



## *Streptococcus pneumoniae* (QRDR mutants) Acute pneumonia

### Procedure Summary

- Immunocompetent New Zealand rabbits
- *S. pneumoniae*
  - Wild-type strains
  - QRDR mutants : *parC*, *gyrA*, *parC-gyrA*, *efflux*
- Intra-tracheal challenge ( $0.5 \times 10^{10}$  CFU)
- Reference compounds : levofloxacin, moxifloxacin, gatifloxacin
- Simulated human dosing (PK) for 48h

### Experimental readouts

- Bacterial burden in lung tissue and spleen
- Weight loss, food intake
- Fever, Clinical disease severity score
- Survival rate
- Gross pathology of lungs
- Detection of resistant mutants, Mutant Selection Window identification

### Optional Services

- Broncho Alveolar Lavage Fluid
- Histology
- Cytokine and chemokine analysis
- Immune cell counts

### References

- Croisier *et al*, JAC 2002, vol 50 : 349-360
- Croisier *et al*, AAC 2004, vol 48 : 1699-1707
- Etienne *et al*, JID 2004, vol 190 : 1472-1475

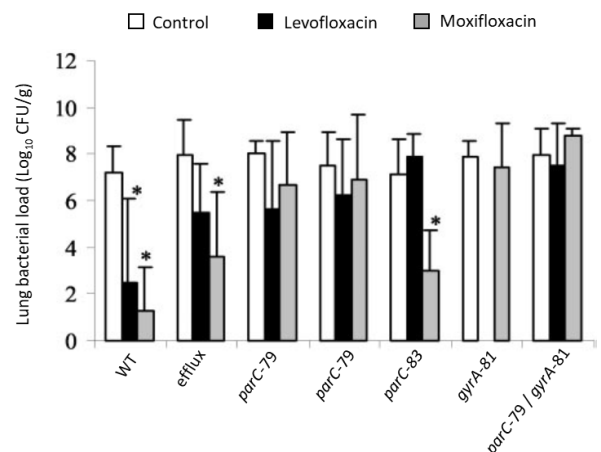
### Facilities

- These assays are performed at our BSL2 laboratory / zootechnical center in Dijon, France

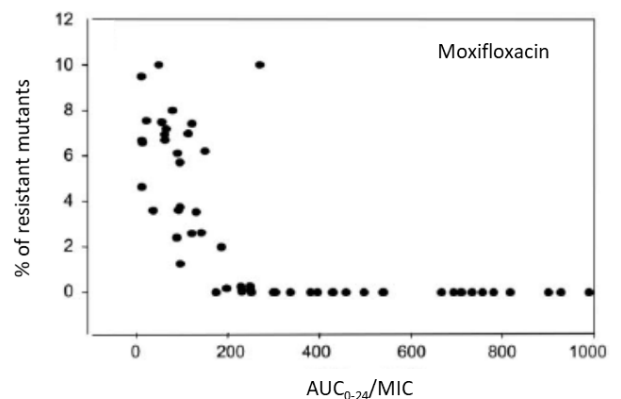
### Animal Welfare

- Each experimental protocol is approved by the local ethics committee for animal experimentation of Grand Campus Dijon (Burgundy, France) and performed in accordance to the current recommendations of the European Institute of Health EU Directive 86/609.

Pulmonary residual bacterial content in rabbits infected with *S. pneumoniae* strains exhibiting various levels of susceptibility to fluoroquinolones



Relationship between fraction of cells recovered as mutant and moxifloxacin exposure in rabbits infected with a *parC* mutant *S. pneumoniae* strain.



Our scientific team will readily accommodate client-specific alterations and will provide expert advice and guidance for your efficacy studies

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