

# Repurposing clinically approved cephalosporins for tuberculosis therapy

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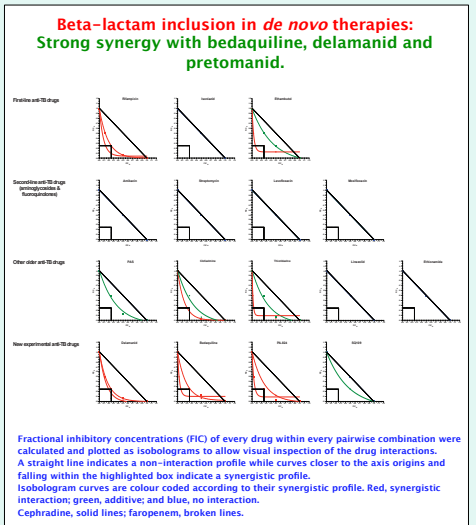
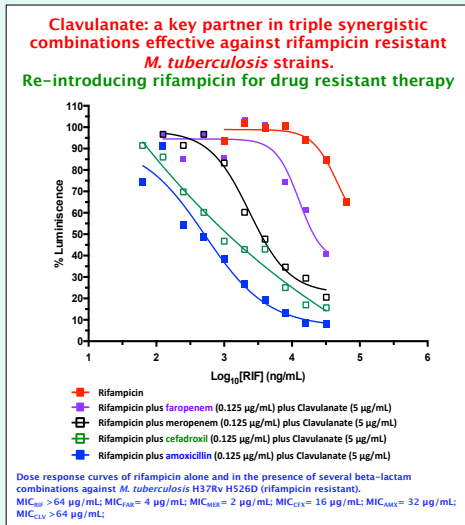
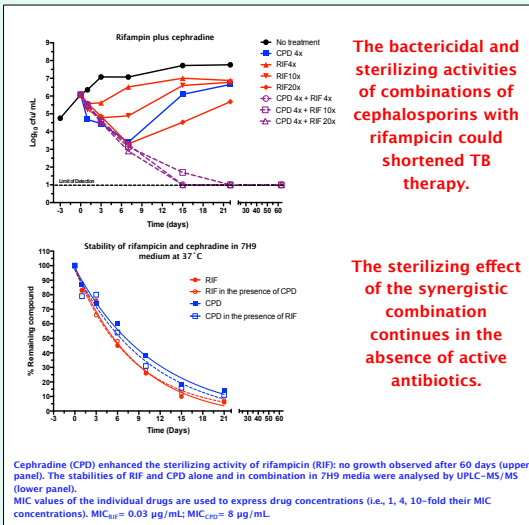
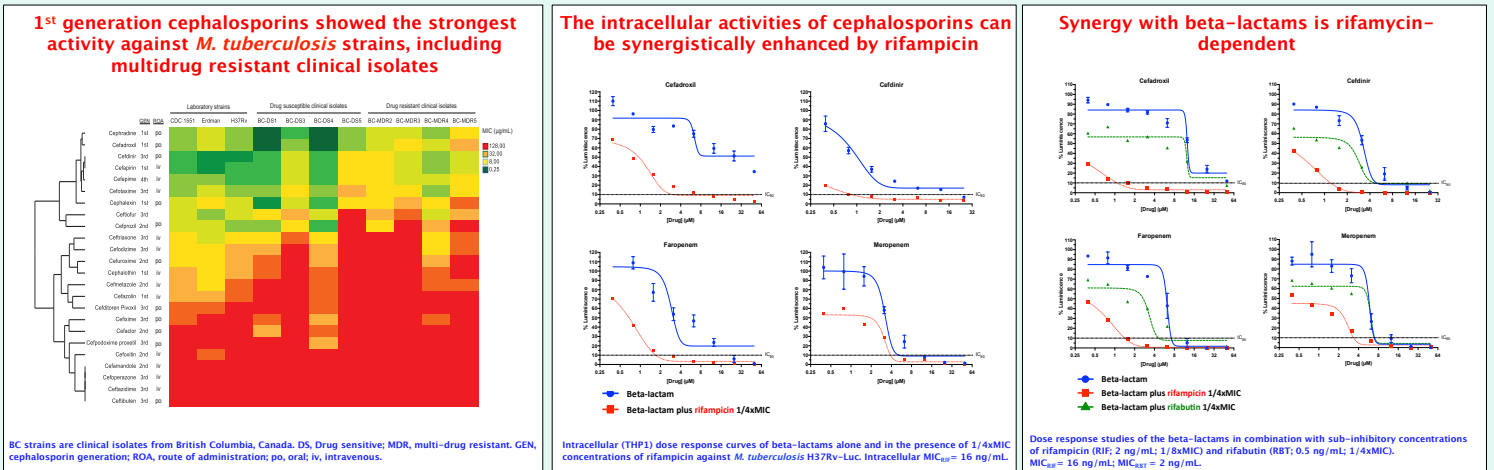
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**INTRODUCTION.** Rifampicin, the cornerstone drug for TB therapy, is not administered at its optimal clinical dose due to long-established toxicity concerns. If the anti-mycobacterial activity of rifampicin could be increased, TB therapy could be shortened, thus reducing the rate of transmission and the emergence of drug resistance.

While modern cephalosporins developed for broad spectrum antibacterial activities have never been pursued for tuberculosis (TB) therapy, we explored their potential repositioning as new anti-TB drugs alone and in synergistic combinations with rifampicin and other anti-TB drugs.

**RESULTS.** We screened an *in-house* library of ca. 600 commercially available antibiotics and identified 1<sup>st</sup> generation cephalosporins having clinically relevant inhibitory concentrations, both alone and in synergistic drug combinations with rifampicin and other anti-TB drugs.

**CONCLUSIONS.** Cefadroxil and cephradine were the most promising cephalosporin for future development. The fact that these cephalosporins are orally bioavailable with good safety profiles, together with their anti-mycobacterial activities alone and in synergistic combinations reported here, suggest that they could be repurposed within new combinatorial TB therapies.



## ACKNOWLEDGEMENTS

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