frontiers

## *Supplementary Material*

# Interplay between mutations and efflux in drug resistant *Mycobacterium tuberculosis* clinical isolates

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## 1 Supplementary Table

**Supplementary Table 1. Putative efflux transporters described in *M. tuberculosis* and their substrates.**

| Transporter | Gene | Function | Substrates | Family | Energy source | Reference |
|---|---|---|---|---|---|---|
| Rv0194 | *Rv0194* | Probable transmembrane multidrug efflux pump | AMP; CHL; ERY; EtBr; NOV; STR; TET; VAN | ABC | ATP | 12 |
| PstB | *pstB* (*Rv0933*) | Phosphate-transport ATP-binding protein | EMB; INH; FQs; RIF | ABC | ATP | 5;8;14;39 |
| Rv1218c–Rv1217c | *Rv1218c-Rv1217c* | Probable tetronasin-transport integral membrane protein | BL; BP; BSP; INH; NOV; PA; PD; PR; RIF | ABC | ATP | 4;16:43 |
| Rv1458c-Rv1457c-Rv1456c | *Rv1458c-Rv1457c-Rv1456c* | Probable unidentified antibiotic-transport integral membrane | EMB; INH; RIF; STR | ABC | ATP | 22 |
| Rv1747 | *Rv1747* | Probable conserved transmembrane ATP-binding protein | EMB; EtBr; INH | ABC | ATP | 7;41 |
| BacA | *bacA* (*Rv1819c*) | Probable drug-transport transmembrane ATP-binding protein | AP; INH; RIF | ABC | ATP | 17;20;25;27 |

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|---|---|---|---|---|---|---|
| Rv2688c-Rv2687c-Rv2686c | *Rv2688c-Rv2687c-Rv2686c* | Antibiotic-transport ATP-binding protein | FQs | ABC | ATP | 7;33 |
| DrrAB | *Rv2936-Rv2937* | Daunorubicin-dim-transport ATP-binding proteins | BCECF; CHL; DAU; DOX; EMB; ERY; EtBr; NOR; PUR; RIF; STR; TET | ABC | ATP | 7;9;27;32 |
| **Mmr** | ***mmr* (*Rv3065*)** | **Multidrug-transport integral membrane protein** | **Dyes; ERY; INH; PY; TPP** | **SMR** | **PMF** | **3;15;30;38** |
| Rv1634 | *Rv1634* | Possible drug efflux membrane protein | FQs; SKI | MFS | PMF | 14;23 |
| Rv0849 | *Rv0849* | Probable conserved integral membrane transport protein | BL; INH; RIF | MFS | PMF | 3 |
| EmrB | *emrB* (*Rv0783c*) | Multidrug resistance integral membrane efflux protein | Several drugs | MFS | PMF | 14 |
| **EfpA** | ***efpA* (*Rv2846c*)** | **Possible integral membrane efflux protein** | **ACR; EtBr; FQs; INH; RIF** | **MFS** | **PMF** | **19;27;30** |
| **P55** | ***p55* (*Rv1410c*)** | **Aminoglycosides/tetracycline-transport integral membrane protein** | **AGs; CFZ; INH; RIF; TET** | **MFS** | **PMF** | **6;11;25;35** |
| **Rv1258c** | ***Rv1258c (tap-like)*** | **Probable conserved integral membrane transport protein** | **EMB; ERY; EtBr; FQs; INH; RIF; SPE; TET** | **MFS** | **PMF** | **1;25;30;37;40** |
| Stp | *stp* (*Rv2333c*) | Integral membrane drug efflux protein Stp | RIF; SPE;TET | MFS | PMF | 36 |
| Rv1877 | *Rv1877* | Conserved membrane protein | ERY; KAN; TET | MFS | PMF | 14 |
| **Rv2459** | ***Rv2459 (jefA)*** | **Conserved integral membrane transport protein** | **EMB; EtBr; INH** | **MFS** | **PMF** | **14;21;30** |
| MmpL3 | *mmpL3* (*Rv0206c*) | Probable conserved transmembrane transport protein | SQ109; BM212; AU; IA | RND | PMF | 26;28;42 |
| MmpL4 | *mmpL4* (*Rv0450c*) | Probable conserved transmembrane transport protein | CMB; MB; RIF | RND | PMF | 13;44 |
| MmpL5 | *mmpL5* (*Rv0676c*) | Probable conserved transmembrane transport protein | AZ; BDQ; CFZ; TET | RND | PMF | 24;31 |
| **MmpL7** | ***mmpL7* (*Rv2942*)** | **Probable conserved transmembrane transport protein** | **INH** | **RND** | **PMF** | **18;30;34** |
| MmpL8 | *mmpL8* (*Rv3823c*) | Probable conserved transmembrane transport protein | SQ109 | RND | PMF | 28 |
| MmpL10 | *mmpL10* (*Rv1183*) | Probable conserved transmembrane transport protein | SQ109 | RND | PMF | 28 |

| | | | | | | |
|---|---|---|---|---|---|---|
| IniBAC | *iniB* (*Rv0341*)<br>*iniA* (*Rv0342*)<br>*iniC* (*Rv0343*) | Isoniazid- inducible protein IniB<br>Isoniazid- inducible protein IniA<br>Isoniazid- inducible protein IniC | ETB; INH | Membrane protein | - | 2;10 |

ABC, ATP-binding cassette; ACR, acriflavine; AGs, aminoglycosides; AMP, ampicillin; AP, antimicrobial peptides; ATP, adenosine triphosphate; AU, adamantyl ureas; AZ, azoles; BCECF, 2',7'-bis-(2-carboxyethyl)-5(6)-carboxyfluorescein; BDQ, bedaquiline; BL, β-lactams; BP, biarylpiperazines; BSP, bisanilinopyrimidines; CFZ, clofazimine; CHL, chloramphenicol; CMB, carboxymycobactins; DAU, daunorubicin; DOX, doxorubicin; EMB, ethambutol; ERY, erythromycin; EtBr, ethidium bromide; FQs, fluoroquinolones; IA, indoleamides; INH, isoniazid; KAN, kanamycin; MB, mycobactins; MFS, major facilitator superfamily; NOR, norfloxacin; NOV, novobiocin; PA, pyrazolones; PD, pyridines; PMF, proton motive force; PR, pyrroles; PUR, puromycin; PY, pyronin Y; RIF, rifampicin; RND, resistance nodulation division; SMR, small multidrug resistance; SPE, spectinomycin; SKI, imidazoline SKI-356313; STR, streptomycin; TET, tetracycline; TPP, tetraphenylphosphonium; VAN, vancomycin. BM212 is a 1,5-diarylpyrrole; SQ109 is an ethylenediamine derivative of ethambutol.
Transporters in bold-type letter corresponded to those evaluated in the present study.

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