[S4-3] [10/17/2002(Thur) 14:50-15:15/Hall B]

Transcriptional Responses of Respiratory Epithelial Cells to Nontypable *H. influenzae* Infection: Identification of Differentially Regulated Genes by Microarray Analysis of Human cDNA

Na-Gyong Lee, Ph.D.

Department of Bioscience & Biotechnology, College of Engineering, Sejong University, Seoul 143-747, Korea

Bacterial infection is a very complex process in which both pathogenic microorganisms and host cells play crucial roles, and it is the outcome of interactions between the two participants. To elucidate the bacterial pathogenesis mechanisms, therefore, it is essential to understand the cellular and systemic responses of the host as well as the virulence factors of the pathogen. Infection of a host by pathogenic bacteria causes drastic changes in the physiology of host cells, leading to activation of a program of various gene expression.

H. influenzae is a Gram-negative bacillus and the causative agent of bacterial meningitis, especially among children. It is classified into six serotypes based on their capsular structures, and among them the most virulent is the type b strain, infection with which is less common due to introduction of safe and effective vaccines. Nontypable *H. influenzae* (NTHi), which is not reactive to the typing antisera against any known capsular structures, is isolated from asysmptomatic carriers and often causes pneumonia and otitis media in children. An airway epithelium is the first line of cells coping with the invading bacteria in NTHi infection. They are not passive bystanders but actively participate in defending the host system, and significant changes occurs inside the cells during the rapid and effective inflammatory responses.

The recent advent of DNA microarray technology made it possible an extensive analysis of changes in gene expression that reflect ongoing infectious processes and physiological changes in the host. In order to identify the genes differentially expressed in human respiratory epithelial cells during infection with NTHi, we have adopted high-density DNA microarrays. DNA microarrays consisting 8,400 human cDNA clones were hybridized with the cDNAs prepared from BEAS-2B human respiratory epithelial cells that had been

cocultued with NTHi strain 2019. The results showed that infection of the cells with NTHi up-regulated various genes, which include genes coding for chemokines, transcription factors, translational factors, several ribosomal proteins, and transmembrane proteins, suggesting activation of cellular metabolism and increase in production of molecules involved in host inflammatory responses.

Lipopolysaccharide (LPS), one of the Gram-negative cell surface components, serves as a molecule that recognizes cellular receptors for invasion and is a strong immune stimulant. LPS of *H. influenzae* does not contain repeating O-antigen units and is called lipooligosaccharide (LOS). We also investigated the modification of cellular gene expression by the infection with an isogenic NTHi strain which expresses truncated LOS due to deficiency in phosphoglucomutase (*pgm*-). Comparison of the wild type and *pgm* mutant strains revealed that several genes, notably IL-8 and NF-kB that had been well-known to be activated during inflammation process, were up-regulated by the wild type NTHi but not by the LOS mutant strain, indicating the involvement of LOS in activating the cellular response to the infection. The potential significance of alterations in expression of these genes will be further discussed.