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Draft genome sequence of lytic bacteriophage KP1 infecting bacterial pathogen *Klebsiella pneumoniae*

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병원균 *Klebsiella pneumoniae*를 감염시키는 용균 박테리오파지 KP1의 유전체 염기서열 초안

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Klebsiella pneumoniae is a Gram-negative, rod-shape bacterium causing disease in human and animal lungs. *K. pneumoniae* has been often found to gain antimicrobial resistance, thus it has been difficult to treat *K. pneumoniae* infection with antibiotics. For such infection, bacteriophage can provide an alternative approach for pathogenic bacterial infection with antimicrobial resistance, because of its sensitivity and specificity to the host bacteria. Bacteriophage KP1 was isolated in sewage and showed specific infectivity to *K. pneumoniae*. Here, we report the draft genome sequence of *Klebsiella pneumoniae* phage KP1. The draft genome of KP1 is 167,989 bp long, and the G + C content is 39.6%. The genome has 295 predicted ORFs and 14 tRNA genes. In addition, it encodes various enzymes which involve in lysis of the host cell such as lysozyme and holin.

Keywords: *Klebsiella pneumoniae*, bacteriophage, draft genome sequence, Illumina Hiseq

Klebsiella pneumoniae is a Gram-negative, rod-shape bacterium. The most common disease caused by *Klebsiella* is pneumonia which form bronchopneumonia and bronchitis. Patients with *Klebsiella* infection have an increased tendency to develop lung abscess, cavitation, empyema, and pleural adhesions, resulting in a high death rate of about 50% even with antimicrobial therapy (Jagessar and Alleyne, 2011). Infection with *K. pneumoniae* can be treated with various antibiotics such as kanamycin, neomycin, and streptomycin. But if the bacterial strains obtain the antibiotic resistance genes it would be difficult to treat using such antibiotics. A recent trend of studies about this problem focuses on the usage of bacteriophage, since bacteriophages have features of specificity to their hosts (Keen, 2012).

To date, the genome sequence of bacteriophage strains that can infect *K. pneumoniae* has been reported from 28 strains. In this study, we isolated a new bacteriophage from the sewage in Chungcheongbuk-do which could infect *Klebsiella pneumonia* and named the phage as KP1. Genome sequencing was performed at Macrogen, Inc. using the high throughput sequencing pipeline with Illumina Hiseq platform. The genomic sequence was assembled *de novo* into 1 contig with Platanus (Kajitani *et al*., 2014). Error correction was performed using Pilon program

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(Walker *et al*., 2014). Genes in the resulting draft genome sequence were annotated with the Rapid Annotation using Subsystem Technology (RASTtk) version 2.0 (Brettin *et al*., 2015) and PHAge Search Tool (PHAST) (Zhou *et al*., 2011). The draft genome of KP1 was 167,989 bp (39.6% G + C content). The genome was dense with genes: only 6,805 bp for spacer regions and 94.9% as genic regions. A total of 295 genes were predicted: 281 protein coding sequences (CDSs) and 14 tRNA including 1 pseudogene. The gene functions were identified with BLASTp against the non-redundant protein sequences (nr) database of NCBI. A majority of the ORFs were annotated as hypothetical or putative proteins. Some genes with known functions were classified into groups such as structure, lifestyle regulation, virion assembly, host cell lysis and DNA replication. In addition, the bacteriophage KP1 has genes involving in host cell lysis: lysozyme murein hydrolase that cleaves the 1,4-beta-linkage in peptidoglycan, phospholipase that hydrolyzes phospholipid, and holin that triggers and controls the degradation of the host's cell wall at the end of the lytic cycle (Young, 1992; Wang *et al*., 2000). The bacteriophage KP1 was infected with various bacterial species including *Klebsiella pneumoniae*, *Salmonella enterica* serovar Typhimurium, *Salmonella enterica* serovar Enteritidis, *Escherichia coli* O78, *Escherichia coli* O148, *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Lactobacillus plantarum*, *Enterococcus faecium*. As a result, *Enteroroccus faecalis*, and the bacteriophage KP1 showed the host specificity on *K. pneumoniae*.

In conclusion, the draft genome of bacteriophage KP1, which can specifically infect *K. pneumoniae*, is presented. It has genes for specific host infection and destruction of the host. Thus, the genomic information of bacteriophage KP1 can be further useful to treat bacterial infection of *K. pneumoniae* with antimicrobial resistance (Wagner and Waldor, 2002).

Table 1. Genomic features of *Klebsiella pneumoniae* phage KP1

Feature type	Genomic feature
Contig	1
Genome size (bp)	167,989
G + C content (%)	39.6
Coding density (%)	94.9
Total gene	295
Protein-coding sequence (CDS)	281
tRNA gene	14
Pseudo-gene	1

Nucleotide sequence accession number

The draft genome sequence of *Klebsiella pneumoniae* bacteriophage KP1 has been deposited in the GenBank MG75-1100. The bacteriophage KP1 strain was deposited to KCCM (Korean Culture Center of Microorganisms) KFCC11674P.

적 요

*Klebsiella pneumoniae*는 그람 음성균에 속하고 막대 형태를 가지며 인간이나 동물의 폐에 감염하여 병을 일으키는 균이다. *K. pneumoniae*는 흔히 항생제 내성을 나타내는데 이로 인해 항생제를 통한 치료가 어려워지게 된다. 이런 상황에서 숙주 균에 특이적이고 민감하게 반응하는 박테리오파지는 항생제 내성균의 치료에 대한 대체적인 접근법으로 제안될 수 있다. 박테리오파지 KP1은 하수처리장에서 분리되었으며 *K. pneumoniae*에 대해 특정적인 감염성이 있다. 본 연구에서는 *Klebsiella pneumoniae* 박테리오파지 KP1의 유전체 초안 분석을 수행하였다. KP1의 유전체 초안은 167,989 bp의 길이, 39.6%의 G + C 비율로 구성되어있다. 295개의 예측된 ORF들과 14개의 tRNA 유전자를 가지고 있다. 또한 이들은 lysozyme, 그리고 holin과 같은 다양한 세포 용해 관련 효소들을 포함하고 있다.

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