

## Fatal attraction: host-pathogen interactions in *B. pseudomallei* infection

N Ketheesan

### Introduction

In some regions, individuals with type 2 diabetes (T2D) are more than ten times over represented among patients with melioidosis. In melioidosis, the severity of the infection and clinical outcomes are determined primarily by the presence or absence of host risk factors such as T2D. Our understanding of the mechanisms underlying susceptibility of individuals with T2D toward *Burkholderiapseudomallei* infection is limited.

### Objectives

Our objective was to determine the early immune responses following *B. pseudomallei* infection in comorbid T2D.

### Methods

To investigate the mechanisms underlying the increased susceptibility of individuals with T2D to *B. pseudomallei* infection, a relevant model of T2D-infection comorbidity was established. The diet induced murine model of T2D reflects the major features of T2D in human. Our studies were conducted by infecting the animals by different routes of infection using both virulent and less virulent strains of *B. pseudomallei*.

### Results& Discussion

The initial systemic inflammatory cytokine response (TNF- $\alpha$ , MCP-1 and IL-12) was delayed in T2D mice during the first 12 hrs of infection and by 24 hrs post-infection *B. pseudomallei* loads were significantly higher in spleen, liver and lung in T2D compared to non-diabetic animals. Following an initial delay in cytokine production, an exaggerated proinflammatory cytokine response was observed in T2D mice by 48 hrs post-infection. T2D mice were highly susceptible to *B. pseudomallei*, with a median survival of 4 days compared to 12 days for non-diabetic mice. Experimental findings suggest that defects in the early immune response to *B. pseudomallei* infection significantly contribute to the greater susceptibility in T2D. Decreased phagocytic and antimicrobial capacity of neutrophils, dendritic cells and macrophages during the initial stages of infection impact on the downstream immunoregulatory functions, predisposing the diabetic host to clinically apparent infection. These dysregulated early responses may also lead to ineffective T cell and protective immune responses.

### Conclusions

Findings in the last few years attribute the failure to mount a robust early immune response to *B. pseudomallei* infection as the fundamental cause of increased susceptibility of individuals with diabetes to this infection.

---

Australian Institute of Tropical Health, Australia

Address for correspondence: Dr Natkunam Ketheesan, Australian Institute of Tropical Health, Australia

+61 410326788 Email: [n.ketheesan@gmail.com](mailto:n.ketheesan@gmail.com)  <https://orcid.org/0000-0002-4870-706X>