Abstract

Whooping cough is a highly contagious acute respiratory disease. Although the disease could be effectively prevented by vaccination, there are worldwide pertussis outbreaks every year. For instance, more than 10 times of cases were reported in the outbreak occurred in Netherlands 1995. Among these cases, a large proportion of them were found to have been vaccinated at least four doses of vaccine. Because of this, it was suspected that a significant genetic variation may emerged between the clinical strains and the vaccine strains that has been long time used for the manufacturing the vaccines. The variation may not any more be able to elicit the high titer of neutralizing antibodies for the effective disease prevention. Therefore, it has become considerably important to analyze the genetic variation among all pertussis strains. Current study has investigated the nucleotide sequence variation of filamentous hemagglutinin among 12 clinical pertussis strains, including 8 domestic strains and 4 strains that were initially obtained from other countries, i.e. strains 10536, Tohama (these two strains are currently used for vaccine production), ATCC 9340 and 18323.

Following the PCR amplification, gene subcloning, and sequencing analysis, we found that no FHA sequence between any two strains were completely identical. In comparison with domestic strains, significant variations were detected in the foreign strains, especially strain ATCC 9340 and 18323. Among all sequences analyzed, the nucleotide variations seem to cluster in certain regions. In another words, some mutation hot spots seem to be present during bacterium evolution. In addition, from the individual strain point of view, some strains even revealed more than 3 variations within a 50 base pair segment. Although the strains used in this study was limited, the degree of variation was so huge that it is possible to use this to evaluate the trends of disease spreading and the sources of pathogens.

Because the nucleotide sequence analysis apparently is not time and cost effective, it is suggested that a pertussis gene bank may be established based on the results of this study, but use the methodology of oligonucleotide polymorphism to analyze all clinical strains. In the meantime, the investigation should also be performed on the strains that currently has been collected form each outbreak. This will contribute to not only the vaccine evaluation, but the disease prevention and human health.

Keywords：genetic variation；Nucleotide sequence；filamentous hemagglutinin