Title:
Preclinical murine models for studying lung infections and antimicrobial treatments of nontuberculous mycobacteria.

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Abstract body:

Pulmonary infections caused by nontuberculous mycobacteria (NTM) have increased significantly, especially in individuals with conditions like chronic obstructive pulmonary disease, bronchiectasis, and cystic fibrosis. This rise emphasizes the urgent need for effective antimicrobial treatments, as NTM is often resistant to standard antibiotics. However, progress in developing these therapies has been slowed by the absence of a standardized and representative murine model of chronic infection.
To address this limitation, we exploited the agar bead method to establish a chronic lung infection with *Mycobacterium abscessus* in immunocompetent mice.
In this model, NTM successfully induced a persistent lung infection with a stable and sustained bacterial loads lasting up to two months with minimal systemic dissemination. Histopathological analysis of lung tissue, bacterial localization, and spatial transcritomics data reveled that chronically infected mice co-localized with pathological areas, including within or surrounding tissue with infiltrating macrophages/granuloma-like structures, or with submucosal inflammatory cells. Moreover, we recently demonstrated that this model can be effectively used for the development of new antimicrobial strategies, including pathogen-directed therapies (Lorè N.I. et al., 2023, *ERJ 2023*; Degiacomi G. et al., *Int J Antimicrob Agents. 2024*) and host-directed therapies (Poerio N. et al., *Microbiol Spectr.* 2022, unpublished).
In conclusion, our refined murine model of chronic lung infection by NTM provides valuable tools for advancing our understanding of bacterial pathogenesis and for evaluating the efficacy of novel antimicrobial therapeutic interventions against NTM lung infection.