PERSPECTIVE


Graduation time

Universities should forego profits from tuberculosis, say **David G. Russell** and **Carl F. Nathan**.

Tuberculosis (TB) is the single leading cause of death from bacterial infection. It is rapidly becoming untreatable, and untreated TB has a fatality rate of about 70% after three years. The challenges in developing new drugs for TB are scientific, logistical, fiscal and societal.

Over the past decade many pharmaceutical firms have abandoned antibiotic research, having failed to discover effective candidates with new mechanisms of action. A further disincentive is the lower return on investment that rapidly curative drugs offer compared with palliative medications for prevalent conditions. The financial picture is particularly bleak for TB, which chiefly afflicts people in low- and middle-income countries. The prospect of even scantier profits makes it all the harder to entice drug companies to work on TB rather than infections that are common in wealthy markets.

The treatment of TB requires combination chemotherapy, because the use of a single agent virtually guarantees the rapid emergence of resistance. When new TB drugs do reach the market, rampant drug-cutting and counterfeiting in poorer countries mean that one or more of the drugs in the combination may be absent, or present at suboptimal concentrations, promoting the accelerated emergence of drug resistance, which is already prevalent to each of the widely used TB drugs. Consequently, one new TB drug is unlikely to do the trick: we need sets of drugs that work together. The difficulty of finding a new combination is more than additive, as each drug must not interfere with the others or with the antiretrovirals used to treat HIV infection (a common co-infection in sub-Saharan Africa). Thus, even if a pharmaceutical company discovers one effective new TB drug (a big if), the chances are that such a drug would be rapidly lost to resistance unless it were used in combination with two or three other new drugs. Embarking on such a search takes an unprecedented level of social consciousness and cross-industry cooperation.

Despite these formidable challenges, a remarkable number of public–private partnerships (PPPs) have been launched for TB drug discovery and development. Among them are the Global Alliance for TB Drug Development, headquartered in New York, the Bill & Melinda Gates Foundation's TB Drug Accelerator (Seattle, Washington), the Lilly TB Drug Discovery Initiative (Seattle), the Tres Cantos Open Lab Foundation (Guildford, UK), and the Innovative Medicines Initiative (Brussels). Many of these consortia pair academic researchers who have an up-to-date understanding of *Mycobacterium tuberculosis* biology and TB pathogenesis with pharmaceutical scientists who have access to chemical compound collections that are larger than those in universities, more suited to drug development, and more extensively curated. Even more important, the pharmaceutical companies bring expertise in medicinal chemistry, chemoinformatics, pharmacology, pharmacokinetics and toxicology, along with the infrastructure to perform clinical trials. Such partnerships provide outstanding opportunities for innovation and efficiency.

Although these PPPs commonly have more open approaches to intellectual property (IP) than are usual in drug development, several pharmaceutical companies have proved willing participants in the search for treatments for neglected diseases. Unfortunately, this enlightened attempt to find a solution to the depleted TB drug pipeline has not been matched by all universities. Many academic institutions are struggling to fill a fiscal deficit. In the United States, as a consequence of the Bayh–Dole Act of 1980, universities in receipt of federal funding are free to license IP as a source of income. Under this profit-driven model, some institutions prefer to save precious patent-filing funds for IP with greater potential return. Some do not want to commit to the distribution of drugs on a non-profit basis in the public markets of low-income countries, a condition required by many of the PPPs. There may also be concerns about sharing ownership of IP with a drug company, or universities may demand a share that is disproportionate with their contribution. Few institutions have heeded the call of the student Universities Allied for Essential Medicines, a global group headquartered in Oakland, California, that challenges universities to adopt IP policies that promote affordable access to medicines and medical technologies for the world's poor.

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Although the technology transfer offices in universities may regard the potential income from the IP associated with the early stages of drug discovery as an attractive source of funds, this expectation is unrealistic for TB drug development because of the limited commercial return. Moreover, any such income pales in comparison with the hundreds of millions of dollars that need to be invested to turn lead compounds into drugs. Who will pay to develop the best candidates that emerge from the PPPs? To conduct the clinical trials? To deliver the drugs to those in need? Regrettably, both a penchant for fiscal conservatism and a zeal for IP protectionism at some universities can obstruct the earliest stages of drug discovery.

The world cannot afford to wait long for answers to these questions, and universities need to play their part in finding solutions. For example, they will need to absorb some of the costs of IP protection and accept the potential for low fiscal returns for IP related to drug discovery for diseases like TB. More broadly, universities should lobby for larger, lasting fixes to the broken antibiotic pipeline, such as those called for by a recent panel of the Institute of Medicine of the US National Academies, based in Washington, DC. We need to examine ways of uncoupling the direct link between the rewards for antibiotic development and income from selling the drugs. As an alternative solution, a global fund — perhaps capitalized by financial transaction taxes — could compensate participating drug discoverers for their activities in proportion to their products' reduction of the burden of disease. This would encourage industry and academia to become partners, promote cooperation, and render counterfeiting non-profitable. At this critical time it is imperative that universities re-evaluate their position and become activists for global health. ■

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