

Table 2. Efflux and Inactivating Genes Modified **April 10, 2022**
Originally modified from AAC 1999 43:2823-30 with permission from ASM Journals

| Resistance Profile | Protein | Genes | Genes included | % homology | | Plasmid /transposon | GenBank # * |
|---|---------------------|-----------------------------|---------------------------|------------|----------|--|--|
| | name | | | DNA | aa | | |
| ABC-F Protein Ribosomal Protection^c | | | | | | | |
| Lincosamide Streptogramin A, Pleuromutilin | Lsa(A) | <i>lsa</i> <i>abc-23</i> | <i>lsa(A)</i> | | | Chromosome | AY225127, AY737526 |
| Lincomycin Streptogramin A | Lsa(B) | <i>orf3</i> | <i>lsa(B)</i> | | | pSCFS1 | AJ579365 |
| Lincomycin | Lsa(C) | | <i>lsa(C)</i> | | | | HM990671 |
| Lincomycin Streptogramin A Pleuromutilin | Lsa(D) | | <i>lsa(D)</i> | | | Chromosome | AXF35727 |
| Lincomycin Streptogramin A Pleuromutilin | Lsa(E) | | <i>lsa(E)^c</i> | | | pEF418 | AF408195 |
| Erythromycin & Streptogramin B | Msr(A) | <i>msr(A)</i> | <i>msr(A)</i> | 98% | 98% | pUL5054 | X52085 |
| | | | <i>msr(SA)</i> | | | pEP2104 | |
| | | | <i>msr(SA')</i> | | | pMS97 | |
| | | | <i>msr(B)</i> | | | | M81802 |
| | Msr(C) | <i>msr(C)</i> | <i>msr(C)</i> | 96% | 95% | Chromosome | AY004350 AF313494 AJ243209 |
| | Msr(D) ^a | <i>msr(D)</i> | <i>mel</i> | 98%-100% | 98%-100% | TnI207.2 | AF227521 |
| | Msr(E) | <i>msr(E)^g</i> | <i>mel</i> | 99% | 98%-100% | chromosomal pKP048, pKSMA0710 pCOP1, pABIR chromosomal, pRSB105EF102240.1, DQ839391.1 pMUR050, pCTX-M3 | FR751518, EU294228 FJ628167.2, FJ917355.1 FJ187822.1, EU294228.1 AY522431.4, AF550415.2 |

| | | | | | |
|---|----------------------|----------------------------------|---|----------------------------------|--|
| | | | <i>orf5</i> | <i>Tn1207.1</i> | AF227520 |
| Erythromycin | Msr(F) | <i>msr(F)</i> ^o | | Chromosome | MN728681, L130509 ¹ |
| | Msr(G) | <i>msr(G)</i> | | Plasmid | CP046364 |
| | Msr(H) | <i>msr(H)</i> | | Chromosome | CP035309 |
| | Msr(I) | <i>msr(I)</i> ^p | | Chromosome | CP065927.1:1658158-1659615 |
| Streptogramin A Pristinamycin II ^d Pleuromutilin, Lincosamides | Vga(A) | <i>vga(A)</i> | <i>vga</i> | pIP524 pCPS32 | M90056 FN806791 |
| Lincosamides | Vga(A) _{LC} | <i>vga(A)</i> _{LC} | | | DQ823382 GQ891882 |
| Pleuromutilin Lincosamide | Vga(A) _v | <i>vga(A)</i> _v | | Chromosome | NG_048553.1 |
| Streptogramin A | Vga(B) | <i>vga(B)</i> | <i>vga(B)</i> | pIP1633 | U82085 |
| Streptogramin A Lincosamides Pleuromutilin ^d | Vga(C) | <i>vga(C)</i> | <i>vga(C)</i> | pKKS825 pCPS49 pKKS825 | NC_013034 , FN377602 FN806792 FN377602 |
| Streptogramin A | Vga(D) | <i>vga(D)</i> | <i>vga(D)</i> | | GQ205627 |
| Streptogramin A Pleuromutilin, Lincosamides | Vga(E) | <i>vga(E)</i> | <i>vga(E)</i> | <i>Tn6133</i> | FR772051 |
| Streptogramin A Pleuromutilin, Lincosamides | Vga(F) | <i>vga(F)</i> ⁿ | <i>vga(F)</i> | Chromosome | MT550884 |
| Streptogramin A Pleuromutilin, Lincosamids | Vga(G) | <i>vga(G)</i>^r | <i>vga(L)</i> <i>Imo0919</i> | Chromosome Chromosome | |
| Oxazolidinones Florfenicol | OptrA | <i>optrA</i> | <i>optrA</i> | pE349 | KP399637 |
| Oxazolidinones Florfenicol | PoxA | <i>poxA</i> ^q | <i>poxA</i> | Chromosome | MF095097 |
| Lincomycin Streptogramin A | Eat(A) _v | | <i>eat(A)</i> _v | Chromosome | gene EFAU004_00630 in <i>E. faecium</i> Aus0004 |

