NOVEL TB BIOMARKERS

Novel urinary TB biomarkers for point of care diagnosis of Tuberculosis disease in low resource settings

BACKGROUND

Tuberculosis (TB) is the leading cause of death in Sub-Saharan Africa and South Africa, and globally, 10.4 million new cases are diagnosed annually. It is a stigmatizing disease that marginalizes patients and their families, and the prolonged morbidity and high death rates are economically debilitating. Detection of TB remains a major problem, with a large majority of patients being co-infected with HIV (approximately 60% of the caseload). Currently diagnosis is difficult, with a number of patients being sputum scarce (cannot produce sputum), others being smear negative (low concentration of TB bacilli in the sputum) and the cases of extrapulmonary TB (EPTB) being as high as 50% in HIV co-infection. Other diagnostic tools are not able to distinguish between latent or active TB infection. There is, therefore a need for new, low cost, Point-of-Care (POC) TB diagnostics. However, the lack of suitable biomarkers for use in different biological samples other than sputum that are able to distinguish active TB disease from latent TB infection is a major hurdle in the development of these diagnostic tests.

TECHNOLOGY DESCRIPTION

A sub-set of novel urinary TB biomarkers have been identified that correlate with disease status, distinguishing active TB from latent TB infection and from non-TB infection. Additionally, a sub-set of biomarkers potentially identify sub-clinical TB, thus making them ideally suited to form the basis of a stand-alone diagnostic for TB and replacement novel mass population screening tool for active case finding. The overall goal is to generate antibodies and/or aptamers against these validated biomarkers and apply them to appropriate diagnostic POC platforms. In contrast to immunological markers in peripheral fluids, the POC test based on these biomarkers will rely on the direct detection of mycobacteria antigens in urine and would give a simple yes/no answer, without the need to define quantitative cut-points. Our goal therefore is to develop a diagnostic test that works with >90% sensitivity and specificity in urine, enabling TB diagnosis at point of care in rural settings for all patients, including those who cannot give a sputum sample, such as HIV positive individuals and children.

VALUE PROPOSITION

Simple, low cost, point-of-care TB diagnostic test for diagnosis of the different disease stages of TB with high sensitivity and specificity. This test utilizes urine samples, allowing for diagnosis of all patients, including those who cannot produce sputum.

CURRENT STATUS

Seven TB biomarkers have been validated in blinded cohorts of patients with active TB disease and non-TB diseased groups from Cape Town, giving PPV = 91% and NPV=94%, irrespective of HIV status. Further validation in cohorts in other regions of South Africa is underway. Future work will include translating the validated urinary biomarkers into appropriate detection platforms and validating these prototypes at point of care.

INTELLECTUAL PROPERTY STATUS & PUBLICATIONS

National phase patent applications based on PCT/IB2014/063987 are pending in South Africa, India and Brazil and granted in China (CN105683757).

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NOVEL TB BIOMARKERS (CONTINUED)

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- Nakedi KC, Calder B, Banerjee M, Giddey A, Nel AJM, Garnett S, Blackburn JM* & Soares NC* (2018) Identification of novel physiological substrates of Mycobacterium Bovis BCG Protein Kinase G (PknG) by label-free quantitative phosphoproteomics. Mol Cell Proteomics. 17, 1365-1377.
- Hermann C, Giddey AD, Nel AJM, Soares NC, Blackburn JM (2019) Cell wall enrichment unveils proteomic changes in the cell wall during treatment of Mycobacterium smegmatis with sub-lethal concentrations of Rifampicin. J. Proteomics 191, 166-179.

OPPORTUNITIES

The University of Cape Town is seeking funding for further biomarker validation and adaption of these biomarkers into existing or novel POC TB diagnostic platforms, including the TB PROTEC and TB SERS Biosensor.

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