Genome sequence of a non-pathogenic *Listeria monocytogenes* serovar 4a strain M7

(Running title: Genomic sequence of *L. monocytogenes* serovar 4a strain)

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Abstract

This report presents the complete and annotated genome sequence of a naturally non-pathogenic *Listeria monocytogenes* serovar 4a strain M7, isolated from cow’s milk in Zhejiang province, China.
Listeria monocytogenes encompasses a diversity of strains with varying virulence and pathogenicity (10, 19). Serovars 4b, 1/2a and 1/2b account for the majority of human listeriosis cases, whereas other serovars, particularly serovar 4a, are rarely associated with listeriosis and seldom isolated from foods (3, 18). To obtain a better understanding of the molecular mechanisms of L. monocytogenes pathogenicity, the genome sequence of a naturally non-pathogenic serovar 4a strain M7, isolated from cow’s milk in Zhejiang province, China (2), was analyzed.

The complete genome sequence of M7 was determined by Solexa Genome Analyzer II platform (100 bp paired-end sequencing library with an insertion size of 500 bp) at Genergy Biotechnology (Shanghai, China). Assembly was performed using SOAPdenovo. Gaps were closed by primer walking and sequencing of PCR products. Coding sequences (CDSs) was predicted using GenDB v2.2 (11) and Glimmer 3.02 (5), and compared with non-redundant protein database to obtain descriptions. Reference genome sequences were obtained from GenBank for five pathogenic L. monocytogenes strains, including serovar 1/2a strains EGD-e (NC_003210) (8), 08-5578 (NC_013766) and 08-5923 (NC_013768) (7), and 4b strains F2365 (NC_002973) (12) and CLIP80459 (NC_012488), as well as L. innocua strain CLIP11262 (NC_003212) (8), L. weishimeri strain SLCC5334 (NC_008555) (9), L. seeligeri strain SLCC3954 (NC_013891) (17).

The genome of M7 consists of a single circular chromosome of 2,976,163 bp, with a GC content of 38.2%. There are 2977 CDSs that represent 89.2% of the genome, with the average length of 297 amino acids, six 16S-5S-23S rRNA operons,
and 67 tRNA genes. M7 harbors no plasmid and carries three prophages bearing 53, 78, and 66 genes respectively. The genome of M7 is highly similar to that of HCC23, a serovar 4a strain isolated from catfish in the US, which contains 2,976,212 nucleotides (NC_011660) (16). Genomic differences were observed on 68 loci (12 deletions, 45 insertions and 11 substitutions) between HCC23 and M7.

Comparative analysis of six \textit{L. monocytogenes} genomes (F2365, CLIP80459, EGD-e, 08-5578, 08-5923 and M7) revealed that \textit{prfA} locus, internalin genes \textit{inlA} and \textit{inlB} and sugar phosphate permease gene \textit{hpt} were conserved in \textit{L. monocytogenes}. Notably, one mutation (G145S) in the positive transcriptional regulator (PrfA) that results in its constitutive activation (6) was identified in M7 but absent in other strains including HCC23. Sixty-four genes that were conserved in pathogenic strains were absent in M7 (prophage genes excepted). At least three internalins (InIC, InIH and InIJ) that contribute to \textit{Listeria} pathogenicity were absent in M7 (13, 14, 15). On the other hand, 151 genes were identified as specific to M7 but absent in pathogenic strains (except the prophage genes). Twenty of these genes were also present in \textit{L. innocua}, a nonpathogenic species closely related to \textit{L. monocytogenes} (4).

A total of 2168 genes constitute the core-genome of \textit{L. monocytogenes}, \textit{L. innocua}, \textit{L. weishimeri} and \textit{L. seeligeri}. The phylogenetic tree based on these genes confirms that M7 constitutes an evolutionary intermediate between \textit{L. monocytogenes} and \textit{L. innocua} (1).

**Nucleotide sequence accession number.** This complete genome has been deposited in GenBank under CP002816.
We thank Dr. Dongyou Liu at Royal College of Pathologists of Australasia Quality Assurance Programs, and Dr. John Bowman at University of Tasmania for great helps on the genome annotation and fruitful discussions. We also thank Jie Mu at Genergy Biotechnology for excellent technical assistance. This study was supported by National Natural Science Foundation of China (30870068). J. C. is supported by the China Postdoctoral Science Foundation (20100481428).

References


innocua subgroups with different evolutionary distances from Listeria monocytogenes.

BMC Microbiol. 10:97.