Pleuromutilin

| | | | | | | | |
|--|--------|--------------------------|---------------|--|--|------------|-----------------------|
| Lincomycin Streptogramin A, Pleuromutilin | Sal(A) | | <i>sal(A)</i> | | | Chromosome | KC693025 |
| Streptogramin A | VarM | <i>varM</i> | <i>varM</i> | | | Chromosome | AB03554 ^{**} |
| Streptogramin A Pleuromutilin, Lincosamides | VmlR | <i>vmlR</i> ^h | <i>vmlR</i> | | | Chromosome | NC_000964.3 |

ABC-F Protein [Mechanism unknown]^f

| | | | | | | | |
|--------------|---------|----------------|----------------|--|--|------------|--------------------|
| Carbomycin | Car(A) | <i>car(A)</i> | <i>car(A)</i> | | | pOJ158, | M80346 AF274302 |
| Oleandomycin | Ole(B) | <i>ole(B)</i> | <i>ole(B)</i> | | | pALOR26E | L36601 |
| Oleandomycin | Ole(C) | <i>ole(C)</i> | <i>ole(C)</i> | | | | L06249 |
| Spiramycin | Srm(B) | <i>srm(B)</i> | <i>srm(B)</i> | | | pKC514 | X63451 |
| Tylosin | Tlr(C) | <i>tlc(C)</i> | <i>tlc(C)</i> | | | | M57437 |
| Lincosamides | LmrC | <i>lmr(C)</i> | <i>lmr(C)</i> | | | Chromosome | EU124663 |

MAJOR FACILITATORS[Efflux]

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|--------------|--------|---------------|---------------|----------|----------|----------|----------|
| Lincomycin | Lmr(A) | <i>lmr(A)</i> | <i>lmr(A)</i> | | | pLST21 | X59926 |
| Erythromycin | Mef(A) | <i>mef(A)</i> | <i>mef(A)</i> | 90%-100% | 91%-100% | p53-6 | U70055 |
| | | | | | | Tn1207.1 | AF227520 |
| | | | | | | Tn1207.2 | AF227521 |
| | | | | | | | AY064721 |
| | | | | | | | AY064722 |
| | | | <i>mef(A)</i> | | | | AY071835 |
| | | | <i>mef(A)</i> | | | | AY071836 |
| | | | <i>mef(E)</i> | | | pAT15-5 | U83667 |

| | | | | | | | |
|--------------|--------|----------------------------|---------------|------|--|------------|---------------------------------|
| | | | <i>mef(E)</i> | | | Chromosome | AF274302, AF376746 |
| | | | <i>mef(I)</i> | 100% | | Chromosome | AJ971089 |
| | | | <i>mef(G)</i> | 100% | | Chromosome | HG423652 |
| | | | <i>mef(O)</i> | 97% | | Chromosome | DQ016305 |
| Erythromycin | Mef(B) | <i>mef(B)</i> | <i>mef(B)</i> | | | pP286 | FJ196385 |
| Erythromycin | Mef(C) | <i>mef(C)</i> | <i>mef(C)</i> | | | pAQU1 | AB571865 |
| Erythromycin | Mef(D) | <i>mef(D)</i> | <i>mef(D)</i> | | | Chromosome | MN728681, LR130509 ¹ |
| Erythromycin | Mef(F) | <i>mef(F)</i> | <i>mef(F)</i> | | | Plasmid | CP046364 |
| Erythromycin | Mef(H) | <i>mef(H)</i> ^m | <i>mef(H)</i> | | | Chromosome | MW269960.1 |
| Erythromycin | Mef(J) | <i>mef(J)</i> ^p | <i>mef(J)</i> | | | Chromosome | CP065927.1:1659729-1660922 |

