Advancing host-directed therapy for Mycobacterium avium infection: identification of drug candidates and potential host targets

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STELLINGEN

behorende bij het proefschrift

Advancing host-directed therapy for *Mycobacterium avium* infection: identification of drug candidates and potential host targets

1. Given the intracellular nature of *Mycobacterium avium* (*Mav*), drug screenings should incorporate cell-based infection models in addition to the broth-based systems currently recommended by guidelines (this thesis, chapter 3).

2. Repurposing clinically approved drugs represents a promising strategy to develop host-directed therapy (HDT) for *Mav* infection, though further optimization is required for clinical applicability (this thesis, chapter 4 and 5).

3. Understanding the mechanism of action of a HDT compound is crucial before progressing it as a therapeutic option for *Mav* infection (this thesis, chapter 5).

4. During early *Mav* infection, macrophage transcriptomic responses are shaped by both intrinsic host immune activation and bacterial factors or pathogen-specific modulation (this thesis, chapter 6).

5. HDT only serves as an adjunct to antibiotics and is not a substitute as a standalone treatment.

6. Systemic administration of therapeutics for mycobacterial lung infections, such as oral or intravenous delivery, is generally preferred over local administration in clinical practice.

7. Non-tuberculous mycobacterial (NTM) infections and disease should be mandatorily reported to public health authorities, as is currently the case for *Mycobacterium tuberculosis*.

8. Traditional sputum culture-based diagnostics are insufficiently sensitive for early detection of NTM, underscoring the need for host-response biomarkers in clinical practice.

9. Acknowledging our ignorance is the first step toward genuine understanding.

10. Science literacy belongs in every classroom, not just the lab (adapted from Neil deGrasse Tyson).

11. Effort without immediate success is not a dead end; it is a side path that enriches the journey with growth toward real achievement (adapted from SpongeBob SquarePants 2018).