Mechanisms of MLS resistance Modified Aug. 1, 2018

<table>
<thead>
<tr>
<th>rRNA methylase</th>
<th>Efflux</th>
<th>ABC-F Ribosomal</th>
<th>ABC-F Protein</th>
<th>Inactivating enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>3</td>
<td>Protection&quot;</td>
<td>function unclear(^a)</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18</td>
<td>6</td>
<td>4 esterase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17</td>
<td>6</td>
<td>2 lyases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17</td>
<td>6</td>
<td>16 transferases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17</td>
<td>6</td>
<td>7 phosphorylases</td>
</tr>
</tbody>
</table>

| erm(A),(B),(C),(D),(E),(F), (G),(H),(I),(N),(O),(Q),(R), (S),(T),(U),(V),(W),(X),(Y), (Z),(30),(31),(32),(33),(34), (35),(36),(37),(38),(39),(40), (41),(42),(43)\(^a\),(44)\(^b\),(45)\(^c\),(46)\(^d\), (47)\(^e\),(48)\(^f\), (49)\(^g\) |
| mef(A),(B),(C)\(^h\), lmr(A)\(^i\) |
| Isa(A)\(^a\), (B),(C),(E)\(^j\) |
| car(A) |
| ere(A),(B),(C)\(^k\) |
| vgb(A),(B) |
| ln(A),(B),(C),(D) |
| mph(A),(B),(C),(D) |
| ln(A)\(^l\), (F),(G),(H)\(^m\),(P)\(^n\), mph(E),(F),(G)\(^o\) |
| vat(A),(B)vat(C),(D), |
| vat(E),(F),(G) |

| optrA\(^p\), eat(A)\(^q\), sal(A)\(^r\), varM, vlmR\(^s\) |
| tle(C) |

S-adenosylmethionine rRNA methyltransferase\(^b\)

4
cfr, cfr(B)\(^n\), cfr(C)\(^p\), cfr(D)\(^q\)

New gene or information since last posting

\(^a\) vga(A)\(_{LC}\) recognized subtype because it is active against both streptogramin A and lincosamides while vga(A) is active against streptogramin A, (Novotna & Janata, 2006) and vga(A) variants confer resistance to lincosamides, streptogramin A and pleuromutilins have been described (Gentry et al., 2008);\(^b\) resistance to
lincosamides, streptogramin A and pleuromutilins [PhLOPSA] but not macrolides (Kadlec, Schwarz 2009); c Schwendener & Perreten, 2012 AAC56:4746; d Isnard et al, 2013 AAC 57:4463 (the original gene eat(A) an innate gene which does not confer resistance but the mutant eat(A), confers resistance to lincosamides, streptogramin and pleuromutilins in E. faecium; e Lisa Nonaka et al., Lett App Microbiol. 2015 61:1-6; f Zhao et al; AAC 2013, 58:1785 (the gene in original host is not functional; i Hot, Berthet, Chesneau, AAC 2014 58: 3335 (innate gene conferring resistance to lincosamides and streptogramin in Staphylococcus sciuri); j Wipf, Schwendener, Perreten, AAC 2014 58:6133; k Wipf et al., 2015 AAC 59:3578-3581; l Steeve Gigurere R. equis (submitted JAC); m Wang et al, JAC 2015, 70:2182-90 resistance to oxazolidinones and phenicols in E. faecalis, E. faecium and Staphylococcus. Data shows it does not confer an efflux protein Schwarz & Yang personnel communication; n Deshpande et al., AAC 2015, 59:6256-6261; Marin et al. 2015, AAC 59:586-589; o Guerin et al., 2016 JAC 71:3046-3049; q Lyras et al., J Bacteriology 2009 191:6345; r Wilpf et al., July 2017, AAC e00066-17 1-6. 
http://aac.asm.org/content/61/7/e00066-17.full.pdf+html; t Tang et al., 2017, JAC, 72:1581; u Luo et al., Intern J Antimicro Agents, 2018, 51:136-139, 2018; v not given official name by nomenclature center, Xing et al., PloSOne 2015 doi:10.1371/journal.pone.0131078; w Sharkey, Edwards, O’Neill, MBio 2016; e01975-15 1-15; Sharkey, O’Neill, 2018 ACS Inf Dis 4:239-246 and Wilson MBio 2016; e00598-16. Demonstrated that lsa(A), and vga(A) are ABC-F proteins that confer resistance by ribosomal protection rather than efflux has been shown in the first paper. Murina et al., Nucl Acid Res 2018, 46:3753-3763 demonstrated that vga(A)LC is ribosomal protection. Thus if an ABC-F protein previously classified as “efflux” and has related proteins that have been shown to be ribosomal protection they are also listed ribosomal protection [n=13]. However, ABC-F proteins have mixed mechanisms of action and this makes it difficult to classify unless biochemical or structural studies have been done on all the other genes [n=6] that Sharkey list as ribosomal protection have not been shown what mechanism of resistance they have though they have some similarity with the proteins experimentally shown to be ribosomal protection. x These genes have been suggested to be ribosomal protection genes but no data to support the mechanism has been done and thus not clear Sharkey, O’Neill, 2018 ACS Inf Dises 4:239-24. y Marinez et al., App Environ Microb 2018 84:e02888-1. aa Martinez et al., AEM 2018, e02888-17. ab Koberska, Kopecky, Olsovksa et al., Folia Microbiol. 2008, 53:395-401. ac Su, Kumar, Ding et al., 2018, May 15, 2018. 115:5157-5162. www.pnas.org/cgi/doi/10.1073/pnas.1803313115 demonstrated that msr(E) codes for a ribosomal protection protein. ad In review, vlmR gene codes for a protein that confers ribosomal protection. ae Reported from Dr. Cattoir lab. af Dr. De-Kang Zhu lab