**Supplementary Table 6. SNPs in virulence genes of *M. orygis*.** Synonymous, nonsynonymous and stop gained or lost SNPs are listed corresponding to the virulence mechanism. ✔ mark indicates presence of the SNP in the gene.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Product** | **Gene** | **Locus Tag** | **Syn-SNP** | **Miss-SNP** | **STOP\_GAIN/LOST** |
| **Amino acid and purine metabolism** | Glutamine synthesis | *glnA1* | MRA\_2237 |   | ✔ |   |
| Lysine synthesis | *lysA* | MRA\_1301 | ✔ |   |   |
| Proline synthesis | *proC* | MRA\_0507 | ✔ | ✔ |   |
| **Anaerobic respiration** | Fused nitrate reductase | *narX* | MRA\_1747 |   | ✔ |   |
| Nitrate reductase | *narG* | MRA\_1172 | ✔ | ✔ |   |
| *narH* | MRA\_1173 | ✔ | ✔ |   |
| Nitrate/nitrite transporter | *narK2* | MRA\_1748 |   | ✔ |   |
| **Anti-apoptosis factor** | NuoG | *nuoG* | MRA\_3184 |   | ✔ |   |
| **Catabolism of cholesterol** | Cyp125 | *cyp125* | MRA\_3584 | ✔ |   |   |
| **Cell surface components** | Carboxylesterase | *caeA* | MRA\_2241 | ✔ |   |   |
|   | *fad23* | MRA\_1195 |   | ✔ |   |
| *fadE5* | MRA\_0253 | ✔ |   |   |
| *gtf1* | MRA\_1538 | ✔ |   |   |
| *gtf2* | MRA\_1536 | ✔ | ✔ |   |
| *mmpL10* | MRA\_1193 | ✔ | ✔ |   |
| *mmpS4* | MRA\_0456 | ✔ |   |   |
| *mps1* | MRA\_0106 | ✔ | ✔ | STOP\_LOST |
| *papA3* | MRA\_1192 | ✔ | ✔ |   |
| *pe* | MRA\_1194 | ✔ | ✔ |   |
| Heparin-binding hemagglutinin | *hbhA* | MRA\_0482 |   | ✔ |   |
| Methyltransferase | *mmaA4* | MRA\_0653 |   | ✔ |   |
| Mycolic acid trans-cyclopropane synthetase | *cmaA2* | MRA\_0511 |   | ✔ |   |
| MymA operon | *adhD* | MRA\_3118 | ✔ | ✔ |   |
| *chp* | MRA\_3119 |   | ✔ |   |
| *fadD13* | MRA\_3121 | ✔ |   | STOP\_GAIN |
| *lipR* | MRA\_3116 | ✔ | ✔ |   |
| *mymA* | MRA\_3115 |   | ✔ |   |
| *tgs4* | MRA\_3120 | ✔ |   |   |
|   | *Undetermined* | MRA\_2985 | ✔ |   |   |
| *Undetermined* | MRA\_2989 | ✔ |   |   |
| *Undetermined* | MRA\_2976 | ✔ |   |   |
| *Undetermined* | MRA\_2982 | ✔ |   |   |
| *Undetermined* | MRA\_2983 |   | ✔ | STOP\_GAIN |
| *ddrA* | MRA\_2962 |   | ✔ |   |
| *fadD22* | MRA\_2975 | ✔ | ✔ |   |
| *fadD26* | MRA\_2956 |   | ✔ |   |
| *fadD28* | MRA\_2967 | ✔ |   |   |
| *fadD29* | MRA\_2977 | ✔ | ✔ |   |
| *lppx* | MRA\_2972 |   | ✔ |   |
| *mas* | MRA\_2966 | ✔ | ✔ |   |
| *mmpL7* | MRA\_2968 | ✔ | ✔ |   |
| *pks1* | MRA\_2973 |   | ✔ |   |
| *ppsA* | MRA\_2957 | ✔ | ✔ |   |
| *ppsB* | MRA\_2958 | ✔ | ✔ |   |
| *ppsC* | MRA\_2959 | ✔ | ✔ |   |
| *ppsD* | MRA\_2960 | ✔ | ✔ |   |
| *ppsE* | MRA\_2961 | ✔ | ✔ |   |
| *tesA* | MRA\_2955 |   | ✔ |   |