ESTERASES

| | | | | | | | |
|--------------|--------|---------------|----------------|----------|----------|----------------------|--------------------|
| Erythromycin | Ere(A) | <i>ere(A)</i> | <i>ere(A)</i> | 92%-100% | 92%-100% | pI1100, pAT63 | M11277 |
| | | | <i>ere(A2)</i> | 92%-100% | 92%-100% | pLQ1723 | AY183454 |
| | | | | | | pLQ1723 | AF099140 |
| | | | | | | pIP1100 | AY183453 |
| | | | | | | | AF326209, DQ157752 |
| | | | | | | AF512546_2, AF512546 | |
| Erythromycin | Ere(B) | <i>ere(B)</i> | <i>ere(C)</i> | 92% | 93% | pLpANDM-1 | FN396877 |
| | | | <i>ere(B)</i> | 99% | 99% | pIP1527 | A15097 |
| | | | <i>ere(B)</i> | | | pAT72 | X03988 |
| | | | <i>ere(C)</i> | | | Chromosome | CP004020 |
| | | | <i>ere(D)</i> | | | Chromosome | KP265721 |

LYASES

| | | | | | | | |
|-----------------|--------|---------------|------------|--|--|--------|--------|
| Streptogramin B | Vgb(A) | <i>vgb(A)</i> | <i>vgb</i> | | | pIP524 | M20129 |
|-----------------|--------|---------------|------------|--|--|--------|--------|

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|---------------------|--------|--------------------------------|--|----------|---------|--|---|
| Streptogramin B | Vgb(B) | <i>vgb(B)</i> | <i>vgb(B)</i> | | | pIP1714 | AF015628 |
| TRANSFERASES | | | | | | | |
| Lincomycin | Lnu(A) | <i>lnu(A)</i> | <i>lin(A')</i> <i>lin(A)</i> | | | pIP856 pIP855 | M14039 JQ861959 |
| Lincomycin | Lnu(B) | <i>lnu(B)</i> | <i>lin(B)</i> | | | pVM25 Chromosome | AJ238249 JQ861959 |
| Lincomycin | Lnu(C) | <i>lnu(C)</i> | | | | MtnLNU pHN61 | AY928180 FJ947048.1 |
| Lincomycin | Lnu(D) | <i>lnu(D)</i> | | | | Chromosome | EF452177 |
| Lincomycin | Lnu(E) | <i>lnu(E)</i> | | | | pStcfr | KF287643 |
| Lincomycin | Lnu(F) | <i>lnu(F)</i> <i>lnu(G)</i> | <i>lnu(F)</i> <i>linF</i> <i>linG</i> | 92%-100% | 93-100% | class 1 integron AHK10349, DQ836009, AEC49683 | EU118119 AJ561197 |
| Lincomycin | Lnu(G) | <i>lnu(G)</i> | | 100% | 100% | | KX470419, CP017962.1 |
| Lincomycin | Lnu(H) | <i>lnu(H)</i> | | | | | AGC41079 |
| Lincomycin | Lnu(P) | <i>lnu(P)</i> | | | | pJIR2774 | FJ589781 |
| Streptogramin A | Vat(A) | <i>vat(A)</i> | <i>vat</i> | | | pIP680 | L07778 |
| Streptogramin A | Vat(B) | <i>vat(B)</i> | <i>vat(B)</i> | | | pIP52 | U19459 |
| Streptogramin A | Vat C) | <i>vat(C)</i> | <i>vat(C)</i> | | | pIP1714 | AF015628 |
| Streptogramin A | Vat(D) | <i>vat(D)</i> | <i>sat(A)</i> | 100% | 100% | pAT15, pAT421 | L12033 AF368302 |
| Streptogramin A | Vat(E) | <i>vat(E)</i> | <i>sat(G)</i> <i>sat(G)</i> <i>vat(E)</i> <i>vat(E-3)</i> | 99% | 98-100% | pIP1803 pLME300 | AF139725, AF229200 AF153312 NC_004566, AJ488494 AF242872 |

| | | | | | | | |
|-----------------|--------|------------------|----------------|--|--|------------|----------|
| | | <i>vat</i> (E-4) | | | | | AY043211 |
| | | <i>vat</i> (E-5) | | | | | AY043209 |
| | | <i>vat</i> (E-6) | | | | | AY043210 |
| | | <i>vat</i> (E-7) | | | | | AY043212 |
| | | <i>vat</i> (E-8) | | | | | AY043213 |
| Streptogramin A | Vat(F) | | <i>vat</i> (F) | | | Chromosome | AF170730 |
| Streptogramin A | Vat(G) | | <i>vat</i> (G) | | | | GQ205627 |

