This thesis discusses the structure-function studies on triosephosphate isomerase (TIM) from *Plasmodium falciparum* (*Pf*), directed towards understanding the roles of highly conserved residues by site directed mutagenesis. **Chapter 1** provides an introductory overview to the relevant literature on triosephosphate isomerase. In addition, this Chapter provides an analysis of conserved residues in TIM, and amino acid diversity at specific positions in the structure using a dataset of 503 TIM sequences. **Chapter 2** reports the work on the completely conserved residue, C126 in TIM, which is proximal to the active site. Five mutants, C126S, C126A, C126V, C126M and C126T have been characterized. Crystal structures of 3-phosphoglycolate (PGA) bound C126S mutant and the unliganded forms of the C126S and C126A mutants have been determined at a resolution of 1.7 Å to 2.1 Å. Kinetic studies reveal a ~5 fold drop in $k_{cat}$ for the C126S and C126A mutants, while a ~ 10 fold drop is observed for the other three mutants. All the mutants show reduced stability at lower concentration and higher temperature. **Chapter 3** presents the kinetic and structural characterization for the E97Q and E97D mutants of *Pf* TIM. A 4000 fold reduction in $k_{cat}$ is observed for E97Q, 100 fold reduction for the E97D mutant, while a ~ 9000 fold drop in activity for the control mutant, E165A. A large conformational change for the critical K12 side chain is observed in the crystal structure of the E97Q mutant, while it remains unchanged in the E97D structure. The results are interpreted to invoke a direct role for E97 in the catalytic proton transfer cycle, eliminating the need to invoke the formation of the energetically unfavorable imidazolate anion at H95. **Chapter 4** reports investigations with position 96 by the biochemical and structural characterization of single mutants, F96Y, F96A and the double mutants, F96S/S73A and F96S/L167V. F96Y showed ~100 fold drop in activity, F96A revealed ~10 fold drop in activity, while F96S/S73A showed 100 fold lower activity than that of the wild type enzyme. Interestingly, the double mutant F96S/L167V proved to be a partial pseudorevertant, showing 10 fold higher activity than the single mutant, F96S. **Chapter 5** describes the cloning, and preliminary kinetic and biophysical characterization of the enzyme, *Dm* TIM. A survey of disease causing mutations in TIM and the relationship of these sites of mutation to the active site and the dimer interface of TIM is presented in this Chapter.