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# Comment on: Resistance gene naming and numbering: is it a new gene or not?

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**Comment on: Resistance gene naming and numbering: is it a new gene or not?**

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1 **Comment on: Resistance gene naming and numbering: is it a new gene or**  
2 **not?**

3

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15

16 Sir,

17 Recently, Hall and Schwarz<sup>1</sup> have suggested the need for a universally consistent  
18 antibiotic resistance gene nomenclature system in order to replace the current  
19 multiple and incompatible systems which exist. They arbitrarily proposed a threshold  
20 value of  $\geq 2\%$  difference of either the nucleotide or amino acid sequence, or both, as  
21 the cut-off for assigning a new gene in order to stimulate debate within the field.

22

23 We welcome this suggestion and subsequent discussions, and agree that resistance  
24 gene nomenclature systems need updating and aligning in order to address the  
25 increasing availability of genetic data and our understanding of the molecular  
26 evolution of resistance genes. We would, however, like to add a note of caution that  
27 the arbitrary  $\geq 2\%$  cut-off may not be universally appropriate.

28

29 In the case of the tetracycline resistance genes, covering the three known  
30 mechanistic classes of protein (ATP-dependant efflux, ribosomal protection and  
31 enzymatic inactivation), the nomenclature system is based on amino acid identity. A  
32 new determinant must show  $< 80\%$  amino acid identity to known determinants to be  
33 designated a new class.<sup>2</sup>

34

35 While Hall and Schwartz<sup>3</sup> suggest a cut-off of  $\geq 2\%$  will reduce the number of gene  
36 designations for those encoding OXA  $\beta$ -lactamases, the opposite will in fact be true  
37 for the tetracycline resistance genes, as indicated by Jacoby *et al.*<sup>4</sup> Taking *tet(M)* as  
38 an example, there are well over 100 sequences within the NCBI database under this  
39 gene class. To implement a  $\geq 2\%$  cut-off for new gene designations would  
40 dramatically increase the number of tetracycline resistance genes which once

41 belonged to the *tet(M)* class. Additionally this increase in new gene designations  
42 would be compounded by the fact that there are at least 59 other tetracycline  
43 resistance gene classes currently assigned,<sup>5</sup> many with multiple examples showing  
44  $\geq 2\%$  sequence divergence.

45

46 Furthermore, such a cut-off would also cause confusion and complications in the  
47 identification of a subclass of the ribosomal protection protein encoding genes known  
48 as the mosaic tetracycline resistance genes, which have an atypical evolutionary  
49 path involving naturally occurring recombination between two or more progenitor  
50 genes.<sup>6</sup> These currently have their own version of a nomenclature system indicating  
51 their mosaic ancestry and this would disappear if a  $\geq 2\%$  divergence rule was  
52 implemented.

53

54 We propose here to contact all investigators involved in the historical and current  
55 discovery, annotation, naming and curation of tetracycline resistance genes, and will  
56 facilitate a discussion in order to determine if there is a consensus on any proposed  
57 change to the current nomenclature system. We urge stakeholders to contact the  
58 authors of this comment in order to indicate their interest in participation. Following  
59 this process, we will report any agreement or hurdles perceived within the field. We  
60 suggest other investigators involved in the nomenclature of other resistance genes  
61 do the same and it is possible that these subgroups could form the basis of a larger  
62 committee as proposed by Evans.<sup>7</sup>

63

64

65

66 Transparency declarations

67 None to declare.

68

69 References

70 1. Hall RM, Schwarz S. Resistance gene naming and numbering: is it a new gene  
71 or not? *J Antimicrob Chemother* 2016; **71**(3):569-71

72

73 2. Levy SB, McMurry LM, Barbosa TM *et al.* Nomenclature for new tetracycline  
74 resistance determinants. *Antimicrob Agents Chemother* 1999; **43**: 1523-1524.

75

76 3. Hall RM, Schwarz S. Resistance gene naming and numbering: is it a new gene or  
77 not?—authors' response. *J Antimicrob Chemother* 2016;**71**(6):1743

78

79 4. Jacoby GA, Bonomo RA, Bradford PA, *et al.* Comment on: Resistance gene  
80 naming and numbering: is it a new gene or not? *J Antimicrob Chemother* 2016; Jun

81 3. pii: dkw204

82

83 5. Roberts MC. Mechanism of resistance for characterized *tet* and *otr* genes.

84 <http://faculty.washington.edu/marilynr/tetweb1.pdf> (Correct as of 13th July 2016).

85

86 6. Warburton PJ, Amodeo N, Roberts AP. Mosaic tetracycline resistance genes  
87 encoding ribosomal protection proteins. *J Antimicrob Chemother* 2016; in press.

88

89 7. Evans BA. Comment on: Resistance gene naming and numbering: is it a new  
90 gene or not? *J Antimicrob Chemother* 2016; **71**: 1742-1745.