ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 1999, p. 1523–1524 Vol. 43, No. 6
0066-4804/99/$04.00+0

Nomenclature for New Tetracycline Resistance Determinants

STUART B. LEVY,[1]* LAURA M. MCMURRY,[1]* TERESA M. BARBOSA,[1] VICKERS BURDETT,[2] PATRICE COURVALIN,[3] WOLFGANG HILLEN,[4] MARILYN C. ROBERTS,[5] JULIAN I. ROOD,[6] AND DIANE E. TAYLOR[7]

Department of Molecular Biology and Microbiology, Tufts University School of Medicine, Boston, Massachusetts 02111[1]; Department of Microbiology and Immunology, Duke University, Durham, North Carolina 27710[2]; Unité des Agents Antibactériens, Institut Pasteur, Paris Cedex 15, France[3]; Lehrstuhl für Mikrobiologie, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany[4]; Department of Pathobiology, University of Washington, Seattle, Washington 98195[5]; Department of Microbiology, Monash University, Clayton, Australia[6]; and Departments of Biological Sciences and of Medical Microbiology and Immunology, University of Alberta, Edmonton, Alberta T6G 2H7, Canada[7]

Received 24 February 1999/Accepted 24 March 1999

Letters of the English alphabet have heretofore been used to name tetracycline resistance determinants. Since all 26 letters have now been used, a nomenclature employing numerals is recommended for future determinants, and one laboratory has offered to coordinate the assignment of numerals.

In 1989, a Note describing the nomenclature for tetracycline resistance determinants which employed letters of the English alphabet was published in this journal (14). Since no letters now remain for designating additional determinants, we propose that new determinants be hereafter designated by Arabic numerals. The new system is patterned on the previous letter-based one, with a numeral used instead of a letter to name a determinant. Since 30 determinants have been described (most, but not all, according to the 1989 nomenclature, with the new 1999 nomenclature being used for Tet 30) (Table 1), the next determinant would receive number 31, with no renaming of the earlier determinants. Following the previous system used with letters, the class would be 31, and the determinant would be designated Tet 31 (with a space between "Tet" and "31"). If there were only a single gene in the determinant, it would be designated *tet*(31). If there were more than one structural gene, the first would be designated *tetA*(31) and the second would be *tetB*(31), etc. A regulatory gene would be designated *tetR*(31). Note that the class designation, 31, is not italicized. The names of the corresponding proteins would be Tet(31) or TetA(31), etc. An allele of a gene would be designated by a hyphen followed by an italicized allele number; for example, *tetA*(31)-*1* would be allele number 1 of the *tetA* gene of class 31. If the class designation is not needed within a single communication, it could be omitted.

This system employs some of the conventions from the previous communication (14) and is summarized in Table 2. Usage for previously described determinants should continue to conform to the prior recommendations (14).

Recently, there have been several situations in which tetracycline resistance determinants discovered in different laboratories were nearly given the same designation. To avoid such a problem in the future, we offer the S. B. Levy group to coordinate the naming of new determinants. Such a determinant can be defined as a naturally occurring unit of one or more adjacent genes involved primarily in tetracycline resistance (as opposed to multidrug resistance or other known function) having a sequence significantly different from sequences of currently known determinants. We suggest ≤80% amino acid identity as the dividing line, based on previous usage. Class L has been defined as a single class even though it contains two subgroups

TABLE 1. Known tetracycline resistance determinants[a]

