

Nomenclature of Plasmid-Mediated 16S rRNA Methylases Responsible for Panaminoglycoside Resistance^V

Production of 16S rRNA methylase has recently drawn attention as a novel aminoglycoside resistance mechanism in pathogenic gram-negative bacteria (1). It confers very-high-level resistance to all aminoglycosides that are currently available for parenteral formulation. Six distinct genes, *rmtA*, *rmtB*, *rmtC*, *rmtD*, *armA*, and *npmA*, encoding their respective enzymes have been identified in clinical and veterinary strains from various geographic areas, including East Asia, Europe, and the Americas, since 2003 (1, 10). NpmA is the only enzyme among them that methylates residue A1408, whereas the others methylate residue G1405, both within the aminoacyl site (A site) of the 16S rRNA (7, 10). All six genes are confirmed to be or are likely to locate on plasmids (3, 4, 10, 11, 12, 14). Recent findings also indicate that some of these genes are capable of crossing the barrier between glucose-fermenting and nonfermenting species. For instance, *armA* has been identified in both members of the family *Enterobacteriaceae* and in *Acinetobacter baumannii* (5, 13), and *rmtD* has been identified in *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (unpublished data). We will likely see an increasing number of reports about this resistance mechanism, including identification of genes encoding new 16S rRNA methylases.

Historically, the nomenclature of genes and enzymes for many resistance mechanisms has become complicated and nonsystematic (6). An extreme example is that of aminoglycoside acetyltransferases, where new gene names are arbitrarily assigned from one of the two coexisting nomenclature systems (9). The situation is somewhat better with β -lactamases and macrolide resistance genes, due to a registry and guidelines, respectively (<http://www.lahey.org/Studies/>) (8). To prevent confusion over the nomenclature of 16S rRNA methylases, we would like to propose practical rules for the nomenclature of these enzymes, which shall apply to any relevant enzymes to be identified in the future.

Currently, the highest and lowest identities of amino acid sequences among the G1405 16S rRNA methylases are 81.7% between RmtA and RmtB and 25.8% between ArmA and RmtD, respectively (2, 3). On the other hand, identities lower than 10% are observed between the G1405 16S rRNA methylases and the NpmA that methylates A1408 (10) (Table). Thus, we propose the following rules. A gene that has an amino acid identity greater than 95% with the closest known 16S rRNA methylase gene will be assigned a variant number starting from two in the order of the dates on which the sequences are deposited in the GenBank/EBML/DDBJ, e.g., *rmtA2* and then *rmtA3*, analogous to the nomenclature of the *qnr* genes. A gene that has between 50 and 95% amino acid identity with the closest known 16S rRNA methylase gene will be assigned a new alphabet letter according to the closest existing gene name, e.g., *rmtE*, *rmtF*, *armB*, or *armC*, provided that the gene is shown to confer a consistent aminoglycoside resistance profile. A gene that has either an amino acid identity of less than 50% with the closest known 16S rRNA methylase gene or that is proven to methylate a new residue of 16S rRNA may be assigned a brand new gene name, like *npmA*, contingent upon demonstration of 16S rRNA methylation activity of the gene product and attributable resistant phenotype. Data regarding 16S rRNA methylase genes in pathogenic bacteria

TABLE 1. Identity of amino acid residues among the sequences of plasmid-mediated 16S rRNA methylases

Methylase	Amino acid sequence identity (%) ^a					
	RmtA	RmtB	RmtC	RmtD	ArmA	NpmA
RmtA	100	81.7	27.7	41.2	29.2	<10
RmtB		100	29.5	41.3	28.9	<10
RmtC			100	26.0	27.8	<10
RmtD				100	25.8	<10
ArmA					100	<10
NpmA						100

^a Identities were calculated by GENETYX, Macintosh version 14.0.1 (SDC Co., Ltd., Tokyo, Japan).

will be accumulated and provided at the following website http://www.nih.go.jp/niid/16s_database/index.html.

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Yohei Doi

*Division of Infectious Diseases
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania*

Jun-ichi Wachino**Yoshichika Arakawa***

*Department of Bacterial Pathogenesis and Infection Control
National Institute of Infectious Diseases
4-7-1 Gakuen
Musashi-Murayama, Tokyo 208-0011
Japan*

*Phone: 81-42-561-0771, ext. 500

Fax: 81-42-561-7173

E-mail: yarakawa@nih.go.jp

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