Murine Pneumonia Models with Colistin Resistant and Carbapenem Resistant *Acinetobacter Baumannii* to Evaluate Treatments for AMR Lung Infections

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BACKGROUND

Acinetobacter baumannii are among the most common and difficult to treat opportunistic pathogens in nosocomial infections such as ventilator-associated pneumonia. Carbapenem resistant *A. baumannii* (CRAB) is ranked by WHO as a critical priority pathogen for the development of new antibiotics. To support the development of new antibiotics, we established a mouse pneumonia model with carbapenem and colistin resistant *A. baumannii* for evaluating novel treatments.

METHOD

A panel of MDR *A. baumannii* clinical isolates from Denmark was selected and MICs were determined accordioning to CLSI guidelines. 3 CRAB clinical isolates and 7 colistin resistant *A. baumannii* clinical isolates were evaluated for virulence in the murine pneumonia model in Balb/C mice utilizing intranasal inoculation and monitoring disease progression and bacterial growth over 26 hours. Methodology was aligned to recommendations published by the COMBINE consortium.

RESULTS

All 3 CRAB isolates increased in bacterial loads in the lungs with > 1 log_{10} CFU and mice developed severe clinical signs of infection 17-21 hrs after inoculation (Fig 1).

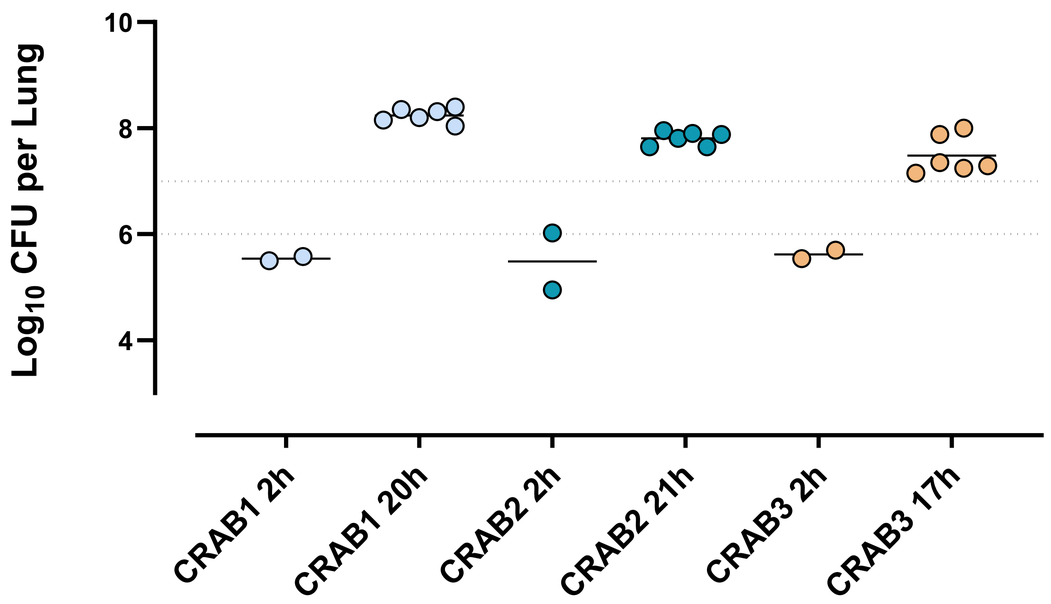

Figure 1. Virulence of 3 CRAB isolates

7 colistin resistant *A. baumannii* clinical isolates were first tested for virulence during 8 hrs in neutropenic Balb/C mice. All isolates increased in bacterial loads in the lungs with 0.5 – 1.3 log_{10} CFU and mice developed clinical signs of infection. 3 of these isolates were selected for further analysis in the 26h model (Fig 2). All 3 isolates increased in bacterial loads in the lungs with >1 log_{10} CFU and mice developed severe clinical signs of infection at 22-23 hrs after inoculation.

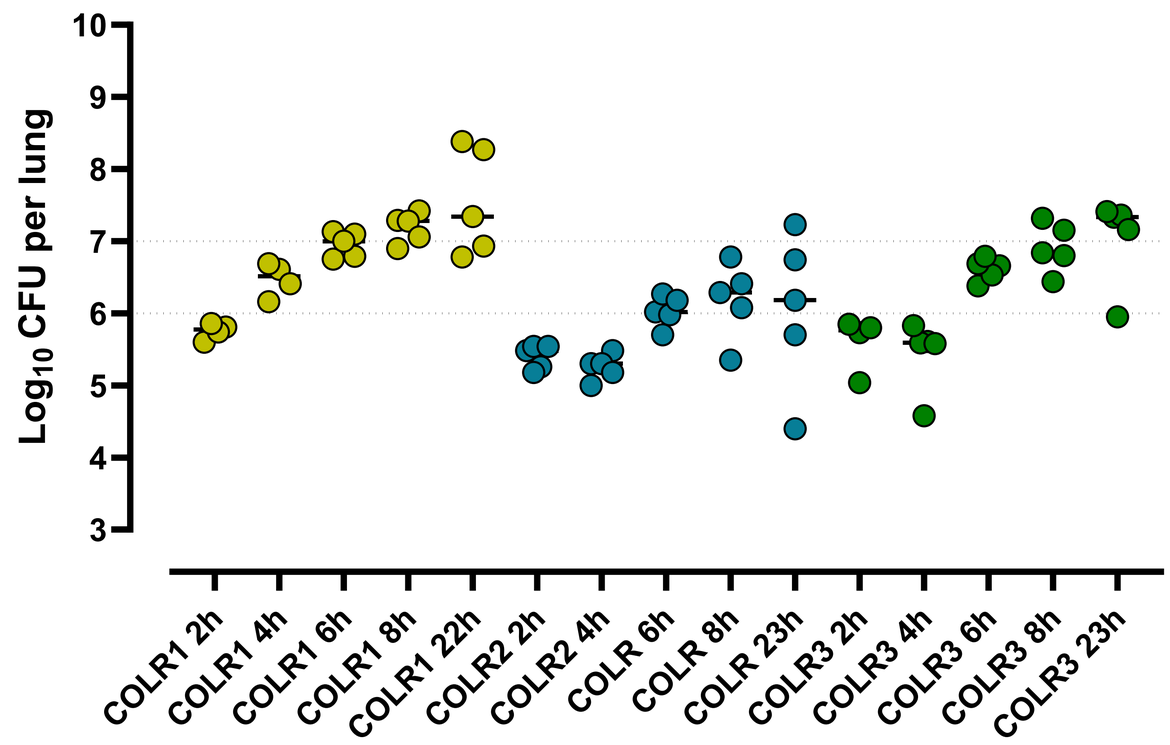

Figure 2. Virulence of 3 Colistin Resistant CRAB isolates

CONCLUSIONS

We have established preclinical mouse pneumonia models with 3 CRAB and 3 colistin resistant *A. baumannii* isolates suitable for evaluating novel antibacterial treatments.

Table 1 MIC (mg/L)	Meropenem	Ciprofloxacin	Gentamicin	Colistin
CRAB 1	> 16	> 8	16	< 0.5
CRAB 2	> 16	> 8	> 32	< 0.5
CRAB 3	> 16	> 8	> 32	< 0.5
COL R 1	> 16	> 8	> 32	> 16
COL R 2	> 16	0,25	1	16
COL R 3	> 16	> 8	> 32	> 16

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