Tuberculosis POCT: An Integrated Photonic Biosensor for Tuberculosis Detection

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Tuberculosis (TB) is an old but re-emerging global health threat caused by the *Mycobacterium tuberculosis* (Mtb). One third of the world's population is infected with Mtb and new infections occur at a rate of one per second. Despite the greatest global health impact of TB, case detection rates are low, posing serious hurdles for TB control. Current methods for the detection of TB are either time consuming or require expensive instruments. Furthermore, these tests have several limitations and perform poorly in populations affected by the HIV epidemic, are thus are not suitable for point-of-care diagnosis. Therefore, accurate, novel, rapid, more sensitive and cost effective diagnostics are urgently needed.

In this respect, the goal of the European FP7 Pocket project is to establish a framework to combine several state-of-the-art concepts for the development of a novel and cost-effective point-of-care test for tuberculosis using patients' urine as non-invasive sample. The new tuberculosis POCT consists of a small photonic chip combined with a microfluidic cartridge (disposable part) and a graphical user interface instrument, used for optical readout and data processing (Figure 1). An integrated label-free photonic circuit is used as biosensor, a low-cost mechanism due to its small size and the compatibility with mature CMOS fabrication technology. The sensing circuit is implemented, combining a highly sensitive Mach-Zehnder interferometer with an on-chip spectral filter, hence replacing the conventional tunable laser by a much cheaper broadband light source. Flood illumination on the input grating couplers was used to reduce the cost and to increase POCT compatibility. The successful development of a POCT TB test depends on an Mtb-specific biomarker. A special focus was set on the most promising markers; cell wall lipopolysaccharide lipoarabinomannan (LAM) and Ag85 complex. Novel, high-quality and selective antibodies were developed against Mtb LAM and Ag85 complex biomarkers. This unique cocktail promises to significantly enhance the sensitivity and specificity far beyond current TB tests. In a preliminary experiment, sensor chips were functionalised using an Azide-ended silane by vapour phase deposition and antibodies were bio-conjugated by click-chemistry using a PEG-based linker. Initial results indicate the successful detection of 250 pg/ml of LAM antigen, thus demonstrating its potential for use in resource-limited area and for the on-line diagnosis of TB. In the new POCT, the safety of sample process has been successfully implemented using microfluidic chip as transfer medium. The designed chip has very low fabrication costs, allowing cost-effective disposable chips to be fabricated in mass production. This chip is plugged into the measurement tool, which contains the required components for optical readout, an automated system to circulate the urine into the chip as well as a computer for data processing.

Due to rising health-care costs, all health-care stakeholders are forced to shift their onus from a 'pay for intervention' to a 'pay for performance' model. This highly promising TB POCT shall be evaluated in order to determine a universal threshold, especially in endemic countries as well as its performance in the field.

Acknowledgement: The Pocket project was funded by the European Commission under grant agreement no FP7 610389.

Attachment: Figure 1: TB POCT Instrument and the disposable chip parts