### Additional Table 2 - Kinetic constants of the enzymes in *M. tuberculosis* model-1 and model-2.

Vmax refers to maximal rate of an enzymatic reaction. $K_{S1}$ and $K_{S2}$ refer to the $K_M$ values of substrates, and, $K_{P1}$ and $K_{P2}$ refer to the $K_M$ values of products of the reactions. They are numbered in the order they appear in the chemical equations shown in the table.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Enzyme</th>
<th>Abbreviation</th>
<th>Vmax (in nmol/min/mg protein)</th>
<th>Vmax (mM/min)</th>
<th>$K_{S1}$ (mM)</th>
<th>$K_{S2}$ (mM)</th>
<th>$K_{P1}$ (mM)</th>
<th>$K_{P2}$ (mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$ACA + OAA = COA + CIT$</td>
<td>citrate synthase</td>
<td>CS</td>
<td>405 [1]</td>
<td>64.8</td>
<td>0.05 [2]</td>
<td>0.012$^a$ [2]</td>
<td>0.5</td>
<td>0.12</td>
</tr>
<tr>
<td>$CIT = ICIT$</td>
<td>aconitase</td>
<td>ACN</td>
<td>195 [1]</td>
<td>31.2</td>
<td>1.7$^a$ [2]</td>
<td>0.7$^c$ [2]</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>$ICIT = aKG$</td>
<td>$i$-isocitrate dehydrogenase 1</td>
<td>ICD1</td>
<td>64 [1]</td>
<td>10.2</td>
<td>0.03 [2]</td>
<td>5</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>$ICIT = aKG$</td>
<td>$i$-isocitrate dehydrogenase 2</td>
<td>ICD2</td>
<td>-</td>
<td>9.965$^d$</td>
<td>0.06$^d$</td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$aKG = SCA$</td>
<td>α-ketoglutarate dehydrogenase complex</td>
<td>KDH</td>
<td>-</td>
<td>57.344$^f$</td>
<td>0.1$^f$</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$SCA = SUC$</td>
<td>succinyl-CoA synthetase</td>
<td>ScAS</td>
<td>7.5 [1]</td>
<td>1.2</td>
<td>0.02$^g$ [2]</td>
<td>5$^h$ [2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$aKG = SSA$</td>
<td>α-ketoglutarate decarboxylase</td>
<td>KGD</td>
<td>-</td>
<td>48.3$^i$</td>
<td>0.48 [1]</td>
<td>4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$SSA = SUC$</td>
<td>succinic semialdehyde dehydrogenase</td>
<td>SSADH</td>
<td>40.7 [1]</td>
<td>6.51</td>
<td>0.015$^j$ [2]</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$SUC = FA$</td>
<td>succinate dehydrogenase</td>
<td>SDH</td>
<td>6.4 [1]</td>
<td>1.02</td>
<td>0.15$^k$ [2]</td>
<td>0.12$^k$ [2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$MAL = OAA$</td>
<td>malate dehydrogenase</td>
<td>MDH</td>
<td>1149 [1]</td>
<td>184</td>
<td>0.833$^m$ [2]</td>
<td>0.0443$^m$ [2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$ICIT = SUC + GLY$</td>
<td>isocitrate lyase 1</td>
<td>ICL1</td>
<td>1.83 [3]</td>
<td>1.172$^n$</td>
<td>0.145 [2]</td>
<td>0.59$^f$</td>
<td>0.13$^f$</td>
<td></td>
</tr>
<tr>
<td>$ICIT = SUC + GLY$</td>
<td>isocitrate lyase 2</td>
<td>ICL2</td>
<td>-</td>
<td>0.391$^o$</td>
<td>1.3 [4]</td>
<td>5.9$^o$</td>
<td>1.3$^o$</td>
<td></td>
</tr>
<tr>
<td>$GLY + ACA = MAL + COA$</td>
<td>malate synthase</td>
<td>MS</td>
<td>125 [3]</td>
<td>20</td>
<td>0.057 [2]</td>
<td>0.03 [2]</td>
<td>1$^f$</td>
<td>0.1$^f$</td>
</tr>
</tbody>
</table>

**Notes for additional table 2**

$^a$Value taken from *Bacillus megaterium*

$^b$Value taken from *Bacillus subtilis*

$^c$Value taken from *Bacillus cereus*

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Additional file 2 to the paper titled “Kinetic modeling of tricarboxylic acid cycle and glyoxylate bypass in *Mycobacterium tuberculosis*, and its application to assessing drug targets” submitted by Vivek Kumar Singh and Indira Ghosh
Banerjee et al. [5] estimated the Vmax of purified ICD1 and ICD2, and Tian et al. [1] estimated the Vmax of ICD1 in cell lysate. Using the ratio of Vmax of purified ICD2 to Vmax of purified ICD1, and the Vmax of ICD1 in cell lysate, the Vmax of ICD2 in cell lysate was estimated. Similar logic was used to estimate the $K_M$ value of ICIT for ICD2.

This reaction is present only in \textit{M. tuberculosis} model-1.

Value taken from \textit{E. coli}.

Value taken from \textit{Calliphoridae}.

Value taken from \textit{Nitrosonomas europaea}.

Value was not available in cell lysate condition, so average of the Vmax of all TCA cycle enzymes was used.

Value taken from \textit{Sus scrofa}.

Value taken from \textit{Mycobacterium phlei}.

Value taken from bacterium.

Multiply the calculated Vmax ($=0.293 \text{ mM/min}$) by 4 because ICL activity increases 4-fold in persistent mycobacteria [3].

Logic similar to that used for the estimation of Vmax for ICD2 was used to estimate Vmax for ICL2 and $K_M$ value of ICIT for ICL2. The data on purified ICL1 and ICL2 were obtained from Bentrup et al. [4].

Since the $K_M$ of ICIT for ICL2 is 10 times the $K_M$ of ICIT for ICL1 [4], the $K_M$ of the products i.e. SUC and GLY were also increased 10 fold.

References


Abbreviations of metabolites

- ACA: acetyl-CoA
- OAA: oxaloacetate
- COA: CoA
- CIT: citrate
- ICIT: isocitrate
- aKG: $\alpha$-ketoglutarate
- SCA: succinyl-CoA
- SUC: succinate
- FA: fumarate
- MAL: malate
- GLY: glyoxylate
- SSA: succinic semialdehyde