

## **Abstract**

### **Aims**

The study is aimed to investigate mechanism of enterovirus 71 in inducing central nervous system (CNS) disease. a highly virulent YN3-4a virus and an avirulent Neu-R8 strain were used for this study In this study, the role of 3A viral protein of enterovirus 71 will be investigated to examine the interactions of 3A viral protein and cytokine expression during the process of induction of CNS disease.

### **Methods**

- (1) Genetic analysis revealed the differences between a highly virulent YN3-4a virus to suckling mice and an avirulent Neu-R8 strain.
- (2)To examine the production of virus and the expression of cytokine mRNA during the periods of HTB11 (human neuroblastoma cells) infected with either strain YN3-4a or Neu-R8 strain.
- (3) To construct a clone expressing non-structure viral protein 3A or structure viral protein VP1 for transfecting the clone to HTB11 (human neuroblastoma cells) and to investigate the effects of 3A and VP1viral proteins on cytokine expression during infection neuron cells.

### **Main results-**

- (1) YN3-4a strain grew fast and well in HTB11 cells; however, NeuR8 did not grow well in HTB11 cells.
- (2) When YN3-4a infected HTB11 cells, continuous expressions of GM-CSF, IL-1  $\beta$  [HH], IL8 and TNF-  $\alpha$  mRNA was induced, in company with an increasing production of virus.
- (3) When NeuR8 infected HTB11 cells induced the expression of GM-CSF、IL-1  $\beta$ 、IL6、TNF-  $\alpha$  mRNA appeared in the early period of infection, and increased afterward.
- (4) When HTB11cells were transfected with plasmid containing 3A or VP1viral protein, the 3A viral protein induced the expression of TNF-  $\alpha$  and IL8; however, VP1viral protein only induced the expression of TNF-  $\alpha$ .
- (5) When RD cells were transfected with plasmid containing 3A or VP1viral protein. The 3A viral protein induced the expression of IL6、IL8 and IL-1  $\alpha$ . The VP1 viral protein induced the expression of IL6、IL8、TNF-  $\alpha$  and IL-1  $\beta$  mRNA.

### **Conclusion and suggestions**

This study showed that the pattern of cytokines expression was varied when HTB11 cells were infected with different EV71 virus strains. Although strain YN3-4a and NeuR8 could induce the expression of GM-CSF, IL-1  $\beta$  [HH], IL8 and TNF-  $\alpha$  mRNA, the expressions of those cytokine in response to NeuR8 infection decreased after 12 hours postinfection, suggesting the continuous expression was related with the ability of virus production in HTB11 cells. Moreover, structural protein VP1 and nonstructural protein 3A could induce different expressing pattern of cytokine.

**Keywords :** enterovirus71 ; mouse neuroblastoma ; human neuroblastoma ; cytokine ; 3A viral protein