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.

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**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.

**In vitro assays**

- **Anti-bacterial and anti-viral testing**
  - Wide range of susceptible and multi-drug resistant bacterial strains including all ESRAPE 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.

- **Galleria mellonella screening model**
  - Wax moth larve model for early in vivo compound screening for efficacy and toxicity

**In vivo models**

- **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.

**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
- Relative Cell Number
- T Cell
- Phagocytosis
- Adhesion
- Metabolic
- Receptors

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**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.

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

**Example**

- **Viral E<sub>C50</sub> determination:** Rescue of influenza (H1N1) infected MDCK cells by zanamivir treatment.
- **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.

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

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