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Complete Genome Sequence of the Hemotrophic *Mycoplasma suis* Strain KI3806▽

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***Mycoplasma suis*, a member of the hemotrophic mycoplasma (HM) group, parasitize erythrocytes of pigs. Increasing evidence suggests that *M. suis* is also a zoonotic agent. Highly pathogenic strains of *M. suis* (e.g., *M. suis* KI3806) have been demonstrated to invade erythrocytes. This complete sequenced and manually annotated genome of *M. suis* KI3806 is the first available from this species and from the HM group. The DNA was isolated from blood samples of experimentally infected pigs due to the lack of an *in vitro* cultivation system. The small circular chromosome of 709,270 bp, encoding an unexpectedly high number of hypothetical proteins and limited transport and metabolic capacities, could reflect the unique lifestyle of HM on the surface of erythrocytes.**

Hemotrophic mycoplasmas (HM) are epierythrocytic, wall-less bacteria that comprise a single phylogenetic cluster within the genus *Mycoplasma* (5). HM infections are found in a wide range of animals (e.g., *Mycoplasma suis* in pigs), causing infectious anemia (3, 4). The unique life cycle of *M. suis* and other HM on erythrocytes implies special features allowing HM to adhere to erythrocytes or to perform metabolic exchanges. Moreover, *M. suis* can invade erythrocytes, leading to high virulence and resistance to antibiotics (2). So far, HM cultivation in cell-free medium has failed, indicating that HM have a special metabolism and/or a high adaption to their hosts.

We determined the genome of *M. suis* strain KI3806, a highly pathogenic and invasive strain. DNA was isolated from experimentally infected piglets using pulsed-field gel electrophoresis and sequenced (EurofinsMedigenomix; Germany) (1, 2).

The circular chromosome of *M. suis* KI3806 is composed of 709,270 bp with a 31%-GC content. The genome includes 32 tRNAs and a single-copy 16S rRNA which is separated from the 23S and 5S rRNA by ~165 kb and encoded on the opposite strand. The predicted 809 open reading frames (ORFs) comprise a density of 1.119 genes per kilobase. The average protein size is 259 amino acids, with a coding percentage of 87%. The low number of estimated paralogs (36 coding determining regions [CDS]; 70% identity) corresponds to only one putative transposase. The genome differs from other mycoplasma genomes in the high portion of predicted proteins without functional assignment (64.6%; 523/809), which may reflect the adaptation of *M. suis* to a special environment but could also be a result of large integration events due to the unit-like organization of these proteins (RG1_33888.0.50303 [region_position], RG2_77345.0.182976, RG3_214881.0.233523, RG4_416009.0.454949, RG5_456815.0.523918, and RG6_581193.0.614049). These six regions encode 19 proteins of unknown function per unit at least and sum up to ~280 kb, which does not include housekeeping genes but does include sequences for 413 unassigned proteins. A similar scenario is known for the integrative conjugative elements (ICEs) from *Mycoplasma agalactiae* (6), but ICEs show different genetic content. In *M. suis* some phage-related proteins, i.e., an integrase, a tape measure protein, a tail protein, and a terminase, are encoded, indicating a phage-derived origin of these large regions. However, in *M. suis* genome extension is suggested to act against genome condensation due to the limited number of transporters and metabolic capacities. Transporters for spermidine/putrescine, hemin, ferrichrome, cobalt, magnesium, and probably amino acids and phosphate are encoded. *M. suis* generates ATP through glycolysis, but the tricarboxylic acid cycle, arginine hydrolysis, or urea hydrolysis is incomplete or missing. Glycolysis is fed by the uptake of glucose via the phosphoenolpyruvate-dependent sugar phosphotransferase system and conversion by glucose 6-phosphate isomerase. Nucleotide biosynthesis lacks reductases (*nrd*A, *nrd*B, and *nrd*D) and also the nucleoside diphospate kinases (*ndk*). The proton gradient is probably regulated by the F1F0 ATPase system.

Altogether, the genome sequence of *M. suis* KI3806 will provide the basis for a better understanding of the nature of HM, especially their nutritional requirements, which have prevented *in vitro* cultivation so far, and the pathogenicity-determining mechanisms.

Nucleotide sequence accession number. The nucleotide sequence accession number of the complete *M. suis* KI3806 genome sequence is FQ790233.

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