

# SgN Immunology Seminar



## Prof. Hardy Kornfeld

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USA

### TB and Diabetes

#### Host

Dr Amit Singhal  
Singapore  
Immunology  
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#### Date

**Friday**  
**27 February**  
**2015**

#### Time

11am – 12pm

#### Venue

SgN Seminar  
Room  
Immunos  
Building  
Level 4  
Biopolis

Diabetes mellitus increases the risk for progression from latent TB infection to active disease, and for unfavorable TB outcomes including delayed sputum conversion, treatment failure, death and relapse. Four of five people with diabetes live in low and middle income countries where TB burden is also high. Despite the significance of this association, mechanisms of TB susceptibility in diabetes are incompletely understood and knowledge about the clinical impact that diabetes has on human TB comes mostly from retrospective data.

We are investigating this comorbidity in mouse models combining hyperglycemia with aerosol *M. tuberculosis* (Mtb) infection, and with clinical studies in India which has the highest dual burden. Data so far suggest that TB susceptibility, like other diabetic complications, is driven mainly by chronic hyperglycemia which increases oxidative stress and causes pathological protein modifications (including glycation) as well as epigenetic reprogramming in affected tissues. These complication pathways result in a delayed innate immune response to inhaled Mtb in mice and consequently to late priming and expression of adaptive immunity. Once underway, the cell-mediated response of diabetic mice (and people) is poorly regulated and exacerbates lung damage. Clinical correlations of mouse and human data, and the cumulative impact of other comorbidities common in diabetic patients will be reviewed.

There is growing urgency to address the dual burden of TB and diabetes. New and better data are needed at every level from fundamental and clinical studies to implementation research. Gaps in current knowledge as well as translational research opportunities will be discussed.

Supported by NIH grant HL081149 and a grant from the Indo-U.S. Vaccine Action Program