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Poster abstract submission

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Poster title

Standardization of the COMBINE Pneumonia Model in mice with Pseudomonas aeruginosa and Klebsiella pneumoniae.

Poster abstract

Reliable pre-clinical efficacy data generated in animal infection models is essential to accelerate antibiotic development, and standardized murine infection models can improve the reproducibility and comparability of efficacy data across laboratories. The choice of animal infection model for efficacy evaluation of novel antimicrobial candidates should be driven by the target clinical indication, while also balancing feasibility. The mouse lung infection model is commonly used for evaluating compounds targeting bacterial species causing pneumonia. This study establishes and validates the performance of a standardized murine pneumonia model with Klebsiella pneumoniae and Pseudomonas aeruginosa isolates using a consensus lung infection protocol across 3 independent laboratories.
Female outbred CD-1 mice 6-9 weeks of age were rendered neutropenic and inoculated intranasally to generate a bacterial burden of 6-7 log10 in the lung at 2 hrs after inoculation. Out of 32 isolates tested, 8 isolates met predefined virulence criteria—showing at least a 1 $\log_{10}$ increase in bacterial load from baseline to endpoint, while maintaining mouse survival for at least 12 hours post-inoculation at all of the 3 independent laboratories. For the 4 K. pneumoniae isolates (DSM 30104, 116098, 116099, 116109), the time to endpoint varied slightly, but in most cases all mice survived the entire observation period. An exception was DSM 30104, where 66% of mice (30/45) reached the humane endpoint between 18–26 hours. Among P. aeruginosa isolates, DSM 50071, 116110, 116114, and 116116 displayed reproducible in-vivo performance with >1 $\log_{10}$ CFU increase, with minor exceptions: one DSM 116110 experiment yielded a mean 0.96 $\log_{10}$ increase and one DSM 116114 experiment showed only a mean 0.39 $\log_{10}$ increase.

These 8 isolates are now made available to the research community from the COMBINE Preclinical Bacterial Strain Repository (PBSR) at DSMZ. Based on this work, we propose a standardized experimental pneumonia model using this isolate panel to support robust preclinical testing of new antibacterial therapies. We believe the COMBINE pneumonia model protocol can enhance the reliability, consistency, and clinical relevance of preclinical findings of efficacy assessments.

Research topic

PK/PD