| Potassium/proton antiporter | *kefB* | MRA\_3277 | ✔ |   |   |
| Proximal cyclopropane synthase of alpha mycolates | *pcaA* | MRA\_0476 | ✔ |   |   |
| Sulfolipid-1 biosynthesis and transport | *mmpL8* | MRA\_3863 | ✔ | ✔ |   |
| *papA1* | MRA\_3864 | ✔ | ✔ |   |
| *papA2* | MRA\_3860 |   | ✔ |   |
| *pks2* | MRA\_3865 | ✔ | ✔ |   |
| *stf0* | MRA\_0304 | ✔ |   |   |
| Trehalose-recycling ABC transporter | *chp1* | MRA\_3862 | ✔ | ✔ |   |
| *fad23* | MRA\_3866 | ✔ | ✔ |   |
| *lpqY* | MRA\_1244 | ✔ |   |   |
| *icl2* |   |   | ✔ |   |
| *sugB* | MRA\_1246 |   | ✔ |   |
| **Copper uptake** | Copper exporter | *ctpV* | MRA\_0976 | ✔ | ✔ | initiator\_codon\_variant |
| **Iron uptake** | ABC transporter | *irtA* | MRA\_1356 | ✔ | ✔ |   |
| *irtB* | MRA\_1357 | ✔ | ✔ |   |
| Heme uptake | *Undetermined* | MRA\_0211 | ✔ |   |   |
| *mmpL11* | MRA\_0210 | ✔ |   |   |
| *mmpL3* | MRA\_0214 | ✔ | ✔ |   |
| Iron-dependent regulator | *ideR* | MRA\_2739 |   | ✔ |   |
|  | *fadD33* | MRA\_1353 |   | ✔ |   |
| *mbtB* | MRA\_2406 | ✔ | ✔ |   |
| *mbtC* | MRA\_2405 | ✔ |   |   |
| *mbtD* | MRA\_2404 |   | ✔ |   |
| *mbtE* | MRA\_2403 |   | ✔ |   |
| *mbtF* | MRA\_2402 | ✔ | ✔ |   |
| *mbtG* | MRA\_2401 |   | ✔ |   |
| *mbtH* | MRA\_2400 |   | ✔ |   |
| *mbtI* | MRA\_2409 | ✔ |   |   |
| **Lipid and fatty acid metabolism** | Isocitrate lyase | *icl* | MRA\_0473 | ✔ |   |   |
| Lipase | *lipF* | MRA\_3527 |   | ✔ |   |
| Lipid phosphatase | *sapM* | MRA\_3351 |   | ✔ |   |
|  | *panD* | MRA\_3640 |   | ✔ |   |
| *plcB* | MRA\_2370 | ✔ |   |   |
| *plcC* | MRA\_2369 | ✔ |   |   |
| **Magnesium uptake** | Magnesium transport | *mgtC* | MRA\_1823 | ✔ | ✔ |   |
| **Mammalian cell entry (mce) operons** | Mce1 | *mce1A* | MRA\_0177 | ✔ | ✔ |   |
| *mce1B* | MRA\_0178 |   | ✔ |   |
| *mce1C* | MRA\_0179 | ✔ | ✔ |   |
| *mce1D* | MRA\_0180 | ✔ |   |   |
| *mce1E* | MRA\_0181 | ✔ | ✔ |   |
| *mce1F* | MRA\_0182 | ✔ | ✔ |   |
| Mce2 | *mce2A* | MRA\_0596 |   | ✔ |   |
| *mce2B* | MRA\_0597 | ✔ |   |   |
| *mce2C* | MRA\_0599 | ✔ | ✔ |   |
| *mce2F* | MRA\_0602 | ✔ | ✔ |   |
| Mce4 | *mce4C* | MRA\_3537 | ✔ |   |   |
| *mce4E* | MRA\_3535 | ✔ | ✔ |   |
| *mce4F* | MRA\_3534 |   | ✔ |   |
| **Manganese uptake** | P(1)-type Mn2+ transporting ATPase | *ctpC* | MRA\_3311 | ✔ | ✔ |   |
| **Phagosome arresting** | PE family protein | *PE\_PGRS30* | MRA\_1662 | ✔ | ✔ |   |
| **Protesase** | Zn++ metallophrotease | *zmp1* | MRA\_0206 | ✔ |   |   |
|  | DevR/S | *devS* | MRA\_3164 |   | ✔ |   |
| MprA/B | *mprA* | MRA\_0988 |   | ✔ |   |
