UoL Research Achievements

The main focus of our research is on improving TB treatment using a spectrum of multidisciplinary approaches at all stages of drug development.

Preclinical development

UoL was the academic co-ordinating institution for the highly successful PreDiCT-TB consortium, a major public-private partnership involving 18 academic and 3 large industrial partners (GSK, Sanofi and Janssen) funded by the EU Innovative Medicines Initiative (€15.3m). The consortium is the first systematic re-appraisal of the value of in vitro and in vivo preclinical models for identifying the best combinations of tuberculosis drugs to progress into clinical trials and will result in novel approaches to the development pathway involving new biomarkers, experimental designs and integration of information through mathematical models.

Pharmacokinetics and pharmacogenetics

UoL is the UK centre of pharmacokinetic expertise in tuberculosis, leading and collaborating on numerous observational studies describing the behaviour of first-line drugs and drawing attention to ways in which their dosing could be optimised in adults and children. These studies have also explored the pharmacogenetic basis of variability in pharmacokinetics to explain differences between populations worldwide (Peru, South Africa, Malawi and Thailand). UoL was the lead institution of the Wellcome Trust-funded PKPDia consortium (£850k) which successfully developed sustainable expertise in pharmacokinetic-pharmacodynamic modelling in TB, HIV and Malaria in three WT-supported major overseas programmes.

Clinical studies

UoL collaborated with Harvard University on a key Phase II clinical trial of higher doses of rifampicin which supported the safety and improved efficacy of doses of this key agent twice as high as currently recommended using innovative methodology in Lima, Peru (HIRIF trial NIAID £5.5m). Another major theme of our research has been the identification of better models and biomarkers of treatment response. We developed a new approach to statistical modelling of quantitative bacteriology data in clinical trials (Rustomjee IJTLD 2008) which has been implemented in several studies and we have shown how to combine this with direct measurements of persister-like organisms in sputum specimens in order to better predict long-term treatment response (Sloan CID 2015).

Evidence synthesis

UoL has also been active in conducting systematic reviews of tuberculosis treatment in collaboration with the Cochrane Infectious Diseases group (Davies CLSR 2007, Ziganshina CLSR 2013). As part of the activities of PreDiCT-TB, a comprehensive review of all existing Phase II and III clinical trial data in the tuberculosis literature has recently been completed which summarises the existing state of knowledge about the performance of current agents and the predictive performance of early bacteriological data against long-term outcomes (Bonnett CID 2017). In addition, in collaboration with Critical Path to TB Regimens in the US, PreDiCT-TB has helped to develop the WHO-supported TB-PACTS data-sharing platform, the first viable repository for individual patient data in TB clinical trials which will facilitate improved such analyses in the future.