What's in a Name? IS*Swi1* Corresponds to Transposons Related to Tn*2* and Tn*3*

Sally R. Partridge

Centre for Infectious Diseases and Microbiology, Westmead Millennium Institute for Medical Research, The University of Sydney, Westmead Hospital, New South Wales, Australia

With the rapid expansion in generation of DNA sequence data, including data from long-read methods that greatly simplify assembly, it is increasingly important to address annotation issues. In bacteria, exactly the same mobile genetic element may be found in different locations, and consistent annotation greatly simplifies comparative analyses. Registries such as ISfinder (https://www-is.biotoul.fr/) (1), which includes a searchable database of insertion sequences (IS) and assigns IS names, are important resources in achieving this. Nomenclature is becoming more complex as the traditional distinction between IS (containing essentially only transposition functions for their own movement) and unit transposons (Tn; larger, more complex elements that also carry "passenger" gene[s]) is becoming blurred: elements closely related to known IS families but carrying passenger gene(s) are being identified (2), as well as elements closely related to known transposons that lack passenger genes.

As their numbers suggest, Tn*1*, Tn*2*, and Tn*3* were among the earliest transposons to be identified (3–5). Their sequences are closely related overall, but identity is lower in short regions adjacent to the resolution (*res*) site, suggesting generation by different recombination events (6). Tn*3* and Tn*2* each carry a $bla_{\text{TEM-1}}$ gene encoding the TEM-1 β-lactamase, but with different "frameworks" (i.e., patterns of synonymous single nucleotide changes [7]) designated 1a and 1b, respectively. Tn*1* carries $bla_{\text{TEM-2}}$, which encodes TEM-2 with a single amino acid change. All known TEM enzymes ($n > 200$) (http://www.lahey.org/Studies/), including "extended-spectrum" variants conferring resistance to clinically important third-generation cephalosporin antibiotics, are derived from TEM-1 or TEM-2. Correctly identifying these transposons is important in understanding resistance epidemiology, but Tn*2*, the most common variant in antibiotic resistance plasmids, is often misannotated as Tn*3* (8), as are other members of the larger Tn*3* family (9).

In a recent paper (10), He and colleagues, in their Fig. 5a, used the name IS*Swi1* for transposons that correspond to Tn*2*, Tn*3*, or different "hybrids" of these (Fig. 1a). Reference 10 also discusses an "IS*Swi1* derivative, IS*Swi1*-m1 (also called Tn*1331*)." Tn*1331* is a well-described derivative of Tn*3* that contains the *aacA4-aadA1a-*$bla_{\text{OXA-9}}$ cassette array from a class 1 integron (11). "IS*Swi*-m1" in pNJST258N5 and "IS*Swi*-m2" (with a deletion) in pNJST258C2 include different regions that match Tn*2* rather than Tn*3* (Fig. 1b). Other "IS*Swi*-m2" elements shown in Fig. 5a of reference 10 are almost identical to the corresponding parts of Tn*1331* (Fig. 1b), suggesting this as the direct ancestor. A minor variant of Tn*1331*, with differences including two nucleotide changes in *aacA4* [*aac*(*6′*)-*Ib*] that lead to a ciprofloxacin-resistant variant (Fig. 1b), has been designated Tn*6238* (12). Reference 10 also used the name IS*Acsp1* for Tn*5403*, a Tn*3* family element without passenger genes (13).

Developing consistent nomenclature for bacterial mobile genetic elements, deciding on meaningful identity cutoffs for whether elements should be considered the same or different, as well as dealing with "hybrids" are clearly important. While the historic nomenclature may not be perfect, using names based on those already established for elements such as Tn*1*, Tn*2*, Tn*3*, Tn*1331*, and Tn*5403* seems sensible in order to avoid adding to the already considerable confusion in nomenclature related to antibiotic resistance.

