

The nucleotide sequence of the tetracycline resistance determinant tetM from Ureaplasma urealyticum

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The tetracycline resistance gene, tetM, first detected in Gram-positive streptococci (1), has also been found in pathogenic Gram-negative bacteria (2). This determinant confers high-level resistance and is frequently located on conjugative transposable elements (3). Recently, a tetM gene has been detected in and cloned from Ureaplasma urealyticum (J.T. Brown and M.Roberts,submitted). Here we report its nucleotide sequence.

A total of 3425 bp were sequenced by the Sanger method (4) using unpurified synthetic primers (5). An open reading frame (ORF), starting from a Met codon at position 956 that is preceded by a putative ribosome binding site, TGGAGGA, codes for a protein of 639 amino acids (MW= 72,611 Daltons). This molecular weight is in agreement with previous data (6). The amino acid composition suggests a cytoplasmic protein (6), differing from other tetracycline resistance determinants involved in tetracycline efflux (7).

Comparison of the tetM nucleotide sequence from Ureaplasma (isolated in Seattle in 1984) with that obtained from S. pneumoniae (6; isolated nearly 7 years earlier in Paris) reveals a close relationship. The ORFs show a 95% homology at the amino acid level. Most of the differences are conservative. Remarkably then, the tetM gene has been conserved over time, geographical distance and passage between distantly related bacteria (9).

It has been suggested that Mycoplasmatales (such as U. urealyticum) do not utilize the typical TGG codon for Trp, but instead employ the termination triplet TGA (8). The tetM gene described here contains four TGG codons, implying normal Trp codon usage in U. urealyticum. The sequence does not contain a TGA termination; therefore, whether or not the organism can additionally utilize TGA as a Trp codon remains unclear.

1 GCTCTCATGTGATACAGTACGCCAAGATATTCCTGATCGCTCTGTAAAGAGGATTCAGATATGACGGTAGAGCCCACTGGCACAATAGTTFATGTAACTCAAGTGTAGACCAG
121 CTCATTACAGAGGGAAAATACAAGACCGCTCCACTCTGCTTATATAGTGAAGTGTCTATGTAGATGTGTTCTGGAAAATATGTGTACTGGTTAAGAAATCCCGACCAATTACCAACATACCTAAG
241 AAATCAAGTTATAACCAAAAGCCATTGAAGTGGAGGGACGGTGTATCCATTACACCAATGAATCAATGAGTTTTTAACAGCGTTCTTCAAGCTCTATCTACAGCGACAGCCGAGT
361 GAACCTTCCCTACTATGTGAAATGACGGGATATTAACCAATCGAALAGAGTACATCTTTCAMGAACGTGTAATCTTATCACAAATCGTAMGGAATATCAGTCCAGGTAATCGGGCTGA
481 CAGTGGAGTATATCGACCAGCAGCAAGCAGCGATATCAAAATTTGATTTGGTACTTGAALAGACGGGGATAATGGGAATGTAACAAATATGGTACATGATTACA
601 GATACTTTGATACATGACTCTTTTATAAAAATGGAGATCTCCCTTACAAATATGCTCTTACGCTATATATTAAGTACTATTAALAGAGTAAATAAATATGGCAAGGTA
721 TCTTAATAAATCTCAATTTGATACCGGGCAAAATAATATGATGCTCTTTTTAGGAGGGCTTAGTTTTTGGTACCCAGTTAAGAAATACCTTTATCATGTGATTTCAAAATATGCA
841 CAGAAATCTGTATGCTTGTGATACCTTATGCTTGTGATGATCAAAAAATCCCAAGTATGAAAGTATTTATCACTGGGATTTTTAGGCCCTTTTGGATTTTGAATGGAGAAAATCACATGAAA MetLys 2
961 IIEIIEASNIIEGLYVALLLEALASIVALSVALASPLGLYETHRTHRLAUHRLGLUHLERLEULERTYASNSERGLYALIEIETHRLGLUHLERVALASPLGLYTHRLALYS Arg Lys 42
ATATTAATATATGGATTTTATGCTATGTTGATGCGGAAAACCTTATACAGAAAGCTTATATATACAGTGGACGGATACAGATTAAGCGTAAAGTACACAGAGC AA
1081 THRASPASHTHRLAUHLERGLUARGGLYLIEIETHRLGLUHLERLEULERTYASNSERGLYALIEIETHRLGLUHLERVALASPLGLYTHRLALYSVALASPLGLYTHRPROGLYIIEIETHRASPHELEU Arg Lys 82
ACGGATAATACGCTTTTGAACGCTCAGAGAGGAATTACAATTCAGACAGGATAAACCTCTTTTACGTGCGAAAATACGAAAGTGAACATCATAGCACCGCCAGGCATATGGAATTCCTTA T
1201 ALAGLUVALTRYARGSERLEULERVALLEULASPLGLYALIEIETHRLGLUHLERLEULERTYASNSERGLYALIEIETHRLGLUHLERVALASPLGLYTHRLALYSVALASPLGLYTHRPROGLYIIEIETHR Arg Lys 122
CGAAGATATATGCTTCAATTTATGCTATGTTGATGCGGAAAACCTTATACAGAAAGCTTATATATACAGTGGACGGATACAGATTAAGCGTAAAGTACACAGAGC AA
1321 THRILEPHEIIEASLYIIEASPLASPLGLYIIEASPLSERTHRVALTRYGLASPLIIEIETHRLGLUHLERLEULERTYASNSERGLYALIEIETHRLGLUHLERVALASPLGLYTHRPROGLYIIEIETHR His 162
ACAACTTTTTATCAATAAGTTCAGCAAAATGGAATTAATCAACCGTTATACAGGATATTAAGAGAACTTCTCGCAAAATGTAATCAACAGAGGATAGACTTATCCCT C

