SUPPORTING INFORMATION

Enzyme Architecture: The Effect of Replacement and Deletion Mutations of Loop 6 on Catalysis by Triosephosphate Isomerase‡

Xiang Zhai,† Maybelle K. Go,† AnnMarie C. O'Donoghue,‡ Tina L. Amyes,† Scott D. Pegan,‡
Yan Wang,§ J. Patrick Loria,§,§ John D. Mesecar,§ and John P. Richard†,*,†

†Department of Chemistry, University at Buffalo, Buffalo, NY, 14221
‡Department of Chemistry, Durham University, Durham, DH1 3EL, UK
§Department of Pharmaceutical and Biomedical Sciences, University of Georgia, Athens, GA 30602
§Department of Chemistry, Yale University, New Haven, CT 06520
§Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT 06520
§Departments of Biological Sciences and Chemistry, Purdue University, West Lafayette, IN 47907

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* Author to whom correspondence should be addressed
Tel: (716) 645 4232
Fax: (716) 645 6963
Email: jrichard@buffalo.edu
Table S1. Statistics from X-ray Data Collection and Refinement for the Loop 6 Replacement Mutant.

| Data Collection Statistics               |
|------------------------------------------|
| Space Group                              | C2                      |
| Unit Cell Dimensions                      |
| a, b, c (Å)                              | 79.4, 56.0, 105.8       |
| β (°)                                    | 92.8                    |
| Resolution (Å)                           | 50.0 – 1.34             |
| No. Reflections Observed                 | 281,998                 |
| No. Unique Reflections                   | 98,338                  |
| $R_{\text{merge}}$ (%)$^a$               | 6.1 (37.0)$^b$          |
| $I/\sigma I$                             | 27.7 (2.4)$^b$          |
| % Completeness                           | 95.8 (88.1)$^b$         |

| Refinement Statistics                    |
|------------------------------------------|
| Resolution Range                         | 50.0 – 1.34             |
| No. Reflections in Working Set           | 93,220                  |
| No. Reflections in Test Set              | 4,916                   |
| $R_{\text{work}}$ (%)$^c$                | 16.6                    |
| $R_{\text{free}}$ (%)$^c$                | 20.5                    |
| RMS deviation:                           |
| Bond Lengths (Å)                         | 0.01                    |
| Bond Angles (°)                          | 1.1                     |
| Protein / Water Atoms                    | 3777 / 765              |
| Average B-Factors (Å$^2$)                | 21.5                    |

$^aR_{\text{merge}} = \frac{\Sigma_\delta \Sigma_i |I_i(h)| - <I(h)>|}{\Sigma_\delta \Sigma_i I_i(h)}$, where $I_i(h)$ is the $i^{th}$ measurement and $<I(h)>$ is the weighted mean of all measurements of $I(h)$.  $^b$ The last resolution shell is shown in parentheses.  $^c$ $R_{\text{work}}$ and $R_{\text{free}} = h(|F(h)_{\text{obs}}| - |F(h)_{\text{calc}}|) / h|F(h)_{\text{obs}}|$ for reflections in the working and test sets, respectively.  R.m.s., root mean square.
Figure S1. Dependence of the apparent second-order rate constant \((k_{\text{cat}}/K_m)_{\text{app}}\) for the isomerization of GAP, catalyzed by the L6RM of cTIM, on the concentration of PGA at pH 7.5 (30 mM TEA buffer), 25 °C, and I = 0.1 (NaCl).
**Figure S2.** Divergent-eyed stereo view of the residues in LRM loop 6 with the gray mesh representing $2F_o-F_c$ kicked simulated annealing map contoured to 1.0 $\sigma$. Kicked Simulated annealing maps were generated by Phenix version 1.8.1.¹

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