REFERENCES

1. **Siguier P, Perochon J, Lestrade L, Mahillon J, Chandler M.** 2006. ISfinder: the reference centre for bacterial insertion sequences. Nucleic Acids Res **34:**D32–D36. http://dx.doi.org/10.1093/nar/gkj014.
2. **Siguier P, Gagnevin L, Chandler M.** 2009. The new IS*1595* family, its relation to IS*1* and the frontier between insertion sequences and transposons. Res Microbiol **160:**232–241. http://dx.doi.org/10.1016/j.resmic.2009.02.003.
3. **Hedges RW, Jacob AE.** 1974. Transposition of ampicillin resistance from RP4 to other replicons. Mol Gen Genet **132:**31–40. http://dx.doi.org/10.1007/BF00268228.
4. **Heffron F, Sublett R, Hedges RW, Jacob A, Falkow S.** 1975. Origin of the TEM-β-lactamase gene found on plasmids. J Bacteriol **122:**250–256.
5. **Kopecko DJ, Cohen SN.** 1975. Site specific *recA*-independent recombination between bacterial plasmids: involvement of palindromes at the recombinational loci. Proc Natl Acad Sci U S A **72:**1373–1377. http://dx.doi.org/10.1073/pnas.72.4.1373.
6. **Partridge SR, Hall RM.** 2005. Evolution of transposons containing bla_{TEM} genes. Antimicrob Agents Chemother **49:**1267–1268. http://dx.doi.org/10.1128/AAC.49.3.1267-1268.2005.
7. **Goussard S, Courvalin P.** 1999. Updated sequence information for TEM β-lactamase genes. Antimicrob Agents Chemother **43:**367–370.
8. **Bailey JK, Pinyon JL, Anantham S, Hall RM.** 2011. Distribution of the bla_{TEM} gene and bla_{TEM}-containing transposons in commensal *Escherichia coli*. J Antimicrob Chemother **66:**745–751. http://dx.doi.org/10.1093/jac/dkq529.
9. **Nicolas E, Lambin M, Dandoy D, Galloy C, Nguyen N, Oger CA, Hallet B.** 2015. The Tn*3*-family of replicative transposons, p 272–302. In Craig NL, Chandler M, Gellert M, Lambowitz AM, Rice PA, Sandmeyer S (ed), Mobile DNA III. ASM Press, Washington, DC.
10. **He S, Hickman AB, Varani AM, Siguier P, Chandler M, Dekker JP, Dyda F.** 2015. Insertion sequence IS*26* reorganizes plasmids in clinically isolated multidrug-resistant bacteria by replicative transposition. mBio **6:**e00762-15. http://dx.doi.org/10.1128/mBio.00762-15.
11. **Tolmasky ME.** 2000. Bacterial resistance to aminoglycosides and β-lactams: the Tn*1331* transposon paradigm. Front Biosci **5:**D20–D29. http://dx.doi.org/10.2741/Tolmasky.
12. **Quiroga MP, Orman B, Errecalde L, Kaufman S, Centrón D.** 2015. Characterization of Tn*6238* with a new allele of *aac*(*6′*)-*Ib-cr*. Antimicrob Agents Chemother **59:**2893–2897. http://dx.doi.org/10.1128/AAC.03213-14.
13. **Rinkel M, Hubert JC, Roux B, Lett MC.** 1994. Identification of a new transposon Tn*5403* in a *Klebsiella pneumoniae* strain isolated from a polluted aquatic environment. Curr Microbiol **29:**249–254. http://dx.doi.org/10.1007/BF01577436.

Published 6 October 2015

Citation Partridge SR. 2015. What's in a name? IS*Swi1* corresponds to transposons related to Tn*2* and Tn*3*. mBio 6(5):e01344-15. doi:10.1128/mBio.01344-15.

Address correspondence to sally.partridge@health.nsw.gov.au.

