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# RACP Foundation Research Awards

# FINAL REPORT

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| **Project / Program Title** | | A comparative proteomic study of the protein repertoires of two bacteria to provide insights into disease mechanisms of tuberculosis |
| **Name** | | Dr Megan Rees |
| **Award Received** | | 2015 Robert and Elizabeth Albert Travel Grant |
| **Report Date** | | 27 July 2018 |
| **Funding Period** | Start Date: | 4 January 2015 |
| | Finish Date: | 4 January 2016 |

## PROJECT SUMMARY

Proteomics was used to unravel the differences between two species of mycobacteria and identify disease causing proteins.

Mycobacterium tuberculosis (M.tb) and Mycobacterium kansasii (M.kan) possess similarities and differences; their genomes are similar and both organisms can cause pulmonary disease with similar radiologic and immunologic findings. However, the organisms have a very disparate biology; the former is a professional pathogen that transmits from person-to-person; the latter is an environmental bacterium that presents in clinical medicine as a non-transmissible opportunistic pathogen. This contrast in their biology is likely to be explained by the production of different proteins.

Proteomics can characterise a broad repertoire of proteins as they are generated by the living organism in an unbiased manner. These features make it an ideal platform to explore the contrast between these two organisms, ultimately identifying proteins present in the exclusive human pathogen (M.tb) but absent from the predominately environmental organism (M.kan). Identifying proteins unique to living M.tb will provide insights into disease causing mechanisms employed by this significant human pathogen

## PROJECT AIMS / OBJECTIVES

I performed a proteomic characterization of both M.tb and M.kan simultaneously to examine these differences, which was conducted in the laboratory of Dr Marcel Behr, Microbiologist in Chief, McGilll University Health Centre and Director of the McGill International TB Centre, Montreal Canada. Proteomic analysis can provide valuable additional information not gleaned from genomic and transcriptional studies as the actual proteins that have been expressed can be identified including any post translational modifications.

I endeavoured to identify the whole proteomes of both M.tb and M.kan, under identical bacterial culture conditions; this includes a qualitative and quantitative analysis of expressed proteins as

well as the identification of post translational modifications, using high throughput mass spectrometry.

## SIGNIFICANCE AND OUTCOMES

Experimental work was carried out as planned with triplicate cultures of both species of bacteria grown in liquid culture under identical conditions, and proteins from the whole cell lysate and secreted proteins were collected and de-complexed with SDS gel separation.

The expressed protein repertoire of each species was characterized with high throughput mass spectrometry using the sensitive Orbitrap instruments. The protein repertoires were analyzed in terms of identity, abundance and post translational modifications. Gene expression of the same samples was also conducted with RNA-seq and this transcriptome was compared to the proteome.

We were able to characterize groups of proteins only present in the pathogenic M. tuberculosis which are likely to represent novel virulence factors and biomarkers. This is also one of the first studies to comprehensively compare the transcriptome and proteome of mycobacteria other than M. tuberculosis.

## PUBLICATIONS / PRESENTATIONS

These results have provided protein candidates of interest for further work at the Behr laboratory.

The results were presented to the Victorian Branch of the Thoracic Society of Australia and New Zealand quarterly meeting on 25 June 2016.