

**Establishment of a young mouse model and  
identification of an allelic variation of zmpB in  
complicated pneumonia caused by  
Streptococcus pneumoniae**

陳志榮

**Hsieh YC;Tsao PN;Chen CL;Lin TL;Lee WS;Shao  
PL;Lee CY;Hsueh PR;Huang LM;Wang JT**

摘要

**Abstract**

**OBJECTIVE:** Complicated pneumonia, including necrotizing pneumonia, lung abscess, and empyema, caused by *Streptococcus pneumoniae* in children has been increasing. We thus determined to investigate its virulence in an animal model and to identify virulence factors of *S. pneumoniae*. **DESIGN:** Prospective, randomized, controlled animal study. **SETTING:** University medical laboratory. **SUBJECTS:** Male Balb/c-strain mice, 3 wks old. **INTERVENTIONS:** We used a young mouse model to monitor bacterial virulence and a microarray to compare gene expression between *S. pneumoniae* from children with complicated and noncomplicated pneumonia. Deletion and complementation of a candidate gene were performed to study its role on the virulence of *S. pneumoniae*. **MEASUREMENTS AND MAIN RESULTS:** A model of complicated pneumonia in young mice infected with strains of *S. pneumoniae* from children with complicated pneumonia was established. Using a microarray analysis, differences in zinc metalloprotease B (zmpB) RNA hybridization between two strains from children with complicated pneumonia (NTUH-p28 and NTUH-p15) and a strain (NTUH-p3) from a child with pneumococcal lobar pneumonia were found. Confirmatory assays revealed the signal differences were due to sequence variation in the zmpB gene. Infection with the zmpB deletion mutant of NTUH-p15 showed a significant decrease in the severity of pneumonia and no destructive lung injury. The zmpB complementation strain of NTUH-p15 significantly restored the level of inflammation and caused lung necrosis. For studying the effect of allelic variation of zmpB on the virulence of *S. pneumoniae*, we added zmpB of NTUH-p15 in the zmpB deletion mutant of NTUH-p3, which resulted in a

higher bacterial burden than that in wild-type NTUH-p3. CONCLUSIONS: A young mouse model is established for complicated pneumococcal pneumonia. This model proved that allelic variation of *zmpB* affects the virulence of *S. pneumoniae*.