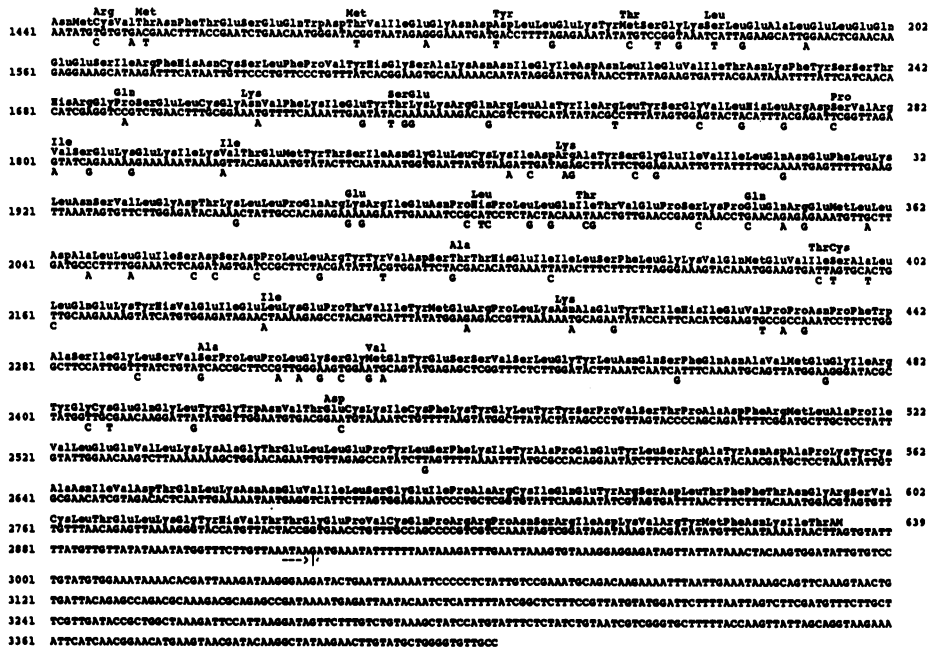


Figure 1.- Nucleotide sequence of the tetM gene from *Ureaplasma urealyticum*. The base differences with the tetM sequence from *Streptococcus pneumoniae* (between arrows) and the predicted amino acid sequence of the tetM gene product from *Ureaplasma urealyticum* are also shown.

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