Tet determinant (or gene, if no determinant name was given)	Mechanism	GenBank accession no.	Reference
Tet A	Efflux	X00006	33
Tet B	Efflux	J01830	11
Tet C	Efflux	J01749	23
Tet D	Efflux	X65876	2
Tet E	Efflux	L06940	1
Tet F	Efflux (ineffective?)	Unsequenced	22, 30
Tet G	Efflux	S52437	34
Tet H	Efflux	U00792	10
Tet I	Efflux (?)	Unsequenced	25
Tet J	Efflux	AF038993	16
Tet K	Efflux	M16217	20
Tet L (plasmid)[b]	Efflux	M11036	13
Tet L (chromosomal)[b]	Efflux	X08034	26
Tet M	Ribosomal protection	X04388	17
(Tet N)	(Withdrawn)		12
Tet O	Ribosomal protection	M18896[c]	28
Tet P	Efflux, ribosomal protection (two genes)	L20800	27
Tet Q	Ribosomal protection	X58717	19
Tet S	Ribosomal protection	L09756	4
Tet T	Ribosomal protection	L42544	5
Tet U	Unknown	U01917	24
Tet V	Efflux	AF030344	7
Tet W	Ribosomal protection	AJ222769	3
Tet X	Modification	M37699	29
Tet Y	Efflux	AF070999	32
Tet Z	Efflux	AF121000	31
otrA	Ribosomal protection	X53401	9
otrB	Efflux	AF079900	18
otrC	Unknown	Unsequenced	21, 25
tcr3 (*tcrC*)	Efflux	D38215	6
tet	Ribosomal protection	M74049	8
Tet 30 [originally unnamed determinant; protein is 46% identical to TetA(A)]	Efflux	AF090987 (wild type)	15

[a] In most cases, we cite the first publication to report the sequence for one or both genes of a determinant. In cases where major (but not minor) errors were later corrected, we cite the later publication. The sequences of many variants of some determinants (particularly Tet L and Tet M) are available but are not given here. Four different unnamed and unsequenced but presumed ribosomal protection determinants (5) are not included.

[b] The proteins encoded by these two Tet L determinants are only 81% identical.

[c] The original sequence is not available electronically, so another is substituted.

* Corresponding author. Mailing address for Stuart B. Levy: Center for Adaptation Genetics and Drug Resistance, Tufts University School of Medicine, 136 Harrison Ave., Boston, MA 02111. Phone: (617) 636-6764. Fax: (617) 636-0458. E-mail: slevy@opal.tufts.edu. E-mail for Laura M. McMurry: lmcmur01@emerald.tufts.edu.

TABLE 2. Proposed nomenclature for new tetracycline resistance determinants

Class[a]	Determinant[b]	Structural[c,d]		Regulatory (repressor)[d]	
		Gene	Protein	Gene	Protein
n	Tet n	*tet*(n)	Tet(n)	*tetR*(n)	TetR(n)

[a] Class n is used as an example, where n is an Arabic numeral (31, 32, 33, etc.), numbered in approximate order of public dissemination.
[b] Note the space between Tet and n.
[c] In the case of multiple structural genes, use the following format: *tetA*(n), *tetB*(n), etc.
[d] After an introductory use, "n" may be omitted where no ambiguity exists.

in which the single proteins only are 81% identical (25, 26), while the proteins of two different classes, M and S, are 79% identical (4, 25). To confirm that a number proposed for a newly discovered tetracycline resistance determinant has not been used, please contact S. B. Levy.

Finally, we note that when looking in databases for a name containing parentheses or a space, such as "*tet*(X)" or "Tet X", quotation marks should be used around the name, as shown, to retrieve the term intact.

This work was supported by grant GM55430 from the National Institutes of Health.