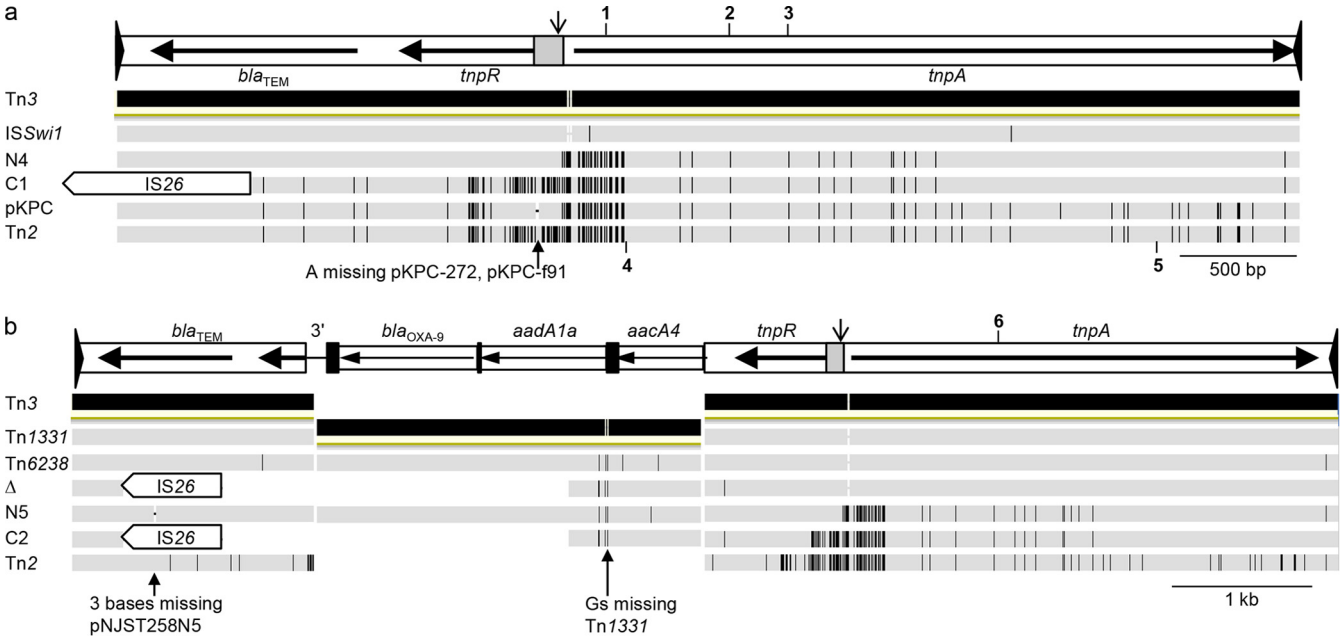

FIG 1 Comparison of transposon sequences. Vertical black lines indicate differences from the reference sequence (top). Genes are shown by labeled arrows, 38-bp terminal inverted repeats are shown as black triangles, and the *res* site is a gray box (the vertical arrow shows the recombination site). Gene cassettes are shown as white boxes labeled with the cassette name, with small black boxes indicating *attC* sites (truncated in the case of *aadA1a*). The 3′ indicates a 111-kb fragment of the class 1 integron 3′-conserved segment. Positions of possible sequence errors (e.g., an A missing from a run of As in pKPC-272 and pKPC-f91; a G missing from two short runs of Gs in Tn*1331*; and 3 bases missing from pNJST258N5) and of various insertions/deletions (1, IS*26* in pKPN-068; 2, Tn*5403* in pKPN-068; 3, Tn*4401* in pKPC-272 and pKPC-f91; 4, IS*Ecp1*-$bla_{CTX-M-15}$ in Tn*2* in pHg; 5, IS*26* truncating Tn*2* in pHg; 6, Tn*4401* in pNJST258C2) are indicated, with selected IS*26* elements shown (pointed end, IR_R). (a) Comparison of IS*Swi1* (from ISfinder) with Tn*3* (GenBank accession number HM749966; the Tn in pKPN-068 CP007733 is identical), Tn*2* (GenBank AY123253; the Tn in pHg CP006662 is identical), and the Tn from pNJST258N4 (N4; CP006928), pKPC-272 (pKPC; CP008825; the Tn in pKPCf-91 CP008826 is identical), and pNJST258C1 (C1; CP006922). (b) Comparison of Tn*3*, Tn*1331* (GenBank AF479774), Tn*6238* (KJ511462), IS*Swi1*-m1 in pNJST258N5 (N5; CP006924), IS*Swi1*-m2 in pNJST258C2 (C2, CP006919), and the identical IS*Swi1*-m2 sequences (Δ) in pAAC154-a50 (CP007728 and CP008828), pKPN-294 (CP008832 and CP009873), pKPN-819 (CP008799), and pKPC-484 (CP008798). This figure was compiled from alignments created using Geneious (Biomatters, New Zealand).