

rRNA methylase	Efflux	ABC-F Ribosomal Protection <sup>w</sup>	ABC-F Protein <sup>x</sup>	Inactivating enzymes			
<b>47</b>	8	<b>26</b>	6	4 esterase	2 lyases	16 transferases	15 phosphorylases
<i>erm</i> (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) <sup>c</sup> ,(44) <sup>j</sup> ,(45) <sup>k</sup> ,(46) <sup>l</sup> ,(47) <sup>o</sup> ,(48) <sup>r</sup> ,(49) <sup>z</sup> ,(50) <sup>ao</sup> ,(51) <sup>an</sup> (52) <sup>aq</sup> ,(53) <sup>ar</sup> , <b>(54)<sup>at</sup></b> , <b>(55)<sup>au</sup></b>	<i>mef</i> (A),(B),(C) <sup>e</sup> , <i>mef</i> (D) <sup>ai</sup> ,(F) <sup>ap</sup> , <i>mef</i> (H) <sup>aq</sup> ,(J) <sup>as</sup> , <i>lmr</i> (A) <sup>aa</sup>	<i>lsa</i> (A),(B),(C),(D) <sup>aj</sup> (E) <sup>e</sup> , <i>msr</i> (A),(C),(D),(E) <sup>ac</sup> ,(F) <sup>ai</sup> , <i>msr</i> (G) <sup>ap</sup> ,(H) <sup>ai</sup> , <b>(I)<sup>as</sup></b> , <i>vga</i> (A) <sup>a</sup> ,(B),(C) <sup>b</sup> ,(D),(E) <sup>e</sup> ,(F) <sup>al</sup> , <b><i>vga</i>(G)<sup>au</sup></b> , <i>optrA</i> <sup>m</sup> , <i>eat</i> (A) <sub>y</sub> <sup>d</sup> , <i>sal</i> (A) <sup>i</sup> , <i>varM</i> , <i>vlmR</i> <sup>ad</sup> , <i>poxtA</i> <sup>am</sup>	<i>car</i> (A), <i>lmr</i> (C) <sup>ab</sup> , <i>ole</i> (B),(C), <i>srm</i> (B), <i>tlc</i> (C)	<i>ere</i> (A),(B),(C) <sup>af</sup> , <i>ere</i> (D) <sup>v</sup>	<i>vgb</i> (A),(B), <i>lnu</i> (A),(B),(C),(D), <i>lnu</i> (E) <sup>f</sup> ,(F),(G),(H) <sup>u</sup> ,(P) <sup>q</sup> , <i>vat</i> (A),(B),(C),(D), <i>vat</i> (E),(F),(G)	<i>mph</i> (A),(B),(C),(D), <i>mph</i> (E) <sup>af</sup> ,(F),(G) <sup>e</sup> , <i>mph</i> (H) <sup>ah</sup> ,(I) <sup>ah</sup> ,(J) <sup>ah</sup> ,(K) <sup>ah</sup> , <i>mph</i> (L) <sup>ah</sup> ,(M) <sup>ah</sup> ,(N) <sup>ah</sup> ,(O) <sup>ah</sup>	

S-adenosylmethionine rRNA methyltransferase <sup>b</sup>

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*cfr*, *cfr*(B)<sup>n</sup>, *cfr*(C)<sup>l</sup>, *cfr*(D)<sup>ae</sup>, *cfr*(E)<sup>ak</sup>

