Members of the globally important CTX-M group of extended-spectrum β-lactamases fall into at least six subgroups (CTX-M-1, -2, -8, -9, -25, and KLUC [<90% amino acid identity between subgroups]), with members of each subgroup differing by one or a few amino acid changes (1). Ancestral members of the different CTX-M subgroups appear to have been captured from the chromosomes of different Kluyvera species, with subsequent mutations leading to variants with advantageous phenotypes (1). Due to their relatedness, bla<sub>CTX-M</sub> genes could also evolve by homologous recombination, and the sequences of three hybrids of bla<sub>CTX-M-1</sub> Group and bla<sub>CTX-M-9</sub> Group genes have been previously reported (1).

The recently described CTX-M-116 was proposed to be composed of parts of the CTX-M-1 Group proteins CTX-M-23 and CTX-M-22 (2). Fursova et al. suggested that recombination to create bla<sub>CTX-M-116</sub> occurred at a “putative 7-bp site of recombination (GTAAAAT)” referred to as a “core site; attC” (positions 436 to 442) in the accompanying GenBank entry (JF966749); i.e., they seem to suggest that recombination has occurred at a sequence found in the middle of bla<sub>CTX-M-1</sub> Group genes that happens to fit the integron/gene cassette-type core site consensus sequence (GTTRRRY) but which is not a full attC site that would be the normal substrate for int-mediated recombination. We agree that bla<sub>CTX-M-116</sub> could be a hybrid of bla<sub>CTX-M-23</sub> which has a nucleotide sequence distinct from those of other bla<sub>CTX-M-1</sub> Group genes, and bla<sub>CTX-M-22</sub> but believe that this would have occurred by homologous recombination, as for bla<sub>CTX-M-64</sub> (3). The site of the crossover cannot be precisely defined, due to identity between the bla<sub>CTX-M-23</sub> and bla<sub>CTX-M-22</sub> sequences in the relevant region, but would lie between position 240, where the match to bla<sub>CTX-M-22</sub> begins, and position 312, where the match to bla<sub>CTX-M-23</sub> ends (see Fig. 1 in reference 2).

Fursova et al. go on to suggest that other bla<sub>CTX-M-1</sub> Group genes (and some bla<sub>CTX-M-9</sub> and bla<sub>CTX-M-25</sub> Group genes) are also made up of 5’ and 3’ “moieties” from different genes delineated by the GTTAAAT sequence (or GTTGAGT for bla<sub>CTX-M-8</sub> and bla<sub>CTX-M-25</sub> Group genes). This boundary is artificial, and we believe that this analysis is misleading. The sequence of the bla<sub>CTX-M-3</sub> gene from GenBank accession no. Y10278 is proposed to include the 5’ moiety of bla<sub>CTX-M-15</sub> As bla<sub>CTX-M</sub> genes (and other bla genes) are named from the protein sequence and different nucleotide sequences can encode the same protein, this gene was designated bla<sub>CTX-M-3a</sub> (4). bla<sub>CTX-M-3</sub> and flanking regions are 100% identical to a region from the Kluyvera ascorbata chromosome (AJ632119), and this gene has been proposed as a progenitor of other bla<sub>CTX-M-1</sub> Group genes (5). bla<sub>CTX-M-15</sub> could then be derived from bla<sub>CTX-M-3a</sub> by a single mutation leading to the D240G substitution that results in increased resistance to cefazidime (6). The sequences of other genes within each group listed in Table 1 of reference 2 (unmarked, own 5’ and 3’ moieties; *, 5’ moiety contributed by another bla<sub>CTX-M</sub> gene; **, both 5’ and 3’ moieties contributed by other bla<sub>CTX-M</sub> genes) could similarly be derived from bla<sub>CTX-M-3a</sub> or bla<sub>CTX-M-15</sub> by a single nucleotide change resulting in one amino acid substitution (Fig. 1).

REFERENCES

FIG 1 Selected bla<sub>CTX-M-1</sub> Group genes that could be derived from bla<sub>CTX-M-1</sub> (as found on the Kluyvera ascorbata chromosome and plasmids) by a single nucleotide change giving rise to a single amino acid substitution (all except bla<sub>CTX-M-39</sub>) or two nucleotide changes giving rise to two amino acid substitutions (bla<sub>CTX-M-39</sub> also called bla<sub>CTX-M-37</sub>).