Rapid Diagnosis and Molecular Epidemiology of *Acinetobacter baumannii*

Abstract:

The *Acinetobacter* species is quite complex. The currently available identification systems fail to clearly differentiate the genomic species. We applied the ASPE suspension array to rapidly discriminate the commonly encountered 13 genomic species, especially the *A. baumannii*, genomic species 3, and 13TU. Furthermore, a combination of the identification results of our study with the resistance profiles provided by NTUH surprisingly showed that most *A. baumannii* isolates were resistant to ciprofloxacin and imipenem, however, the majority of genomic species 3 and 13TU isolates were susceptible to ciprofloxacin and imipenem. This finding has great clinical significance. Because most of the previous studies lumped the *A. baumannii*, genomic species 3, and 13TU together. Our novel array method can differentiate the resistant-prone *A. baumannii* from the other two susceptible-prone species within 8 hours. It is helpful for clinicians using the ASPE suspension array in making decision of antibiotic choice for infections caused by *Acinetobacter* species before conducting the susceptibility tests. This will also indirectly help to alleviate the rapid evolution of MDRAB.

In this study we also investigated the resistant mechanisms of *A. baumannii* to ciprofloxacin in various molecular levels: mutation of *gyrA* and *parC* resistance genes, RNA transcriptive expression of *adeB* gene as well as expression of outer membrane proteins. Our result showed that the ciprofloxacin-resistant *A. baumannii* showed mutations and change the Ser to Leu on the 83 th position of *gyrA* gene and on the 80th position of the *parC* gene. The changes in amino acid sequence of *gyrA* and *parC* genes are highly associated with ciprofloxacin resistance ($P<0.001$). The RNA transcriptional level of *adeB* gene in ciprofloxacin-resistant *A. baumannii* isolates are more than four fold higher than the susceptible ones. Analysis of the expression of outer membrane proteins using 10% SDS-PAGE and silver staining showed that the 29kDa, 33kDa and 44kDa proteins exhibited different expression level between resistant and susceptible isolates. The results pointed out that *A. baumannii* integrates multiple resistant mechanisms to cope with different antibiotics.

In conclusion, within less than one year, we have established a novel multiplex detection method to identify 13 *A. baumannii* genomic species and submit the research finding to a high ranking SCI journal. We also set up the methodology to investigate the resistant mechanisms which enabling us to identify specific differences at DNA, RNA and protein levels. Our collaborative clinicians also confirm that these findings will have substantial contribution towards the treatment and control of *A. baumannii*.

Keywords：*Acinetobacter baumannii*, suspension bead array, resistance