REFERENCES

1. **Allard, J. D., and K. P. Bertrand.** 1993. Sequence of a class E tetracycline resistance gene from *Escherichia coli* and comparison of related tetracycline efflux proteins. J. Bacteriol. **175:**4554–4560.
2. **Allard, J. D., M. L. Gibson, L. H. Vu, T. T. Nguyen, and K. P. Bertrand.** 1993. Nucleotide sequence of class D tetracycline resistance genes from *Salmonella ordonez*. Mol. Gen. Genet. **237:**301–305.
3. **Barbosa, T. M., K. P. Scott, and H. J. Flint.** 1999. Evidence for recent intergenic transfer of a new tetracycline resistance gene, *tet*(W), isolated from *Butyrivibrio fibrisolvens*, and the occurrence of *tet*(O), in ruminal bacteria. Environ. Microbiol. **1:**53–64.
4. **Charpentier, E., G. Gerbaud, and P. Courvalin.** 1993. Characterization of a new class of tetracycline-resistance gene *tet*(S) in *Listeria monocytogenes* BM4210. Gene **131:**27–34.
5. **Clermont, D., O. Chesneau, G. de Cespédès, and T. Horaud.** 1997. New tetracycline resistance determinants coding for ribosomal protection in streptococci and nucleotide sequence of *tet*(T) isolated from *Streptococcus pyogenes* A498. Antimicrob. Agents Chemother. **41:**112–116.
6. **Dairi, T., K. Aisaka, R. Katsumata, and M. Hasegawa.** 1995. A self-defense gene homologous to tetracycline effluxing gene essential for antibiotic production in *Streptomyces aureofaciens*. Biosci. Biotechnol. Biochem. **59:**1835–1841.
7. **de Rossi, E., M. C. J. Blokpoel, R. Cantoni, M. Branzoni, G. Riccardi, D. B. Young, K. A. L. De Smet, and O. Ciferri.** 1998. Molecular cloning and functional analysis of a novel tetracycline resistance determinant, *tet*(V), from *Mycobacterium smegmatis*. Antimicrob. Agents Chemother. **42:**1931–1937.
8. **Dittrich, W., and H. Schrempf.** 1992. The unstable tetracycline resistance gene of *Streptomyces lividans* 1326 encodes a putative protein with similarities to translational elongation factors and Tet(M) and Tet(O) proteins. Antimicrob. Agents Chemother. **36:**1119–1124.
9. **Doyle, D., K. J. McDowall, M. J. Butler, and I. S. Hunter.** 1991. Characterization of an oxytetracycline-resistance gene, *otrA*, of *Streptomyces rimosus*. Mol. Microbiol. **5:**2923–2933.
10. **Hansen, L. M., L. M. McMurry, S. B. Levy, and D. C. Hirsh.** 1993. A new tetracycline resistance determinant, Tet H, from *Pasteurella multocida* specifying active efflux of tetracycline. Antimicrob. Agents Chemother. **37:**2699–2705.
11. **Hillen, W., and K. Shollmeier.** 1983. Nucleotide sequence of the Tn10 encoded tetracycline resistance gene. Nucleic Acids Res. **11:**525–539.
12. **Horaud, T., F. Delbos, and K. Pepper.** 1990. Does a tetracycline resistance determinant of class N exist? Antimicrob. Agents Chemother. **34:**1447–1449.
13. **Hoshino, T., T. Ikeda, N. Tomizuka, and K. Furukawa.** 1985. Nucleotide sequence of the tetracycline resistance gene of pTHT15, a thermophilic *Bacillis* plasmid: comparison with staphylococcal Tc^R controls. Gene **37:**131–138.
14. **Levy, S. B., L. M. McMurry, V. Burdett, P. Courvalin, W. Hillen, M. C. Roberts, and D. E. Taylor.** 1989. Nomenclature for tetracycline resistance determinants. Antimicrob. Agents Chemother. **33:**1373–1374.
15. **Luo, Z.-Q., and S. K. Farrand.** 1999. Cloning and characterization of a tetracycline resistance determinant present in *Agrobacterium tumefaciens* C58. J. Bacteriol. **181:**618–626.
16. **Magalhaes, V. D., W. Schuman, and B. A. Castilho.** 1998. A new tetracycline resistance determinant cloned from *Proteus mirabilis*. Biochim. Biophys. Acta **1443:**262–266.
17. **Martin, P., P. Trieu-Cuot, and P. Courvalin.** 1986. Nucleotide sequence of the *tetM* tetracycline resistance determinant of the streptococcal conjugative transposon Tn1545. Nucleic Acids Res. **14:**7047–7058.
