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Title:	Endoglucanase activity at a second site in <i>Pyrococcus furiosus</i> triosephosphate isomerase—Promiscuity or compensation for a metabolic handicap?
Authors:	Sharma, Perna (/jspui/browse?type=author&value=Sharma%2C+Perna) Guptasarma, P. (/jspui/browse?type=author&value=Guptasarma%2C+P.)
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Abstract:	<p>The eight-stranded (β/α)₈ barrel fold known as the Triosephosphate isomerase (TIM) barrel is the most commonly observed fold in enzymes, displaying an eightfold structural symmetry. The sequences and structures of different TIM barrel enzymes suggest that nature exploits the modularity inherent in the eightfold symmetry to generate enzymes with diverse enzymatic activities and, in certain cases, more than one catalytic activity per enzyme. Here, we report the discovery, verification, and characterization of such an additional activity, a novel endoglucanase/cellulase activity in what is otherwise a triosephosphate isomerase from the hyperthermophile archaeon <i>Pyrococcus furiosus</i> (PfuTIM). The activity is seen in two different ranges of temperatures, with one maximum at 40 °C and a second maximum close to 100 °C. The endoglucanase/cellulase activity is inhibited by norharman, a TIM inhibitor, which is suspected to bind at a site different to that of the regular substrate, glyceraldehyde-3-phosphate (G3P). However, endoglucanase/cellulase activity is not inhibited either by G3P analogs or by glycine-scanning mutations involving residues in loops 1, 4, and 6 of PfuTIM, which are known to be important for TIM activity. It appears, therefore, that two different sites on PfuTIM are responsible for the observed TIM and endoglucanase activities. We discuss possible correlations between this discovery and certain unusual features of the glycolytic pathway in <i>P. furiosus</i>.</p>
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