**Table S1**: Table describing changes in gene essentiality predictions according to changes in GAM and NGAM values that were utilized across different genome-scale reconstructions of *M. tuberculosis*.

|  |  |  |  |
| --- | --- | --- | --- |
|  | iEK1011 NGAM | iSM810 NGAM | sMtb NGAM |
| NGAM | 3.15 (iEK1011) | 1.00 (iSM810) | 0.10 (sMTb) |
| Griffin essentiality MCC | 0.60 | 0.60 | 0.59 |
| DeJesus essentiality MCC | 0.71 | 0.70 | 0.70 |

**Table S2**: List of reactions in iEK1011 that violate the law of mass conservation.

|  |  |
| --- | --- |
| **Unbalanced Reactions** | **iEK1011 reaction string** |
| **TAG** | 10.0 12dgr\_TB\_c + arachcoa\_c + hexccoa\_c + nodcoa\_c + pentdcoa\_c + 2.0 pmtcoa\_c + 3.0 stcoa\_c --> 10.0 coa\_c + 10.0 tag\_TB\_c |
| **LIPY** | 10.0 h2o\_c + 9.0 tag\_TB\_c --> 9.0 12dgr\_TB\_c + arach\_c + 2.0 hdca\_c + 2.0 hexc\_c + 4.0 ocdca\_c |
| **VIUB** | atp\_c + fe3\_e + h2o\_c + 0.0005 mcbts\_c + 0.0005 mcbtt\_c --> adp\_c + fe3\_c + pi\_c |
| **MBTA1** | acac\_c + h\_c + n6hlys\_c + n6hlysmal\_c + nadh\_c + salc\_c + thr\_\_L\_c --> 6.0 h2o\_c + mcbtt\_c + nad\_c |
| **MMM2r** | 0.001 aqcobal\_c + succoa\_c <-- mmcoa\_\_R\_c |
| **MME** | mmcoa\_\_R\_c <-- 0.001 aqcobal\_c + mmcoa\_\_S\_c |
| **NMO** | etha\_c + fmnh2\_c + o2\_c --> acald\_c + fmn\_c + no2\_c |

**Table S3**: Examples of false negatives computed by iEK1011 on the DeJesus et al. gene essentiality dataset that are not within the iSM810 model, and reasoning for its inclusion.

|  |  |  |
| --- | --- | --- |
| IEK1011 FNs | In iSM810? | Reasoning |
| Rv0505c | No but in others | Evidence of gene. Could be regulatory. |
| Rv2895c (viuB) | No but in others | Iron uptake… but described not to be necessary for iron uptake *in vitro*... |
| Rv1739c | No but in others | Sulfate uptake |
| Rv1159 | No but in others | Strong evidence of annotation [68]. Oddly left out of iSM810 when the other non-FNs were included in phosphatidylinositol mannosides (PIMS). |
| Rv3807c | No, only in iOSDD | Putative evidence [69] . Noted in TB Biocyc Database 21.1 The fact that it is not essential may mean that the annotation is incorrect. |
| Rv3825c | No, but in sMtb. | Strong evidence [70] |

**Table S4**: Gene essentiality predictions using the shared set of 472 genes.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Griffin Essentiality Data | | | | | deJesus Essentiality Data | | | | |
|  | MCC | TP | TN | FP | FN | MCC | TP | TN | FP | FN |
| iEK1011 | 0.57 | 160 | 206 | 86 | 21 | 0.66 | 195 | 195 | 49 | 32 |
| sMtb | 0.50 | 152 | 197 | 95 | 29 | 0.53 | 180 | 179 | 65 | 47 |
| iSM810 | 0.45 | 154 | 178 | 114 | 27 | 0.55 | 193 | 170 | 74 | 34 |
| iOSDD | 0.24 | 148 | 122 | 170 | 33 | 0.30 | 186 | 114 | 130 | 41 |
| iNJ661 | 0.22 | 141 | 129 | 163 | 33 | 0.27 | 177 | 119 | 125 | 50 |