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Acinetobacter baumannii: Setup and characterization of pneumonia and septicemia preclinical models with longitudinal monitoring using bioluminescent strains

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Project overview

Bacterial multidrug resistance (MDR) is responsible of up to 4.9 million deaths, with the MDR **ESKAPE** pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp) being the leading cause of nosocomial infections worldwide. Treating these MDR bacteria represents one of the greatest challenges in clinical practice.

Among ESKAPE pathogens, the emergence of rapidly spreading carbapenem-resistant *Acinetobacter baumannii*, combined to the lack of available active antibiotics has led the WHO to raise the threat level to "Urgent" and classify it in the critical group of its Bacterial Priority Pathogens List (2024). These observations call for an urgent need for new anti-microbials.

The goal of this study was to setup preclinical models mimicking the main clinical infections caused by *A. baumannii* (bacteraemia and pneumonia) using bioluminescent strains that allow to perform longitudinal monitoring of the bacterial dissemination and assess antibacterial candidate's efficacy.

MATERIALS:

Bacterial strains:

In collaboration with intensive care units several MDR *A. baumannii* were obtained. After microbiological characterization (antibiogram), 2 strains, isolated from broncho-alveolar or blood samples, were transformed to generate bioluminescent strains and were used to establish the *in vivo* acute pneumonia and septicemia mouse models.

Mice infection:

Neutropenic mice were infected with 10⁷ CFU/mouse by either

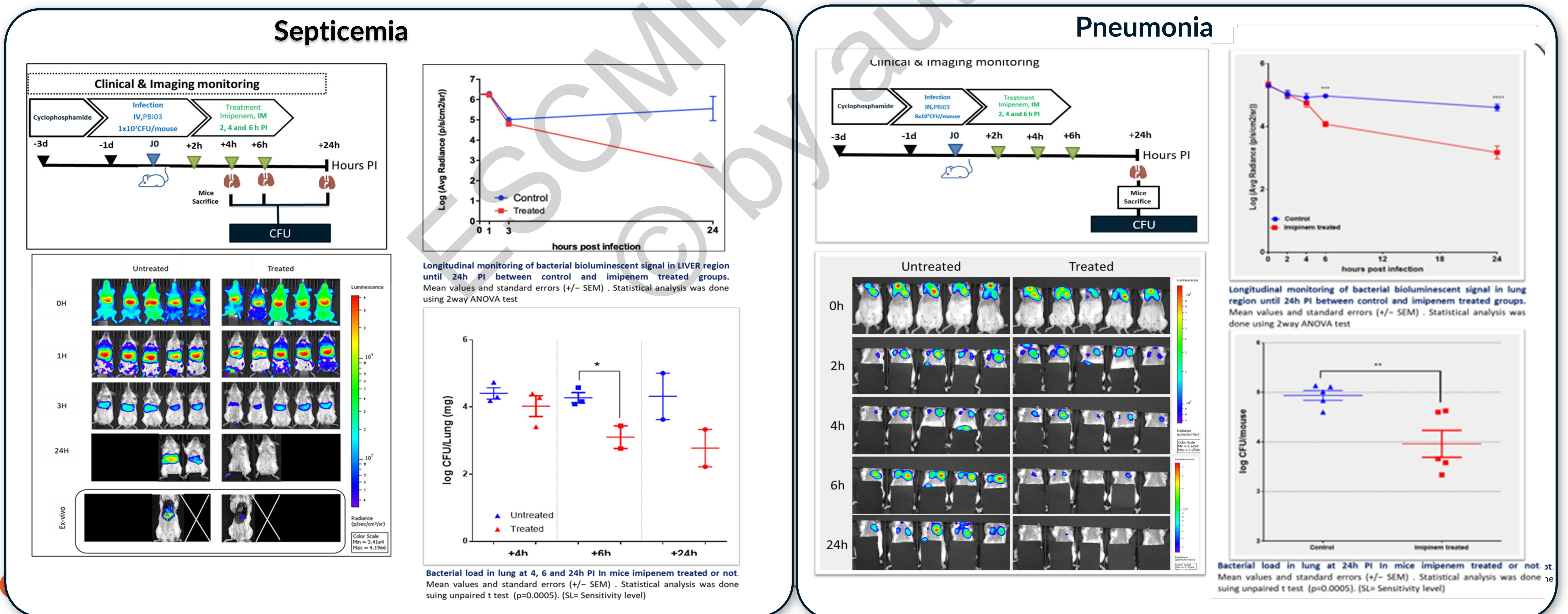
- **Intranasally** route to induce a PNEUMONIA model
- **Intravenously** route to obtain a SEPTICEMIA model

Kinetic of infection and antibacterial efficacy were longitudinally monitored using bioluminescence imaging system (IVIS Spectrum).

