

# Complete Genome Sequence of *Neisseria meningitidis* Serogroup A Strain NMA510612, Isolated from a Patient with Bacterial Meningitis in China

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**Serogroup A meningococcal strains have been involved in several pandemics and a series of epidemics worldwide in the past. Determination of the genome sequence of the prevalent genotype strain will help us understand the genetic background of the evolutionary and epidemiological properties of these bacteria. We sequenced the complete genome of *Neisseria meningitidis* NMA510612, a clinical isolate from a patient with meningococcal meningitis.**

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*Neisseria meningitidis* is a leading cause of bacterial meningitis worldwide (1). Among its 6 serogroups (A, B, C, X, Y, and W135) involved in invasive meningococcal disease, serogroup A strains caused pandemic waves and large epidemics in China and Africa during the last century (2). Interestingly, most of the epidemics before the 1990s were associated with a clone of subgroup III, called sequence type 5 (ST5) (3, 4), whereas replacement of ST7 strains occurred thereafter in both China and the African meningitis belt (5). Molecular genotyping of organisms involved in epidemics showed that ST7 strains with P1.20,9 represented over 86% of isolates in China after 2000 (6). Herein, we present the complete genome sequence of serogroup A strain NMA510612, a type strain of the ST7 genotype, which was isolated in China in 2006 from a patient with acute bacterial meningitis. The genome of NMA510612 will further our understanding of the molecular evolution of the hyperinvasive lineage of *Neisseria meningitidis*.

The NMA510612 strain was grown in a chocolate plate incubated overnight in 5% CO<sub>2</sub> at 37°C. The chromosome DNA extraction was performed according to the protocol provided with the DNA extraction kit (Promega, Madison, WI, USA). For *de novo* sequencing, a fragment library with an average length of 500 bp was constructed and then sequenced with a Roche/454 GS FLX Titanium instrument (Roche Diagnostics, Penzberg, Germany). The raw data set of 219,392 reads (126 Mb) was assembled using Newbler version 2.6 (Roche), which produced 106 large contigs (>500 bp) with an average size of 19 kb. Then, gaps between these contigs were closed by genomic PCR and primer walking methods with conventional Sanger sequencing (7). Glimmer3 and tRNAscan-SE were used to predict protein-coding sequences (CDS) and tRNA genes, respectively. Annotation of the CDS was performed with BLAST searches of the GenBank nonredundant protein database followed by manual curation using Z2491 as a reference (GenBank accession no. AL157959.1) (8).

The complete sequence of the NMA510612 genome consists of

one circular chromosome with a size of 2,188,020 bp, and the average G+C content is 51.5%. The chromosome is predicted to possess 4 rRNA operons, 163 insertion elements (IS), 59 tRNAs, and 2,462 CDS. The NMA510612 genome was demonstrated to be highly collinear with that of WUE2594 (GenBank accession no. FR774048), a strain of the ST5 genotype isolated from Germany in 1991 (9). The NMA510612 genome is smaller than the WUE2594 genome due to lack of a 42-kb Mu-like prophage region. On the other hand, it specifically harbors several genes, such as *tetA* and *hmbR*. Previous studies have demonstrated the presence of tetracycline resistance determinants like *tet(M)* and *tet(B)* (10, 11). The distribution of the hemoglobin receptor gene *hmbR* was investigated and observed at a significantly higher frequency among disease isolates than among carriage isolates (12). In addition, we found that polymorphic regions exist in genes encoding type IV pilus proteins and type I restriction enzymes. These variations may be involved in a rearrangement of surface-exposed proteins in this ST7 clone and enable the bacteria to overcome the herd immunity generated by the presence of the ST5 strain in the population.

**Nucleotide sequence accession number.** The genome sequence of *N. meningitidis* NMA510612 has been deposited in GenBank under accession no. CP007524.

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## REFERENCES

1. Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM. 2001. Meningococcal disease. *N. Engl. J. Med.* 344:1378–1388. <http://dx.doi.org/10.1056/NEJM200105033441807>.
2. Harrison LH, Trotter CL, Ramsay ME. 2009. Global epidemiology of meningococcal disease. *Vaccine* 27(Suppl 2):B51–B63. <http://dx.doi.org/10.1016/j.vaccine.2008.10.030>.

