

Laboratory science in tropical medicine

From laboratory and clinical sciences through to public health...

Much of the investment given to alleviating the burden imposed by diseases of poverty is focused on public health/operational research, as part of the delivery and monitoring of existing interventions. However, in the face of a continuing need to develop new therapies and diagnostics due to changing demands imposed by pathogen evolution or operational constraints, means that discovery science is an important part of the research portfolio.

As the first institute in the world dedicated to research and teaching in tropical medicine, the Liverpool School of Tropical Medicine (LSTM) has a long track record of contributions to promoting improved health in less developed countries by providing a balanced portfolio of activity from laboratory and clinical sciences through to public health.

The relationship between the host and pathogen is a fascinating and important one, providing insights into complex biological processes, co-evolution and molecular pathogenesis, as well as information for the development of novel products aimed at reducing disease. As part of its commitment to basic science research, LSTM opened its Centre for Tropical and Infectious Diseases (www.lstmliverpool.ac.uk/research/research-environment/ctid) in 2008.

This centre brings together teams of multidisciplinary scientists in state-of-the-art facilities to promote research on tropical diseases, which, while often being very much within the realm of discovery science, has a clear goal of translation into product development. This is considered to be the first phase of translation, bringing new discoveries through into realistic programmes aimed at making new

therapeutic products, and this operates within an environment that also houses the second phase of translation, ensuring that research influences policy and products reach practice.

Having both phases of translation within a single institute allows integration of both 'communities', ensuring that the laboratory researcher is answering relevant questions and creating appropriate products for resource-poor settings, and providing a platform for evaluation and delivery of the new interventions. The latter is the focus of one LSTM's latest strategic developments, through the establishment of a new Centre for Applied Health Research and Delivery.

Taking research findings into product development is not simple, as demonstrated by the paucity of new drugs for infectious diseases being registered, particularly for diseases of poverty. LSTM seeks to address this through the use of conventional academic structures that bring researchers together with appropriate resources to deliver innovative science, but, in addition, works with industrial partners within Product Development Partnerships (PDP):



Innovative Vector Control Consortium (IVCC)

The IVCC (www.ivcc.com), funded by the Bill and Melinda Gates Foundation, is a PDP established as a not-for-profit company and a registered charity. The aim of IVCC is to overcome the barriers to innovation in the development of new insecticides for public health vector control, and to develop information systems and

tools that will enable new and existing pesticides to be used more effectively. It was created by the Director of LSTM Professor Janet Hemingway, who brought together an international team of researchers working on vector control based around the major contributions to research on insecticide resistance from LSTM.

Working with major companies in the agro-chemical business (e.g. Bayer, Vestergaard, Syngenta, DuPont, BASF), it is developing new insecticides to replace existing pyrethroid compounds for which resistance is spreading in mosquito populations across the world. However, this needs to be within a remit of economic and operational constraints imposed by working in areas without access to strong infra-structures. Laboratory research has contributed to the development and testing of new insecticides, as well as field tests for insecticide resistance to inform public health decisions on vector control programmes.



Anti-Wolbachia Consortium (AWOL)

Similar to IVCC, including its BMGF funding base, AWOL (<http://a-wol.com>) consists of academic and industrial partners working to create products suitable for mass drug administration (MDA) programmes for human filariasis, and to discover new alternative treatments in the event of drug-resistance developing to current therapies. The basis for this programme comes from an original laboratory finding made by Professor Mark Taylor, who discovered that the

nematode worms causing elephantiasis and river blindness need a symbiotic bacterium *Wolbachia* to survive.

Direct treatments for the filarial parasites can lead to serious side-effects due to the release of inflammatory factors, whereas using drugs that kill the bacteria within the worms leads to their death without deleterious effects on the host. Tetracycline-based drugs are now being used in a major MDA programme to eradicate disease. Simultaneously, there are efforts to design better medicines with shorter treatment regimens, working closely with another of LSTM's academic centres (Centre for Neglected Tropical Diseases – see below).



LSTM also operates a number of academic centres that inform areas of laboratory science and bring basic and clinical scientists with appropriate skills together. One of the major research centres operates in collaboration with the University of Liverpool and the College of Medicine, University of Malawi – the Malawi-Liverpool-Wellcome Trust (MLW) Clinical Research Programme (www.mlw.medcol.mw). This Wellcome Trust-funded major overseas programme has a laboratory facility that supports hi-tech research conducted in a disease-endemic setting. MLW identifies the priority research questions relevant to the health problems in Malawi and Southern Africa, and provides a focus point for a key part of our strategy, namely capacity strengthening.

Finding sustainable ways of implementing capacity strengthening is a major challenge, particularly in resource-constrained settings such as sub-Saharan Africa. MLW relies significantly on the long-term investment provided by the Wellcome Trust as part of their strategy for capacity development.

MLW is a partnership with mutual benefit that facilitates training and career development in medical research for African scientists, and provides a resource for investigators from high-income countries to answer new research questions to generate relevant and international quality outputs.



'Neglected Tropical Diseases' is a recent term, in part championed by a former Director of LSTM Professor

David Molyneux. Through his lobbying and persistence, funding agencies have recognised the importance of supporting research into a group of tropical diseases with significant mortality and morbidity, but a lower 'profile' than malaria, HIV/AIDS and TB. The Centre for Neglected Tropical Diseases (CNTD) (www.cntd.org), headed by Professor Moses Bockarie, was created in LSTM largely around a DFID-funded programme to eradicate lymphatic filariasis through a range of public health approaches, including MDA. Its portfolio has developed to include laboratory science, both in terms of monitoring infection and drug resistance, as well as linking with AWOL to develop new products for treatment and diagnosis.

Similarly, with tropical medicine often seen in the context of three main infectious diseases, envenoming by snake bite is under-represented, yet it kills at least 125,000 people each year. Victims that survive envenoming often suffer severe tissue damage at the site of the bite, which can cause permanent physical disability and deformity. The majority of snake bite victims are the rural poor in tropical countries with severely under resourced health infrastructures.

The Alistair Reid Venom Unit at LSTM (www.lstmliverpool.ac.uk/research/research-environment/venom-unit) is a

unique resource for snake venom research, headed by Dr Rob Harrison. The unit hosts the largest collection of venomous snakes in the UK, for use in clinical and scientific studies to improve the efficacy, safety and affordability of anti-venoms to treat victims of snakebite, with a focus on the rural poor of Africa. As well as being involved in clinical studies aimed at improving snakebite management, the unit has used genomic technologies to understand the complex mixture of biological components found in venoms, and to design new therapies with better coverage of snake species and fewer adverse reactions on treatment.

Laboratory science has a major role to play in tropical medicine research through the delivery of new knowledge that can be translated into interventions for diseases in resource-poor countries. However, in addition to the standard issues faced by academia in an increasingly competitive environment for funding, it has the added challenges of working frequently in very difficult environments, supporting capacity strengthening for its partners in research and obtaining sufficient recognition by the academic community for the translational research that needs to be undertaken if research findings are to be developed into products.



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