



Fundamental research is the key to eliminating TB

To speed up progress to tackle the disease, basic researchers and those on the front line must talk to each other more, says **Christian Lienhardt**.

Fewer people will contract tuberculosis (TB) this year than last. That is good news, and enough to meet the United Nations Millennium Development Goal that called “to halt and begin to reverse the incidence” of TB. But the pace of progress is too slow. Some 8.6 million people contracted the disease in 2012, and 1.3 million died, including 320,000 people with HIV. As it stands, the world will miss the international target to eliminate TB by 2050. To meet that ambitious goal, we need to modernize the way in which we tackle the disease. This means that fundamental research must play a bigger part in nurturing the development of diagnostics, medicines and vaccines.

Some clinicians in the TB field still do not recognize the power of basic research in developing tools for patients. Indeed, the slow pace of the research often frustrates health workers. In return, basic researchers may not see how their efforts can directly contribute to TB management. The divide between the two approaches sees them often considered at odds with each other.

The past ten years have seen a remarkable rise in the number of research, financing, technical and programme partners involved in building a major pipeline for TB tools. Innovative public-private partnerships and community activism have stimulated faster and more equitable access to such tools. However, without continued studies into the molecular nature of TB, no new interventions will become available to health-care professionals. At a time when health systems still miss about one-third of the new cases each year and as drug-resistant TB strains are signalling a fresh public-health crisis, basic research must be better harnessed and promoted to develop new diagnostic, therapeutic and preventative tools.

To help catalyse this change, the World Health Organization (WHO) has made research one of the three fundamental pillars of its proposed post-2015 global TB strategy. This research pillar seeks to promote the discovery, development and rapid adoption of new tools for TB control. Never before has the WHO so clearly addressed the need for fundamental research in the fight against TB, and it hopes that doing so now will encourage crucial communication across the community. Clinicians and public-health specialists need to help to identify areas in which fundamental research can provide answers, but they also need to learn the rhythms and language of basic research — the constraints, processes and timescales. In exchange, fundamental researchers must learn how to give their studies the most impact on clinical needs and disease burden.

This will require fresh thinking on how to fund and manage cross-disciplinary science. We need to encourage researchers to assemble multidisciplinary teams to work on key public-health research themes with defined outcomes.

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Longitudinal studies of patients and households can be used, for example, to identify biomarkers that characterize the various clinically relevant stages of TB, together with studies on how to prevent transmission and disease development. The power of this type of study has been illustrated in the Framingham Heart Study, established in 1948 to identify the factors behind cardiovascular disease.

A coordinated approach could help to prevent TB. Understanding the biology of *Mycobacterium tuberculosis* — the function of its intracellular machinery and the biochemical pathways critical for its survival and pathogenesis — is essential to combat the pathogen. More-sophisticated studies of the host immune response could help to identify biological mechanisms in people who become infected but never develop active TB, and might reveal how vaccines could mimic the immune response.

In diagnosis, simple tests that use small quantities of body fluids to detect infection would help to prevent progression to active disease. Rapid identification of drug resistance is needed to initiate appropriate, safe and effective treatment.

In treatment, basic and translational research must focus on improving options for people with drug-sensitive and drug-resistant TB alike. These efforts should go beyond the development of better drug candidates and combinations and study why TB cannot be treated with just a few weeks of chemotherapy — as most bacterial infections can be.

None of these studies, however, will be possible without the close collaboration of patients, physicians and basic, translational and clinical researchers, to jointly guide the rational approach to identification of new diagnosis, treatment and preventive options. Broad, cross-discipline research spans a range of funding agencies and cannot be supported by individual funders. To facilitate the funding of cross-cutting work, projects could be designed on the basis of the disciplines involved, and scientists could seek funds from agencies that support work in these respective disciplines, such that multiple funders could ultimately be involved in larger projects.

Crucially, the development of optimal tools to prevent, detect and treat TB depends heavily on public and private funding; the financing gap for TB research is now estimated at about US\$1.4 billion per year. The WHO's objective in promoting this crucial dialogue and change is to bring together the clinical, public-health and research communities to promote and expand TB research and its funding. But the agency also hopes that fundamental researchers from many other scientific fields will consider applying their work to TB. The world needs them. ■

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