3. Wang JF, Caugant DA, Li X, Hu X, Poolman JT, Crowe BA, Achtman M. 1992. Clonal and antigenic analysis of serogroup A *Neisseria meningitidis* with particular reference to epidemiological features of epidemic meningitis in the People's Republic of China. *Infect. Immun.* **60**: 5267–5282.
4. Zhu P, van der Ende A, Falush D, Brieske N, Morelli G, Linz B, Popovic T, Schuurman IG, Adegbola RA, Zurth K, Gagneux S, Platonov AE, Riou JY, Caugant DA, Nicolas P, Achtman M. 2001. Fit genotypes and escape variants of subgroup III *Neisseria meningitidis* during three pandemics of epidemic meningitis. *Proc. Natl. Acad. Sci. U. S. A.* **98**: 5234–5239. <http://dx.doi.org/10.1073/pnas.061386098>.
5. Nicolas P, Décousset L, Riglet V, Castelli P, Stor R, Blanchet G. 2001. Clonal expansion of sequence type (ST)-5 and emergence of ST-7 in serogroup A meningococci, Africa. *Emerg. Infect. Dis.* **7**:849–854. <http://dx.doi.org/10.3201/eid0705.010513>.
6. Zhang X, Shao Z, Zhu Y, Xu L, Xu X, Mayer LW, Xu J, Jin Q. 2008. Genetic characteristics of serogroup A meningococci circulating in China, 1956–2005. *Clin. Microbiol. Infect.* **14**:555–561. <http://dx.doi.org/10.1111/j.1469-0691.2008.01977.x>.
7. Gordon D, Abajian C, Green P. 1998. Consed: a graphical tool for sequence finishing. *Genome Res.* **8**:195–202. <http://dx.doi.org/10.1101/gr.8.3.195>.
8. Parkhill J, Achtman M, James KD, Bentley SD, Churcher C, Klee SR, Morelli G, Basham D, Brown D, Chillingworth T, Davies RM, Davis P, Devlin K, Feltwell T, Hamlin N, Holroyd S, Jagels K, Leather S, Moule S, Mungall K, Quail MA, Rajandream MA, Rutherford KM, Simmonds M, Skelton J, Whitehead S, Spratt BG, Barrell BG. 2000. Complete DNA sequence of a serogroup A strain of *Neisseria meningitidis* Z2491. *Nature* **404**:502–506. <http://dx.doi.org/10.1038/35006655>.
9. Schoen C, Weber-Lehmann J, Blom J, Joseph B, Goesmann A, Strittmatter A, Frosch M. 2011. Whole-genome sequence of the transformable *Neisseria meningitidis* serogroup A strain WUE2594. *J. Bacteriol.* **193**: 2064–2065. <http://dx.doi.org/10.1128/JB.00084-11>.
10. Gascoyne-Binzi DM, Heritage J, Hawkey PM, Sprott MS. 1994. Characterisation of a tet(M)-carrying plasmid from *Neisseria meningitidis*. *J. Antimicrob. Chemother.* **34**:1015–1023. <http://dx.doi.org/10.1093/jac/34.6.1015>.
11. Takahashi H, Watanabe H, Kuroki T, Watanabe Y, Yamai S. 2002. Identification of tet(B), encoding high-level tetracycline resistance, in *Neisseria meningitidis*. *Antimicrob. Agents Chemother.* **46**:4045–4046. <http://dx.doi.org/10.1128/AAC.46.12.4045-4046.2002>.
12. Harrison OB, Evans NJ, Blair JM, Grimes HS, Tinsley CR, Nassif X, Kriz P, Ure R, Gray SJ, Derrick JP, Maiden MC, Feavers IM. 2009. Epidemiological evidence for the role of the hemoglobin receptor, hmbR, in meningococcal virulence. *J. Infect. Dis.* **200**:94–98. <http://dx.doi.org/10.1086/599377>.