### New gene or information since last posting

<sup>a</sup>*vga*(A)<sub>LC</sub> 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);
- <sup>b</sup> resistance to lincosamides, streptogramin A and pleuromutilins [PhLOPS<sub>A</sub>] but not macrolides (Kadlec, Schwarz 2009);
- <sup>c</sup> Schwendener & Perreten, 2012 AAC56:4746;
- <sup>d</sup> 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)<sub>v</sub>* confers resistance to lincosamides, streptogramin<sub>A</sub> and pleuromutilins in *E. faecium*;
- <sup>e</sup> Lisa Nonaka et al., Lett App Microbiol. 2015 61:1-6; <sup>f</sup> Zhao et al; AAC 2013, 58:1785 (the gene in original host is not functional);
- <sup>i</sup> Hot, Berthet, Chesneau, AAC 2014 58: 3335 (innate gene conferring resistance to lincosamides and streptogramin<sub>A</sub> in *Staphylococcus sciuri*);
- <sup>j</sup> Wipf, Schwendener, Perreten, AAC 2014 58:6133; <sup>k</sup> Wipf et al., 2015 AAC 59:3578-3581; <sup>l</sup> Anastasi, Giguere, Berghaus et al. 2015 JAC 70:3184-3190  
doi:10.1093/jac/dkv279
- <sup>m</sup> 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 proteins Schwarz & Yange personnel communications; <sup>n</sup> Deshpande et al., AAC 2015, 59:6256-6261; Marín et al. 2015, AAC 59:586-589;
- <sup>o</sup> Guerin et al., 2016 JAC 71:3046-3049; <sup>q</sup> Lyras et al., J Bacteriology 2009 191:6345;
- <sup>r</sup> Wilpf et al., July 2017, AAC e00066-17 1-6. <http://aac.asm.org/content/61/7/e00066-17.full.pdf+html>; <sup>t</sup> Tang et al., 2017, JAC, 72:1581;
- <sup>u</sup> Luo et al., Intern J Antimicro Agents, 2018, 51:136-139, 2018; <sup>v</sup> not given official name by nomenclature center, Xing et al., PloSOne 2015  
doi:10.1371/journal.pone.0131078;
- <sup>w</sup> 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 as originally speculated. Murina et al., Nucl Acid Res 2018, 46:3753-3763 demonstrated that *vga(A)<sub>LC</sub>* is ribosomal protection. Thus if an ABC-F protein previously classified as an efflux protein and has related proteins that have been shown to be ABC-F ribosomal protection protein .
- <sup>y</sup> 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 that Sharkey list as ribosomal protection. Most not have been shown what mechanism of resistance they have by experimentation
- <sup>x</sup> These genes have been suggested to be ribosomal protection genes but no data other than sequences and aa to support the mechanism. All are from *Streptomyces* species (see Sharkey, O' Neill, 2018 ACS Inf Dis 4:239-24);
- <sup>z</sup> Martinez, Luque, Milani et al., AEM 2018, DOI: 10.1128/AEM.02888-17.; <sup>ab</sup> Kiberska, Kopecky, Olsovska et al., Folia Microbiol. 2008, 53:395-401;
- <sup>ac</sup> Su, Kumar, Ding et al., 2018, May 15, 2018. 115:5157-5162, [www.pnas.org/cgi/doi/10.1073/pnas.1803313115](http://www.pnas.org/cgi/doi/10.1073/pnas.1803313115) demonstrated that *msr(E)* codes for a ribosomal protection protein. <sup>ad</sup> Ero et al., 2019 Protein Science 28:684;
- <sup>ae</sup> Reported from Dr. Cattoir lab GenBank # MG707078; <sup>af</sup> Dr. De-Kang Zhu lab; <sup>af</sup> multiple different sequences have been labeled *mph(E)* in various publications;

<sup>ag</sup> from *Corynebacterium glutamicum* pTZC1 Dr. Nakase; <sup>ah</sup> Not named by the nomenclature center. Dr. Wrights lab named these; most come from WGS sequences from a variety of bacteria [Pawlowski et al. 2018 Nature Communications];

<sup>ai</sup> Schwendener, Dona, Perreten AAC 2020 DOI:1-.1128/AAC.00160

<sup>aj</sup> Shi, Yoshida, Fujlwara, Nishiki Microbial Drug Resist, 2020 <https://doi.org/10.1089/mdr.2020.0218>;

<sup>ak</sup> Stojkovic et al., 2019. AAC2019 doi 10.1128/AAC.01074-19; <sup>al</sup> Chang Beijing, China; <sup>am</sup> Antonelli et al., JAC doi:10.1093/jac/dky088;

<sup>an</sup> Huber, Giguere, Slovis et al., Environ Microb 2020 doi:10.1111/1462-2920.15020;

<sup>ao</sup> Aoli, Nakase, Nakaminami et al, AAC2020 <https://aac.asm.org/content/aac/64/3/e01810-19.full.pdf> ;

<sup>ap</sup> Fernandez, Perreten, Schwendener JAC 2021 <https://doi.org/10/1093/jac/dkaa405>; <sup>aq</sup> Imwattana et al. <https://doi.org/10.1101/2020.11.12.379040>;

<sup>ar</sup> Greninger, Addetia, Starr et al. CID 2020 doi: 10.1093/cid/ciz1060; <sup>as</sup> Guglielmino et al manuscript in preparation;

<sup>at</sup> **Kruger, Ji, Hanke et al. JAC accepted;**

<sup>au</sup> **Alexander, Brown-Elliott, Wallace Jr. in preparation**

<sup>av</sup> **Oswaldi, Luth, Dzierzon et al., <https://doi.org/10.3390/microorganisms10030512>**