Scent Detection Technology with Rats to Tackle Tuberculosis

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The threat of tuberculosis (TB) is a significant health concern. Last year more than 6 million TB cases were reported to the World Health Organization (WHO). [1] Research shows that being a military member is not a risk factor for TB; however, situations enacted by service in the military can present increased risk of infection. Deployment in areas of high prevalence of TB increases exposure rates of the airborne bacteria. [2]

APOPO is addressing the problem of diagnosing TB, the global leading cause of death from an infectious agent after HIV. [3] TB remains a major public health challenge, with an estimated nine million new TB-patients worldwide and 1.5 million TB deaths in 2013. [1]

A researcher with APOPO works with a giant African pouched rat. When trained, these rats can detect TB in a patient's sputum. (Photo courtesy of APOPO)

New diagnostics are a key component to tackling the TB epidemic, and while a number of new diagnostic technologies are implemented globally, significant limitations exist, including the inability to screen large numbers of individuals accurately, rapidly, inexpensively and sustainably over the long term. Resource -limited settings, such as Tanzania and Mozambique, are especially susceptible to these limitations, and technologies that could overcome these limitations are not expected in the coming years.

To bridge the gap in the diagnosis of TB in Africa, regions of which repeatedly require emergency aid from the United States, APOPO developed an innovative, rapid, simple and low cost TB screening tool: trained giant African pouched rats (*Cricetomys gambianus*). [4] The TB detection rats detect a pattern of volatile organic compounds specific for TB bacteria in sputum from individuals who have symptoms suggestive of TB. Training detection rats takes an average of nine months, and they have a working life span of around seven years.

Not only do detection rats have greater accuracy than traditional microscopy, they are unique in their speed of sample screening. [5] The rats can evaluate 100 samples of presumptive TB patients within 20 minutes; this would take a lab technician using conventional microscopic detection up to four days. As these rats are endemic to sub-Sahara Africa there is unlimited access to this resource and this, combined with APOPO's commitment to employing trainers locally, ensures that the technology is suitable and potentially scalable.

APOPO's TB program has been operational in routine care in Tanzania since 2008. Since then, the detection rats consistently increased case detection rates in collaborating TB clinics by about 40 percent and detected more than 6,900 TB patients missed by routine care. In January 2013 a research project designed to replicate the successful results in Tanzania was launched in Maputo, Mozambique. The program, in its second phase of implementation, resulted in the evaluation of more than 47,000 sputum samples and identified more than 1,600 additional TB patients.

The primary goal of APOPO's TB program is to develop and disseminate a cost-effective and high-impact detection-rat technology for use by independent entities in high-TB burden countries. This goal requires accreditation or, at a minimum, approval from national governments and endorsement from international governing agencies such as the WHO. APOPO developed a five year strategic research plan focused on completing a number of key clinical studies aimed at leading to a submission to the WHO's Strategic and Technical

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Advisory Group for Tuberculosis. It is key for APOPO to prove that the detection rat technology adds value compared to existing diagnostics, with regard to accuracy, cost-effectiveness, ease of use and better clinical outcomes for patients.

One goal of this major clinical study is to determine the accuracy of detection rats, compared to traditional diagnostic standards, in a population of presumptive TB patients. The accuracy of the rats will be assessed in individuals with a positive microscopy result and in individuals with a negative result, as well as in individuals living with and without HIV/AIDS; an important factor associated with the accuracy of a diagnostic tool. In total, around 2,000 presumptive TB patients from Dar es Salaam, Tanzania will be included in the study conducted according to international standards of laboratory and clinical trials practice. For this study APOPO is partnering with the Central Tuberculosis Reference Laboratory, the National Institute of Medical Research and the Center for Infectious Disease Research in Zambia.

In addition, the cost-effectiveness of the detection rats are investigated by means of a modelling study. This study will contribute evidence for APOPO and for policy makers on how TB detection rats can be best embedded in a diagnostic pathway (e.g. as an add-on test or a triage test). For this study APOPO is collaborating with the Amsterdam Institute for Global Health and Development.

In parallel to the clinical and cost-effectiveness research APOPO is also conducting behavioral and basic research [6] to improve on the clinical studies, as well as to explore different opportunities for the detection rat technology. One basic research goal, for example, is to get better insight into what the rats are actually detecting, potentially improving the performance of the rats. Based on this research APOPO could improve training procedures for young rats by presenting them sputum samples with known bacteriological loads.

In support of the different ongoing and planned research activities, APOPO has installed a TB Scientific Advisory Committee consisting of a multidisciplinary team of international TB expert. The role of this committee is to provide scientific and medical credibility to the program and research output, to advise on the long term strategic research planning and to identify new opportunities for research, funding and partnerships.

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