFN-γ lacks any therapeutic value in tuberculosis and was rightfully concerned about our "speculation that [our] work is likely to enable future therapeutic trials of IFN-γ for tuberculosis" [1].

We reported a novel mechanism through which *M. tuberculosis* actively exploited IFN-γ to promote nonprotective necrotic death in human macrophages [2]. With this ability to exploit IFN-γ, *M. tuberculosis* might render endogenous or exogenous IFN-γ not only ineffective against *M. tuberculosis* but also hazardous to host macrophages. Our findings, therefore, fit Wallis' interpretation of the data from previous IFN-γ trials. However, we also believe that the true protective effect of IFN-γ has not been determined, probably because of interfering mechanisms of *M. tuberculosis*, such as the ESX-1 secretion system we reported or other yet-to-be-defined mechanisms. Without a thorough understanding of

how *M. tuberculosis* interferes with IFN-γ, it might be premature to completely discard a potential protective effect of IFN-γ against *M. tuberculosis* infections. With this reasoning, we speculated that the efficacy of IFN-γ against tuberculosis might be improved by blocking the ability of *M. tuberculosis* to exploit IFN-γ.

## Notes

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