# End-to-end Capabilities for Infectious Disease Drug Discovery

charles river

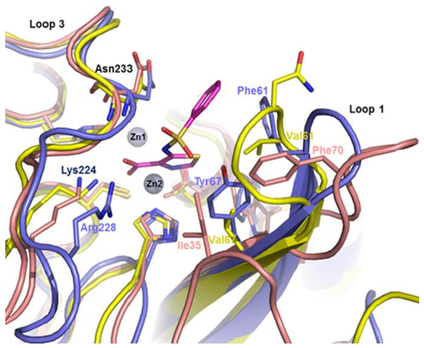
**End-to-end Infectious Disease Drug Discovery at Charles River**

- The development of new drugs, vaccine candidates and assessment of novel drug combinations, is key to help combat the increasing threat of antimicrobial resistance and the spread of infectious disease.
- With our expertise in chemistry, microbiology, immunology, and host-pathogen interactions, we can offer a bespoke end-to-end service to help support your infectious disease drug discovery projects, from early drug discovery, preliminary *in vitro* testing and use of *Galleria mellonella* for early *in vivo* screening, to pre-clinical mammalian model systems and safety assessment.

## Early discovery

**Integrated drug discovery**

- Extensive experience in anti-bacterial, anti-fungal, anti-viral and anti-parasitic drug discovery programs.
- Fully integrated teams including medicinal and synthetic chemists, biologists, structural biologists, DMPK experts, pharmacologists, formulation specialists.
- Multiple client compounds progressed into the clinic.




**Hit Finding**

- State-of-the-art high-throughput screening platforms for the identification of hit compounds across the spectrum of gene and target classes.
- Virtual and fragment-based screening with in-house structural biology support.

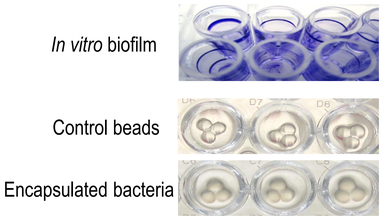
**Medicinal chemistry**

- Lead optimisation to improve biochemical potency and *in vivo* efficacy. Physicochemical and pharmaco-kinetic optimisation to ensure optimal *in vivo* target coverage.
- Computational chemistry and in-house X-ray crystallography to support the design process.
- Novel template design and implementation of challenging synthetic chemistry.
- Process chemistry, pharmaceutics and formulation.
- Patent strategy management. Preparation and support for IND filing.

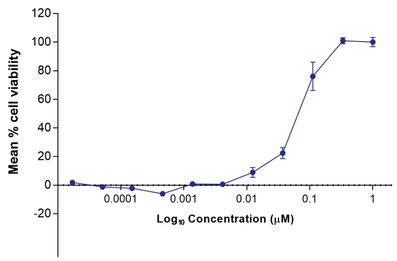
## *In vitro* assays

**Anti-bacterial and anti-viral testing**

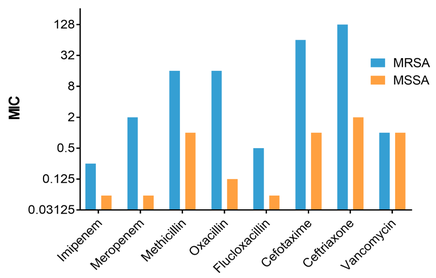
- Wide range of susceptible and multi-drug resistant bacterial strains including all ESKAPE pathogens and luminescent strains.
- Viral strains include Influenza, Herpes simplex and respiratory syncytial virus
- Assays to determine drug tolerance and susceptibility, biofilm formation, and host-pathogen interactions.




*In vitro* biofilm models: top - 96 well plate crystal stain standardised method, bottom two images - alginate bead model system.




Viral $EC_{50}$ determination: Rescue of influenza (H1N1) infected MDCK cells by zanamivir treatment.