| *mprB* | MRA\_0989 |   | ✔ |   |
| PhoP/R | *phoP* | MRA\_0767 |   | ✔ |   |
| *phoR* | MRA\_0768 |   | ✔ |   |
| PrrA/B | *prrA* | MRA\_0910 |   | ✔ |   |
| *prrB* | MRA\_0909 |   | ✔ |   |
| Sigma H | *sigH* | MRA\_3263 |   | ✔ |   |
| Sigma L | *sigL* | MRA\_0743 |   | ✔ |   |
| Sigma M | *sigM* | MRA\_3950 |   | ✔ |   |
| **Secreted proteins** | Antigen 85 complex | *fbpA* | MRA\_3844 |   | ✔ |   |
| *fbpB* | MRA\_1897 |   | ✔ |   |
| Protein kinase G | *pknG* | MRA\_0416 | ✔ | ✔ |   |
| **Secretion system** | Accessory secretion factor | *secA2* | MRA\_1833 |   | ✔ |   |
| ESX-1 (T7SS) | *PE35* | MRA\_3911 | ✔ | ✔ | STOP\_GAIN |
| *PPE68* | MRA\_3912 |   | ✔ |   |
| *eccA1* | MRA\_3907 | ✔ |   |   |
| *eccB1* | MRA\_3908 | ✔ | ✔ |   |
| *eccCa1* | MRA\_3909 | ✔ | ✔ |   |
| *eccCb1* | MRA\_3910 | ✔ | ✔ |   |
| *eccD1* | MRA\_3916 | ✔ |   |   |
| *eccE1* | MRA\_3921 |   | ✔ |   |
| *espA* | MRA\_3652 | ✔ | ✔ |   |
| *espB* | MRA\_3920 | ✔ | ✔ |   |
| *espC* | MRA\_3651 |   | ✔ |   |
| *espD* | MRA\_3650 | ✔ |   |   |
| *espE* | MRA\_3903 |   | ✔ |   |
| *espF* | MRA\_3904 |   | ✔ |   |
| *espI* | MRA\_3915 |   | ✔ |   |
| *espJ* | MRA\_3917 | ✔ | ✔ |   |
| *espK* | MRA\_3918 |   | ✔ |   |
| ESX-2 (T7SS) | Undetermined | MRA\_3927 | ✔ | ✔ |   |
| *PE36* | MRA\_3932 |   | ✔ |   |
| *PPE69* | MRA\_3931 |   | ✔ |   |
| *eccA2* | MRA\_3923 | ✔ | ✔ |   |
| *eccB2* | MRA\_3934 | ✔ | ✔ |   |
| *eccC2* | MRA\_3933 | ✔ | ✔ |   |
| *eccD2* | MRA\_3926 |   | ✔ |   |
| *eccE2* | MRA\_3924 | ✔ | ✔ |   |
| *espG2* | MRA\_3928 |   | ✔ |   |
| *esxD* | MRA\_3930 | ✔ | ✔ |   |
| ESX-3 (T7SS) | *PPE4* | MRA\_0295 | ✔ | ✔ | STOP\_GAIN |
| *eccA3* | MRA\_0291 | ✔ |   |   |
| *eccC3* | MRA\_0293 | ✔ | ✔ |   |
| *eccD3* | MRA\_0299 |   | ✔ |   |
| *eccE3* | MRA\_0301 |   | ✔ |   |
| *mycP3* | MRA\_0300 |   | ✔ |   |
| ESX-4 (T7SS) | *eccB4* | MRA\_3491 | ✔ |   |   |
| *eccC4* | MRA\_3488 | ✔ | ✔ |   |
| *esxT* | MRA\_3485 | ✔ | ✔ |   |
| *mycP4* | MRA\_3490 | ✔ | ✔ |   |
| ESX-5 (T7SS) | *Undetermined* | MRA\_1807 | ✔ | ✔ |   |
| *PE18* | MRA\_1802 | ✔ |   |   |
| *PPE26* | MRA\_1803 | ✔ |   |   |
| *PPE27* | MRA\_1804 |   | ✔ |   |
| *PPE41* | MRA\_2457 | ✔ | ✔ |   |
| *cyp143* | MRA\_1799 | ✔ | ✔ |   |
| *eccA5* | MRA\_1811 |   | ✔ |   |
| *eccB5* | MRA\_1797 | ✔ | ✔ |   |
| *eccCb5* | MRA\_1798 | ✔ | ✔ |   |
| *eccD5* | MRA\_1808 |   | ✔ |   |
| *mycP5* | MRA\_1809 |   | ✔ |   |
| **Stress adaptation** | AhpC | *ahpC* | MRA\_2455 | ✔ |   |   |
| Cu | *sodC* | MRA\_0437 | ✔ |   |   |
| Pore-forming protein | *ompA* | MRA\_0906 |   | ✔ |   |