TB Drug Discovery Facility:
Mycobacteria Research Laboratory for Screening Drugs and Inhibitors
Birkbeck & LSHTM, University of London and UCL

Tuberculosis (TB), an ancient infectious disease, still accounts for the highest human mortality (around 2 million deaths every year) worldwide from its causal pathogen, Mycobacterium tuberculosis, alone. In spite of intensive efforts towards eradicating TB, it remains a challenging health problem not only for the developing countries but also for the developed world. Furthermore, the situation is becoming even more complicated due to issues such as: (a) long, complex and ineffective chemotherapy against newly emerging extensively-drug-resistant (XDR)/total-drug-resistant (TDR)-TB strains, (b) conflicts among the anti-TB and anti-human immunodeficiency virus (HIV) drugs, and (c) no cure for latent TB infection. Therefore, development of a new and more effective drug treatment against TB is urgently required.

A concerted effort has made worldwide towards developing new anti-TB drugs by different consortia such as the global alliance for TB drug development (http://www.tballiance.org/), TB drug discovery (TBDUK) (http://www.tbd-uk.org/), open source drug discovery (OSDD) (http://www.osdd.net/), new medicines for TB (NM4TB) (http://www.nm4tb.org/), the working group on new TB drugs (WGND) (http://www.newtbdrugs.org/), and more medicines for TB (MM4TB) (http://www.mm4tb.org/) resulting in a large number of novel chemical libraries in the pipeline which require a comprehensive phenotypic evaluation at the preclinical stage of TB drug development.

The joint facility offers:
(a) High throughput screening of inhibitor libraries against the whole cell Mycobacterium species including drug resistant mycobacterial strains from in vitro to ex vivo including determination of MIC (Minimum Inhibitory Concentration) & MBC (Minimum Bactericidal Concentration).

(b) High throughput screening of inhibitor libraries for their mammalian cell toxicity and determination of SI (Selectivity Index) values.

(c) High throughput screening of inhibitor libraries against the following novel therapeutic targets in Mycobacterium: (i) ATP-dependent Mur ligases (MurC/D/E/F) (ii) Arylamine N-acetyltransferase (NAT), (iii) Oxidoreductases and (iv) a number of other novel targets (research in progress).

We use the following bacterial strains for whole cell screening:
Mycobacterium smegmatis, Mycobacterium phlei, Mycobacterium aurum, Mycobacterium marinum, Mycobacterium bovis BCG, Mycobacterium tuberculosis (Control: Escherichia coli, MRSA & Pseudomonas sp. for antibiotic specificity)

We use RAW 264.7 mouse macrophage cells and SPOTi & MABA as whole cell assay methods.

Key Publications:

Please contact Dr Sanjib Bhakta (s.bhakta@bbk.ac.uk), Head of ISMB Mycobacteria Research Laboratory for MTA/ CDA/ contract research or academic collaboration.