Assessment of MIC for different antibiotics against *S. aureus* MRSA and MSSA strains

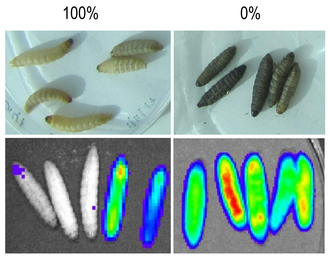
## *In vivo* models

***Galleria mellonella* screening model**

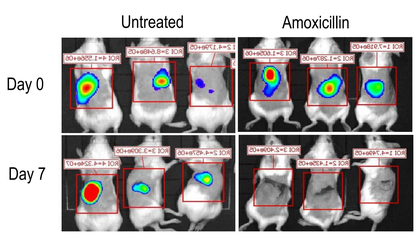
- Wax moth larvae model for early *in vivo* compound screening for efficacy and toxicity

**Mammalian bacterial and viral infection models**

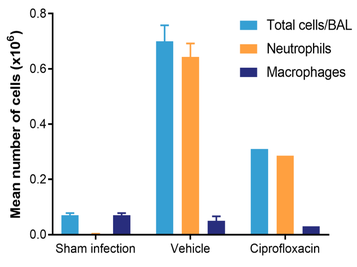
- Pre-clinical screening for efficacy of antimicrobial and antiviral therapy.
- Range of acute and chronic models offered; skin, lung, sepsis, UTI, deep wound, thigh infection, influenza, and vaccination models with challenge.



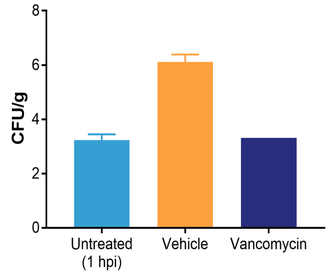

*In vivo* bacterial burden in *Galleria.*



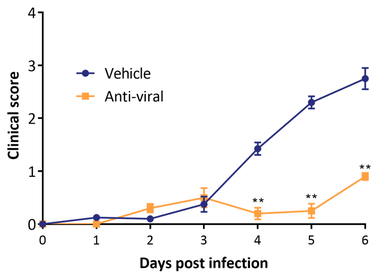

Bacterial burden following wound infection and successful treatment with Amoxicillin.




Bioanalysis on bronchial lavage fluid shows an influx of inflammatory cells following infection and treatment with ciprofloxacin.




Intravenous infection with *Staphylococcus aureus* can be rescued following treatment with Vancomycin.




Anti-viral treatment is effective at blocking clinical signs of H1N1 infection in mice (p value < 0.001).

## Safety assessment

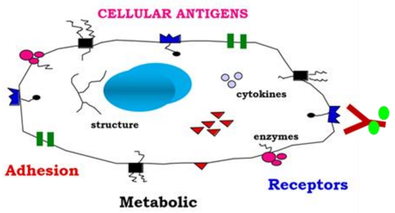
**PK/PD**

**IND Enabling Studies**

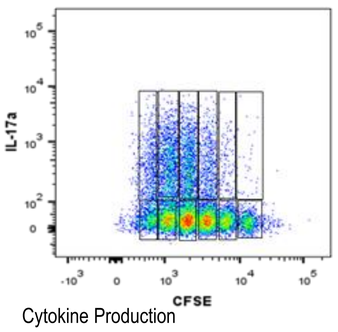
**Fast Track Expertise**

***In Vivo* Support**

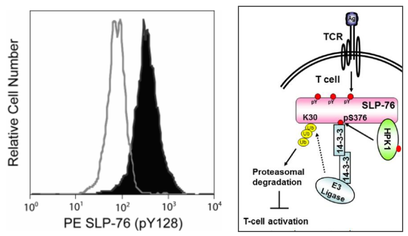
- Flow Cytometry
- Immunohistochemistry (IHC)
- T-Cell-Dependent Antibody Response (TDAR)
- Cytokine Analysis
- Gene Expression




Phenotypic Analysis




Cytokine Production




Cell Signaling