

**UNIVERSITI TEKNOLOGI MARA**

**CHARACTERISATION OF  
IMMUNOSTIMULATORY  
COMPOUNDS IN *Streptococcus  
pneumoniae* TOWARDS  
UNDERSTANDING THE HOST  
PATHOGEN INTERACTION**

**EZARINA BINTI ABDUL RAHIM**

**MSc**

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## AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student : Ezarina Binti Abdul Rahim  
Student I.D. No. : 2013169091  
Programme : Master of Medical Science (Microbiology)  
-MD750  
Faculty : Medicine  
Thesis Title : Characterisation of Immunostimulatory  
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Towards Understanding The Host Pathogen  
Interaction  
  
Signature of Student : .....  
Date : December 2016

## ABSTRACT

*Streptococcus pneumoniae* is a common cause of morbidity and mortality worldwide. *S. pneumoniae* cause many types of infections such as meningitis, bacteremia, sepsis, acute sinusitis, and otitis media. *S. pneumoniae* has more than 92 different serotypes based on its capsular structure. The aim of the study is to investigate the effect of serotypic variation on genes encoding virulent determinants in relation to capsular properties, the role played by the neuraminidase in the colonisation and the patterns of toll-like receptor signaling responses in A549 human lung epithelial cell line towards understanding the host pathogen interaction. In this study, serotype 14 appears to have an additional chemical shift peak by using proton nuclear magnetic resonance (NMR), thus may be the reasons of reduced affinity to penicillin. The sequence variation in pneumococcal genes was observed by using polymerase chain reaction. The differential expression level of neuraminidase was done using reverse transcription polymerase chain reaction. Higher NanA gene expression in serotype 23F and 19F suggests that these serotypes are more invasive. In contrast, NanB gene showed low-level expression in serotype 23F and 19F. This postulates that NanA and NanB gene may have different function or mechanism in the pathogenesis of *S. pneumoniae*. Lastly, the toll-like receptor (TLR) signaling responses in A549 cells upon infection with pneumococcal cell wall were investigated by using RT<sup>2</sup> Profiler PCR Array. The involvements of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6 and TLR10 in modulating the immune response were detected. TLR2 showed the highest expression indicates it is important in recognition of cell wall components. Serotype 1, 3, and 5 that able to induce higher TNF $\alpha$  and IL-1 $\alpha$  have shown to be more immunogenic. The study would give a better insight into pneumococcal pathogenesis and host pathogen interaction in relation to different serotypes.

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