In vivo imaging:

In vivo optical imaging was used to longitudinally follow the infections by bioluminescence.

Bacteraemia and Pneumonia models setup



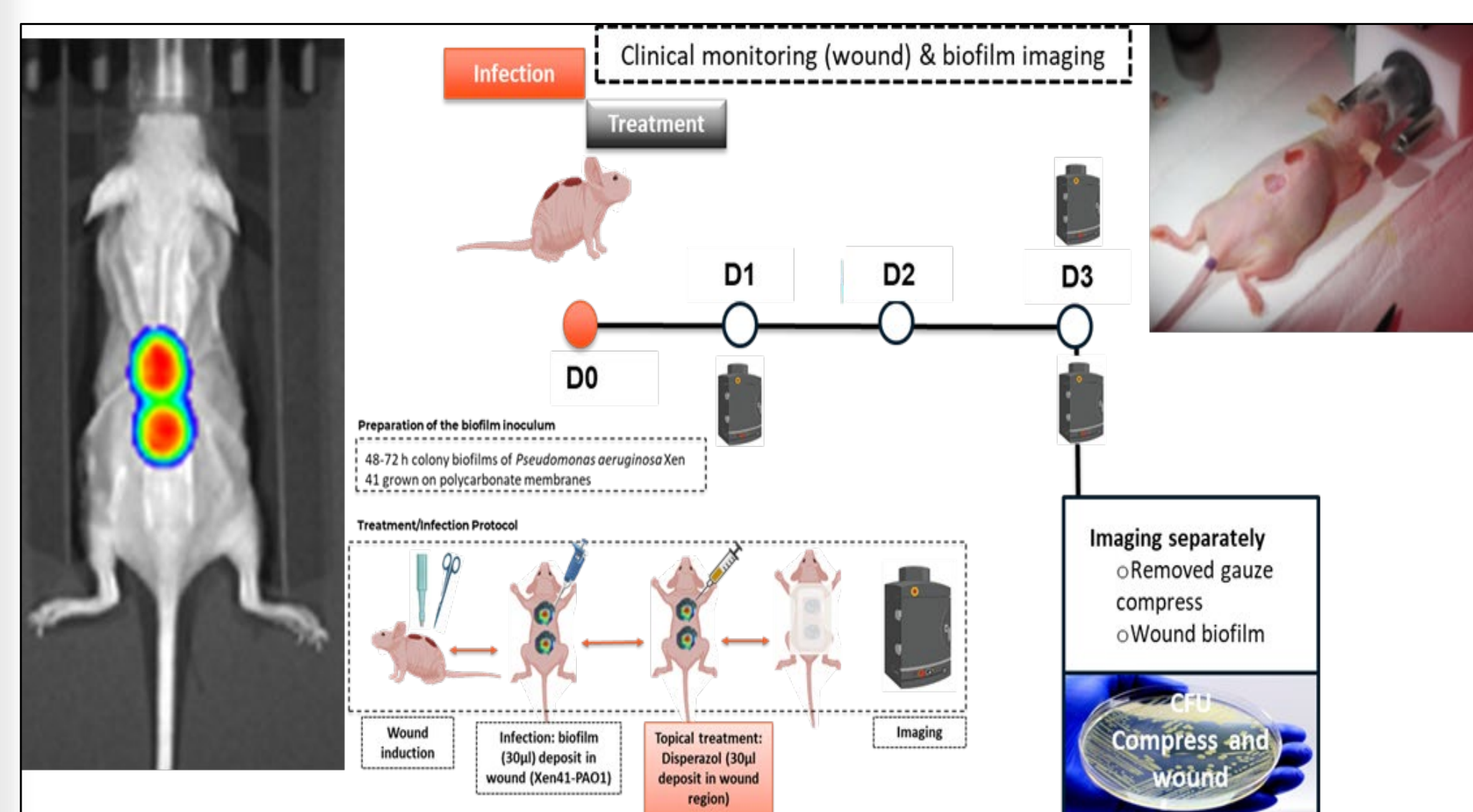
Conclusions

We established **two** relevant *A. baumannii*

PNEUMONIA and **SEPTICEMIA** infection models in mice and validated them as relevant preclinical models to study bacterial virulence/dissemination and to evaluate antimicrobial drug efficacy.

Next steps

- Setup Biofilm in wound model



- Lung model
- Multibacterial infection model
- Evaluate bacterial infection vs Microbiota (cutaneous)

We are open for collaboration!