



Title of PhD project	Antibody and aptamer approach to diagnosis of TB based on secreted proteins of Mycobacterium tuberculosis	
Supervisor	Professor Rajko Reljic	SGUL
Co-Supervisor	Professor Graham Bothamley	LSHTM
Brief description of project	<p>Diagnosis of TB remains problematic, requiring a combination of lab-based and clinical methods to distinguish between active disease and latent TB infection (LTBI). Sero-diagnosis, despite its early promises, has failed to identify MTB antigens that can discriminate these two forms of infection. MTB secretes a multitude of antigens when grown in culture and these antigens are very likely to be present in infected tissues at higher levels during active disease than LTBI, which is represented by sparse, metabolically inactive organisms. We therefore postulate that targeting these secreted antigens by their serum immunoreactivity, or directly in patient's sputum by proposed novel aptamer technology, could lead to a novel test for TB.</p> <p>The specific objectives of this PhD are therefore to develop a novel diagnostic approach for active TB based on culture filtrate (CF) proteins of MTB, utilising sera samples from two existing clinical cohorts of TB patients, LTBI and BCG vaccinated individuals, and sputum samples to raise aptamers that can directly identify these antigens. The project will include a range of immunological and microbiological techniques, as well as clinical sample processing and analysis. The aptamer generation will be sourced out to a specialist commercial entity. It is expected that, by the end of the project, the student will generate conclusive experimental evidence as to the potential of these two complementary approaches to be translated into a novel diagnostic test for TB.</p>	
Skills we expect a student to develop/acquire whilst pursuing this project	<ol style="list-style-type: none"> 1. Awareness and contribution to preparing ethics application. 2. Storage, processing and analysis of clinical samples. 3. Immunological techniques, including ELISA, electrophoresis, Western blotting, and flow cytometry. 4. Microbiological techniques, including liquid and solid plate culture of mycobacteria. 	

	<ol style="list-style-type: none"> 5. Work in containment level 2 and 3. 6. Molecular cloning and protein expression. 7. Data analysis by statistical packages. 8. Mass-spectrometry understanding (though this will be sourced out). 9. Generic skills, including literature search, writing, oral presentations and other forms of scientific communication.
Particular <u>prior</u> educational requirements for a student undertaking this project	Master in Science or Research in a biomedical/medical field (1st or 2i). Good knowledge of immunology required and a keen interest in infectious diseases. Previous experience in laboratory setting also required.
Project key words	<p>Tuberculosis Diagnosis Serology Aptamers Latent infection</p>
Possible under 1+4 route? Master's options identified.	No
MRC Core Skills developed through this project	<p>Interdisciplinary skills Whole organism physiology</p>
MRC LID themes	<p>Translational and Implementation Research Infectious Disease</p>
Further reading	<p>Mucosal Therapy of Multi-Drug Resistant Tuberculosis With IgA and Interferon-γ</p> <p>A Novel Human IgA Monoclonal Antibody Protects against Tuberculosis</p> <p>Prognostic value of interferon-γ release assays and tuberculin skin test in predicting the development of active tuberculosis (UK PREDICT TB): a prospective cohort study</p> <p>Male Sex Bias in Immune Biomarkers for Tuberculosis</p>