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Nomenclature of Genes Encoding Aminoglycoside-Modifying Enzymes

Enzyme modification remains the most important mechanism of aminoglycoside resistance. The genetic determinants of these enzymes are easily disseminated even in bacterial populations with no apparent genetic relationship. The availability of molecular techniques has enabled researchers to distinguish more accurately the various genes involved in aminoglycoside resistance and to study more in depth the heterogeneity of these genes. Genetic analysis has revealed a high degree of heterogeneity in the genes encoding these modifying enzymes. Inevitably, this has led to a very complex situation that has generated some confusion and controversy, particularly when it concerns the nomenclature of these genes. Moreover, the picture has become even more intricate by the use of two systems of nomenclature. In the standard nomenclature for bacterial plasmids proposed by Novick et al. (3), the genes encoding the aminoglycoside acetyltransferases, nucleotidyltransferases, and phosphotransferases are designated *aac*, *aad*, and *aph*, respectively. In the family of the acetylating enzymes, *aacA* stands for a 6′-*N*-acetyltransferase, while *aacB* and *aacC* stand for a 2′-*N*-acetyltransferase and a 3-*N*-acetyltransferase, respectively. This designation can be followed by a number to indicate a subdivision. In this nomenclature, *aacA7* is supposed to be the seventh discovered gene encoding a 6′-*N*-acetyltransferase enzyme. In the second widely used nomenclature (see reference 4), the gene designation is written in the same way as in the enzyme designation, but in italic and lowercase characters. In this nomenclature, the *aacA* gene would be described as an *aac(6′)* gene. This designation can be followed by a roman numeral to indicate a subdivision and a lowercase character to distinguish the various genes encoding a particular enzyme. Hence, the *aac(6′)-Im* gene is the 13th gene encoding a 6′-*N*-acetyltransferase type I enzyme. It is clear that the simultaneous use of two systems of nomenclature can be the cause of misunderstandings and confusion. Indeed, a given designation can refer to various genes and vice versa.

To illustrate this, we would like to refer to our recently published article on a gene encoding a 6′-*N*-aminoglycoside acetyltransferase, which we arbitrarily called *aac(6′)-Il* (2). However, Bunny et al. had already published an article on an *aacA7* gene that encoded a protein designated AAC(6′)-Il, indicating that the gene, *aacA7*, was to be considered as the equivalent of the *aac(6′)-Il* gene (1). Thus, unintentionally and in error, we used a designation that had already been used. To avoid confusion, we propose to rename our gene the *aac(6′)-Im* gene. Interestingly, both genes were found to be associated with a *sulI*-type integron. The *aacA7* gene was found on the multidrug-resistant plasmid pBWH301 and was linked with the *catB3*, *aadB*, *oxa2*, and *orfD* gene cassettes. However, comparison of the derived amino acid sequences of the newly described AAC(6′) proteins encoded by the two genes revealed that the two predicted proteins were different. In a 154-amino-acid overlap with the *aacA7* gene product, the protein corresponding with the *aac(6′)-Im* gene possessed 21.0% identity and 47.6% similarity. These two amino acid sequences have been compared to the different amino acid sequences of the AAC(6′)-I family. After inclusion of the *aacA7* gene, we reconstructed the phylogenetic tree (see Fig. 2 in reference 2). From the deduced phylogeny of these sequences, it was found that the product of the *aacA7* gene belonged to the second subfamily of AAC(6′)-I enzymes comprising AAC(6′)-Ig, -Ik, -Ij, -Ih, -Id, -If, and -Ic. The AAC(6′)-Il protein was more related to -Id, -If, and -Ic than to the cluster of proteins encoded by genes found in *Acinetobacter* spp. The protein encoded by the *aac(6′)-Im* gene is located in the third subfamily together with AAC(6′)-Ia and AAC(6′)-Ii and is closely related to AAC(6′)-Ia (64.2% identity and 77.6% similarity with a 165 amino acid overlap) (2).

In conclusion, it seems highly desirable to come to a consensus on the gene nomenclature. It is not our intention to promote one system or another but rather to launch the discussion. The main aim of a uniform nomenclature is clarity in order to enhance communication. This can be achieved only if the nomenclature is generally accepted and consequently used. Furthermore, it cannot be denied that there is an urgent need for a central and easily accessible database, such as a Website. This will certainly facilitate the exchange of information and avoid further confusion. It is our opinion that the American Society for Microbiology can play a catalyzing role in this discussion.

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