18. **McMurry, L. M., and S. B. Levy.** 1998. Revised sequence of OtrB (Tet347) tetracycline efflux protein from *Streptomyces rimosus*. Antimicrob. Agents Chemother. **42:**3050.
19. **Nikolich, M. P., N. B. Shoemaker, and A. A. Salyers.** 1992. A *Bacteroides* tetracycline resistance gene represents a new class of ribosome protection tetracycline resistance. Antimicrob. Agent Chemother. **36:**1005–1012.
20. **Noguchi, N., T. Aoki, M. Sasatsu, M. Kono, K. Shishido, and T. Ando.** 1986. Determination of the complete nucleotide sequence of pNS12, a staphylococcal tetracycline-resistance plasmid propagated in *Bacillus subtilis*. FEMS Microbiol. Lett. **37:**283–288.
21. **Pang, Y., B. A. Brown, V. A. Steingrube, R. J. Wallace, Jr., and M. C. Roberts.** 1994. Tetracycline resistance determinants in *Mycobacterium* and *Streptomyces* species. Antimicrob. Agents Chemother. **38:**1408–1412.
22. **Park, B. H., M. Hendricks, M. H. Malamy, F. P. Tally, and S. B. Levy.** 1987. Cryptic tetracycline resistance determinant (class F) from *Bacteroides fragilis* mediates resistance in *Escherichia coli* by actively reducing tetracycline accumulation. Antimicrob. Agents Chemother. **31:**1739–1743.
23. **Peden, K. W. C.** 1983. Revised sequence of the tetracycline resistance gene of pBR322. Gene **22:**277–280.
24. **Ridenhour, M. B., H. M. Fletcher, J. E. Mortensen, and L. Daneo-Moore.** 1996. A novel tetracycline-resistant determinant, tet(U), is encoded on the plasmid pKQ10 in *Enterococcus faecium*. Plasmid **35:**71–80.
25. **Roberts, M. C.** 1996. Tetracycline resistance determinants: mechanisms of action, regulation of expression, genetic mobility, and distribution. FEMS Microbiol. Rev. **19:**1–24.
26. **Sakaguchi, R., H. Amano, and K. Shishido.** 1988. Nucleotide sequence homology of the tetracycline-resistance determinant naturally maintained in *Bacillus subtilis* Marburg 168 chromosome and the tetracycline-resistance gene of *B. subtilis* plasmid pNS1981. Biochim. Biophys. Acta **950:**441–444.
27. **Sloan, J., L. M. McMurry, D. Lyras, S. B. Levy, and J. I. Rood.** 1994. The *Clostridium perfringens* Tet P determinant comprises two overlapping genes: *tetA*(P), which mediates active tetracycline efflux, and *tetB*(P), which is related to the ribosomal protection family of tetracycline-resistance determinants. Mol. Microbiol. **11:**403–415.
28. **Sougakoff, W., B. Papadopoulou, P. Nordmann, and P. Courvalin.** 1987. Nucleotide sequence and distribution of gene *tetO* encoding tetracycline resistance in *Campylobacter coli*. FEMS Microbiol. Lett. **44:**153–159.
29. **Speer, B. S., L. Bedzyk, and A. A. Salyers.** 1991. Evidence that a novel tetracycline resistance gene found on two *Bacteroides* transposons encodes an NADP-requiring oxidoreductase. J. Bacteriol. **173:**176–183.
30. **Speer, B. S., and A. A. Salyers.** 1990. A tetracycline efflux gene on *Bacteroides* transposon Tn*4400* does not contribute to tetracycline resistance. J. Bacteriol. **172:**292–298.
31. **Tauch, A., A. Puehler, and J. Kalinowski.** DNA sequence and genetic organization of pAG1, a 19.8-kb R-plasmid of *Corynebacterium glutamicum* encoding a new class of tetracycline efflux and repressor proteins. Submitted for publication. Unpublished data (GenBank accession no. AF121000).
32. **Tietze, E.** 1998. Unpublished data (in GenBank).
33. **Waters, S. H., P. Rogowsky, J. Grinsted, J. Altenbuchner, and R. Schmitt.** 1983. The tetracycline resistance determinants of RP1 and Tn*1721*: nucleotide sequence analysis. Nucleic Acids Res. **11:**6089–6105.
34. **Zhao, J., and T. Aoki.** 1992. Nucleotide sequence analysis of the class G tetracycline resistance determinant from *Vibrio anguillarum*. Microbiol. Immunol. **36:**1051–1060.