Liverpool School of Tropical Medicine
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LSTM
RESEARCH CENTRE FOR DRUGS & DIAGNOSTICS

Leading the way in diseases of poverty in the tropics

The Liverpool School of Tropical Medicine's Research Centre for Drugs and Diagnostics' public–private partnerships and delivery of translational projects help vulnerable people in resource-poor countries.

The Research Centre for Drugs and Diagnostics (RCDD), located at the Liverpool School of Tropical Medicine (LSTM), comprises a multidisciplinary group of experts working to develop new drugs and diagnostics for tropical diseases.

Using state-of-the-art laboratories and equipment, the team at the RCDD regularly works with industry, academia and other nongovernmental organizations to discover, develop and deliver novel therapies and diagnostics against a range of pathogens. The team's extensive experience includes drug discovery and development projects for malaria, tuberculosis and neglected tropical diseases.

"We work on diseases of poverty in the tropics and have expertise across the full spectrum of translational research, from discovery and development all the way through to implementation and policy," said Giancarlo Biagini, pharmacology lead at the RCDD. "Our transdisciplinary research environment is critical for the successful generation of new drugs and diagnostics for vulnerable people in resource-poor countries."

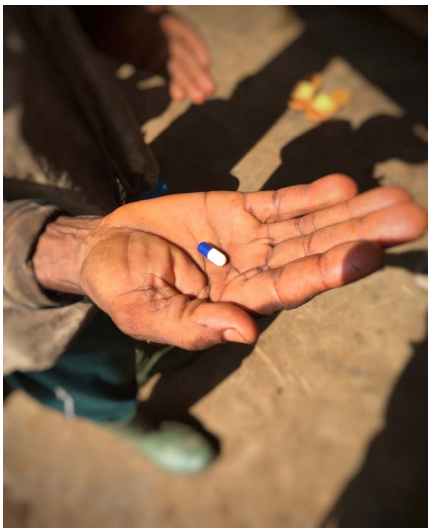
The RCDD offers access to patient populations, and pathways to drug and diagnostic evaluation and implementation, in the UK, Africa, Asia and South America, as well as field sites for monitoring and evaluation in Africa, South America and South East Asia. "We have very strong partnerships with scientists in endemic countries, and our links with industry bridge the gap between pharma and the endemic communities in need and help to strengthen their capacity to deliver new interventions," said Mark Taylor, chair in parasitology at the LSTM.

Product development public–partnerships

The RCDD is involved in a number of product development public–private partnerships, with a portfolio of projects that range from hit identification and expansion through to lead series development and optimization and to preclinical candidate identification.

For example, Taylor is director of the Anti-*Wolbachia* (A-WOL) Consortium, which comprises both academic and industrial partners funded by the Bill & Melinda Gates Foundation, Global Health Technology Fund and the Medical Research Council. A-WOL aims to discover and develop new drugs against onchocerciasis (river blindness) and lymphatic filariasis (elephantiasis). Traditional treatment for these conditions, which are both caused by parasitic filarial nematode worms, requires long-term mass drug administration programs with drugs that target the larval stage.

A-WOL is working to develop novel approaches that are capable of killing adult worms (macrofilaricidal) within a 7-day treatment period by targeting *Wolbachia*, a bacterial endosymbiont essential for the worms' survival. The group has identified a candidate molecule, TylAMac, which is the first next-generation anti-*Wolbachia* drug to be designed specifically as a macrofilaricidal agent. The lead molecule is undergoing formal preclinical evaluation in partnership with AbbVie and DNDi. A-WOL researchers at the RCDD screened 10,000 compounds from a large compound library and identified 6 anti-*Wolbachia* chemotypes with suitable drug-like qualities[1]. The first industrial scale screening of 1.3 million compounds in partnership with AstraZeneca delivered 20,000 hits and a further 10 novel chemotypes as promising new leads.



Louise Hamill, LSTM

A cacao farmer taking doxycycline to cure his river blindness.

A-WOL has also identified two repurposing molecules, high-dose rifampicin and fusidic acid, which significantly reduce treatment times compared to the current gold-standard, doxycycline. In October 2017, RCDD researchers published a proof-of-concept study of a radical improvement made to the targeting of *Wolbachia* via a drug synergy between a common anthelmintic drug (albendazole) and different classes of antibiotics (tetracyclines and rifampicin)[2]. Using the drugs in combination reduced the length of treatment required from several weeks to 7 days, opening up the opportunity to scale-up this approach at the community level.

Delivering translational projects

The RCDD has a track record in the delivery of translational projects and is actively involved in a number of partnerships and consortia both in the UK and internationally. For example, RCDD runs and is part of the Medical Research Council Confidence in Concept Tropical Infectious Disease Consortium, a partnership between leading UK institutes involved in translational research in tropical infectious diseases. In the past 5 years, the consortium has funded more than 50 projects, nearly 40 of which involved industrial partners.

Researchers from the RCDD are also contributing to a project to develop E209, a second-generation peroxide-based drug that has the potential to become the first fully synthetic one-dose malaria treatment[3]. Working in partnership with the University of Liverpool and a global collaborative network of scientists, and with input from Medicines for Malaria Venture, the group designed E209 to have significant improvements over the gold-standard antimalarial treatment artesunate. Data from in vitro studies show that E209 is effective against parasites that express mutations in the *K13* gene, the key genetic marker for artemisinin resistance.

In the field of tuberculosis, the RCDD works closely with partners in developing countries, taking a practical approach to finding the best solutions that can be applied effectively in resource-constrained countries. For example, the RCDD is involved in clinical studies to evaluate new diagnostics for tuberculosis in Nigeria, Ethiopia and Moldova, and to develop health system approaches that facilitate population access to diagnostics and treatment.

RCDD also works with industry to design and improve tuberculosis diagnostics using its extensive culture collection and containment level 3 facilities at LSTM. "We have one of the largest complements of category 3 laboratories in academia in the UK," said Biagini. The suite is a purpose-designed unit for the safe handling of organisms classified as Advisory Committee on Dangerous Pathogens hazard group 3, and offers access to hazard group 3 human pathogens, including *Mycobacterium tuberculosis* and *Plasmodium falciparum*.

The RCDD offers flexible models of collaboration, from open access to commercial service provision.

1. Johnston, K. L. et al. *Sci. Adv.* **3**, eaao1551 (2017).
2. Turner, J. D. et al. *Proc. Natl Acad. Sci. USA* **114**, E9712–E9721 (2017).
3. O'Neill, P. M. et al. *Nat. Commun.* **8**, 15159 (2017).

contact
Giancarlo Biagini, Pharmacology Lead
Research Centre for Drugs and Diagnostics at the Liverpool School of Tropical Medicine
Liverpool, UK
Tel: +44 (0)151 705 3151
Email: giancarlo.biagini@lstmed.ac.uk