PHOSPHORYLASES

| | | | | | | | |
|------------|-----------------------|----------------|---|------|----------|---------------------|------------------------|
| Macrolides | Mph(A) | <i>mph</i> (A) | <i>mph</i> (A) | 99% | 93-99% | pTZ3519 | D16251 |
| | | | <i>mph</i> (K) | | | pGE64 | U36578 |
| Macrolides | Mph(B) | <i>mph</i> (B) | <i>mph</i> (B) | | | pTZ3714, pTZ3723 | D85892 |
| Macrolides | Mph(C) | <i>mph</i> (C) | <i>mph</i> (BM) | 100% | 100% | pMS97 | AB013298 |
| | | | <i>mph</i> (C) | | | pSR1 | AF167161 |
| Macrolides | Mph(D) | <i>mph</i> (D) | <i>mph</i> (D) partial sequence | | | | AB048591 |
| | Mph(E) | <i>mph</i> (E) | <i>mph</i> , <i>mph1</i> <i>mph2</i> | 99% | 99%-100% | Chromosome | FR751518 |
| | | | | | | pKP048, pKSMA0710 | FJ628167.2, FJ917355.1 |
| | | | | | | pCOP1, pABIR | FJ187822.1, EU294228.1 |
| | | | | | | Chromosome, pRSB105 | EF102240.1, DQ839391.1 |
| | | | | | | pMUR050, pCTX-M3 | AY522431.4, AF550415.2 |
| | | | | | | Chromosome | JF769133, |
| | Mph(F) | <i>mph</i> (F) | <i>mph</i> (E) | 100% | 100% | pRSB111 | AM260957 |
| | Mph(G) | <i>mph</i> (G) | | | | pAQU1 | AB571865 |
| | Mph(H) ^k | <i>mph</i> (H) | <i>mph</i> (E) | | | Chromosome | NC_013172.1 |
| | Mph(I) ^k | <i>mph</i> (I) | | | | Chromosome | KX531056.1 |
| | Mph(J) ^{j,k} | <i>mph</i> (J) | | | | Chromosome | KY753883.1 |
| | Mph(K) ^{j,k} | <i>mph</i> (K) | <i>yebJ</i> | | | Chromosome | NC_000964.3 |
| | Mph(L) ^k | <i>mph</i> (L) | | | | Plasmid | ACMJ01000036.1 |
| | Mph(M) ^k | <i>mph</i> (M) | | | | Chromosome | AHFB01000066.1 |

| | | | | |
|---------------------|---------------|---------------|------------|-------------------|
| Mph(N) ^k | <i>mph(N)</i> | | Plasmid | NC_023287.1 |
| Mph(O) ^k | <i>mph(O)</i> | <i>mph(E)</i> | Chromosome | NZ_AGSO01000004.1 |

Blue represents new or changes since last update

**** DNA database bank of Japan; *Not all GenBank # are listed just representative ones**

^aDaly, M., R. Flamm, and V. Shortridge. 2003. The prevalence of *mef(A)* vs *mef(E)* in *S. pneumoniae* and the characterization of associated *msr(A)* homolog element. In: Abstract of the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, C2-71, p. 112, Chicago IL; ^b

Long et al., AAC 50:2500; ^c Only Chinese gene shown to have all resistances; ^d Kadlec et al., J Antimicrob Chemoth. 65:2692, 2010; ;

^e 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; ^f These genes have been suggested to be ribosomal protection genes but no data to support the mechanism has been done and thus not clear of the mechanism of action [Sharkey, O' Neill, 2018 ACS Inf Dis 4:239-24].

^g Su, Kumar, Ding et al., 2018, May 15, 2018. 115:5157-5162, www.pnas.org/cgi/doi/10.1073/pnas.1803313115.

^h Ero et al., 2019 Protein Science 28:684; ^j Does not confer resistance in native host but does in heterologous host;

^k Not named by nomenclature center [Pawlowski et al., 2018 Nature communications doi:10.1038/s41467-017-02680], named by Wright lab which originally included naming multiple different genes *mph(E)*;

^l Found in GenBank do not know if it functions [Perreten]; ^m Imwattana et la. bioRxiv doi: https://doi.org/10.1101/2020.11.12.379040;

ⁿ Yan et al., JAC 202075:868-872. doi:10.1093/jac/dkz545; ^o Fernandez, Perreten, Schwendener 2021. JAC 76; 48-54. doi:10.1093/jac/dkaa405 ;

^p Guglielmino manuscript in preparation; ^q Antonelli, D'Andrea et al. Jac 2018 73:1763-69. Doi:10.1093/jac/dky088;

^r **Oswaldi, Luth, Dzierzon et al. Microorganisms 2022 10, 512. <https://doi.org/10.3390/microorganisms10030512>**

More information on mobile macrolide resistance genes can be found in FeBler, Wang, Wu, Schwarz, 2018; Plasmid. 2018 June 19.

pii: S0147-619X(18)30035-0. doi:10.1016/j.plasmid.2018.06.002, PMID:29932965