Acinetobacter baumannii

- MDR infections tend to occur in immunosuppressed patients, in patients with serious underlying diseases, and in those subjected to invasive procedures and treated with broad-spectrum antibiotics.
- Infections are frequently found in intensive care units (ICUs), where they are implicated as the cause of ventilator-associated pneumonia (VAP), urinary tract infections, and bacteremia.
- Resistance to β-lactams, (β-lactamases: Class A (TEM, SHV, CTX-M), Class B (IMP), Class C and Class D (OXA-23), aminoglycosides, fluoroquinolones (*gyr*A / *par*C), tetracyclines (efflux) and polymixins.

Pseudomonas aeruginosa

- Problematic for seriously ill patients - Responsible for 21% of pneumonias, 10% of urinary tract infections, 3% of bloodstream infections, and 13% of eye, ear, nose, and throat infections within ICUs.
- Most commonly isolated bacterium colonizing severe burns and wound infections.
- Wound infections caused by multidrug resistant (MDR) *P. aeruginosa* have been associated with high morbidity and mortality rates worldwide.

- Based on the clinical issues faced due to both *A. baumannii* and *P. aeruginosa* infections, there exists the need for specific experimental animal models to be developed and used to screen and evaluate efficacy of new treatment options for these infections.
- To be relevant for the evaluation of new therapies to combat MDR *A. baumannii* and *P. aeruginosa* animal models:
  - Need to be representative of current clinical needs
    - Pneumonia, urinary tract infections, wounds/burns, bacteremia
  - Need to make use of relevant bacteria strains
    - Clinical isolates based on indication or site of isolation/infection
  - Need to utilize current strains of concern
    - Based on resistance phenotypes
  - Need to involve proper doses and dosing regimens
    - Treatment of established chronic infections
  - Need to define the measure of efficacy
    - Reduction of bacterial titers at the site(s) of infection

- Murine Lung Infection Model (Bacterial pneumonia)
  - Normal / Neutropenic mice (CD-1, Balb/c, C57Bl/6)
  - Intranasal inoculation
  - Treatment delayed 4 - 24 hrs post-infection (single/multiple dose regimens and routes – parenteral, oral and aerosol delivery)
  - Lung titer / Survival endpoints / PK-PD estimates (plasma & ELF)
  - Established for *A. baumannii* & *P. aeruginosa* endotracheal clinical isolates of various resistance phenotypes

- Murine Ascending Pyelonephritis (Urinary Tract Infection)
  - Normal / diabetic mice (C3H/HeJ)
  - Transurethral inoculation
  - Treatment initiated 4 days post-infection (established ascending model)
  - Kidney / Bladder / Urine titer endpoints
  - Established for multiple *P. aeruginosa* urine clinical isolates

- Murine Skin Infection Models (Skin & Skin Structure Infection)
  - Normal / Partial neutropenic mice (CD-1)
  - Intradermal (superficial) or subcutaneous (abscess) infection types
  - Treatment initiated 4 - 24 hrs post-infection, single/multiple dose regimens, both topical and parenteral
  - Bacterial titer / wound healing endpoints
  - Established for *A. baumannii* & *P. aeruginosa* wound clinical isolates (including mixed infection with *S. aureus)*

- Murine Septicemia (Systemic Bacteremia)
  - Normal mice (CD-1)
  - Intraperitoneal or intravenous inoculation
  - Treatment initiated 1 - 4 hrs post-infection (single/multiple dose regimens)
  - Survival (ED_{50}) / Blood & Spleen titer endpoints (time course)
  - Established for *A. baumannii* & *P. aeruginosa* bloodstream clinical isolates, including characterized resistant strains (IMP-4, OXA, TEM, SHV, KPC, NDM)