In a recent article in your journal, Rather et al. (11) discussed the cloning and characterization of an aminoglycoside resistance determinant that they called the aac(3)-Vb gene. Without meaning to detract from the scientific merits of the paper, we would like to comment on the nomenclature used by the authors to indicate the 3-N-acetylator enzymes and the genes encoding them.

As far as the genetic name is concerned: according to the generally accepted nomenclature proposed by Novick et al. (10), the proper name for the gene is aacC, not aac(3).

A more controversial point concerns the isoenzyme classification. What the authors now call the AAC(3)-V or AAC(3)-Va enzyme is identical to the enzyme they used to call AAC(3)-II (9), a name still in use by other authors (4, 12–14). Regrettably, this has not been mentioned by the authors. In our experience, the use of two names for a single protein is very confusing for those who are not dealing with this matter on a daily basis.

For your information, and in an attempt to shed some light on this matter, we present some historical data. In 1974, Le Goffic et al. (8) reported the isolation of an R factor from a clinical isolate of Klebsiella (R-176) that coded for a 3-N-acetyltransferase causing resistance to gentamicin, tobramycin, and kanamycin. Since this was the second enzyme exhibiting 3-N-acetyltransferase activity and since it differed physically from the first, the authors proposed the name AAC(3)-II. After these two enzymes were discovered, AAC(3)-III, a Pseudomonas-specific enzyme, was found in 1976 (3) and AAC(3)-IV was found in 1978 (6).

In 1980, Gomez-Lus et al. (7) described the isolation of a 3-N-acetyltransferase that, in their opinion, differed from the other four. However, they did not purify the enzyme, and basically the substrate profile of the novel enzyme resembled that of AAC(3)-II. Still, Gomez-Lus et al. classified the enzyme into a separate group: AAC(3)-V.

When the gene coding for this supposed AAC(3)-V enzyme was cloned and hybridized to DNA of other isolates with known acetylating enzymes (2), it appeared to be identical to a gene sequenced by Allmansberger et al. (1). By misinterpreting susceptibility data, Allmansberger et al. believed that the gene they studied was the AAC(3)-III-encoding gene. However, we have unequivocally shown that their gene is in fact identical to the original AAC(3)-II-encoding gene isolated from the R-176 plasmid (14). The mistake of Allmansberger et al. can be explained by the fact that the original clinical isolate contained both AAC(3)-II and an APH(3') enzyme (10a). This frequently occurring combination results in a resistance phenotype that can easily be confused with the AAC(3)-III phenotype.

The result of all this is that we now have two names for a single enzyme. This situation is all the more unfortunate and confusing because in articles dealing with AAC(3)-V, such as the one by Rather et al., the original name, AAC(3)-II, is not even mentioned.

Now that a novel enzyme that the authors call AAC(3)-Vb has been characterized, we think that this is a unique opportunity to stop the confusion and to provide clarity.

Our proposal would be to give the name AAC(3)-II to the enzyme that erroneously has been called AAC(3)-V or, more recently, AAC(3)-Va and to use the name AAC(3)-V for the novel enzyme called AAC(3)-Vb by Rather et al.

We realize that this solution may cause some discomfort to some authors, but the advantages of uniformity and clarity outweigh this by far.

REFERENCES

11. Pipersberg, W. Personal communication.


Jos A. M. van de Klundert
John S. Vliegenthart
Department of Medical Microbiology
University Hospital
P.O. Box 9600
NL 2300 RC Leiden
The Netherlands

Author’s Reply

In response to the comments of Dr. van de Klundert and Dr. Vliegenthart, we address the issue of the isoenzyme classification and the series of events leading to our choice of enzyme nomenclature. We have recently published our work on the characterization of a gene encoding a 3'-N-acetyltransferase (5) which has a substrate specificity resembling those of two previously described 3'-N-acetyltransferases, the AAC(3)-II enzyme described by LeGoffic et al. (4) and the AAC(3)-V enzyme described by Gomez-Lus et al. (3). The AAC(3)-V profile was defined again by Shimizu et al. (7) and used by Barg (2), who developed a DNA probe for the gene encoding this enzyme from plasmid pC190. Shimizu et al. (7) switched from the AAC(3)-II to the AAC(3)-V nomenclature on the basis of slight differences in the resistance profiles reported by Gomez-Lus et al. (3). In retrospect, this may have been in error, since the enzymes encoding the resistance profiles AAC(3)-II and AAC(3)-V are likely to be identical.

The AAC(3)-V probe developed by Barg (2) hybridized with a strain containing the plasmid pWP113a, which had been incorrectly described in Allmansberger et al. (1) as encoding an AAC(3)-III enzyme. In fact, the plasmid from which this AAC(3)-V probe was obtained was highly similar to pWP113a. Therefore, on the basis of this study, it seemed appropriate that an AAC(3)-V enzyme was encoded by pWP113a. Interestingly, the AAC(3)-V probe did not hybridize with a strain obtained from Bristol, producing an AAC(3)-II enzyme (2). In retrospect, it is likely that this AAC(3)-II strain may carry the same gene described by us (5) or a third isoenzyme.

The DNA sequence of another 3'-N-acetyltransferase was subsequently determined by Vliegenthart et al. (8). Even though this gene had complete homology to the gene on pWP113a, already described as encoding an AAC(3)-V enzyme (2), it was described as encoding an AAC(3)-II enzyme.

At Schering-Plough Research Institute, the AAC(3)-Va probe obtained from pC190 (2) was routinely used to examine the presence of aminoglycoside resistance genes. A Serratia marcescens strain classified as AAC(3)-V did not hybridize to this probe, even under conditions of moderate stringency (6). Therefore, there existed two distinct genes encoding AAC(3)-V enzymes. Since the probe had already been described in the literature as AAC(3)-V, we decided to name the enzyme in this S. marcescens strain AAC(3)-Vb, with the original enzyme now called AAC(3)-Va.

The nomenclature that we have been using, described by Shimizu et al. (7), is based on a unique aminoglycoside resistance profiles (1, -II, -III, -IV, and -V) and more recently, the individual genes encoding enzymes with identical resistance patterns (a, b, c, and d) (5, 6). Therefore, van de Klundert’s proposal to call one enzyme AAC(3)-II and the second one AAC(3)-V is inappropriate, since the different designations would imply that the resistance profiles are different when in fact they are the same. However, in the interest of uniformity, we agree to use the designation AAC(3)-IIa for the enzyme previously designated AAC(3)-Va and AAC(3)-IIb for the enzyme previously designated AAC(3)-Vb. This nomenclature is fully described in Shaw et al. (6). We hope that this review article will help to clarify a number of different designations that have been previously utilized for identical enzymes.

REFERENCES


P. N. Rather
VA Medical Center
10701 East Boulevard
Cleveland, Ohio 44106

K. J. Shaw
R. S. Hare
G. H. Miller
Schering-Plough Research Institute
201 Galloping Hill Road
Kenilworth, New Jersey 07003