PFK1 and PFK2 encode the alpha and beta subunits, respectively, of phosphofructokinase, a key enzyme of glycolysis that catalyzes the formation of fructose 1,6-bisphosphate from fructose 6-phosphate and ATP. Unlike other enzymes of glycolysis, phosphofructokinase and pyruvate kinaseonly function in the forward direction; hence these enzymes are specific to glycolysis and are not involved in gluconeogenesis.Glycolysis is the lysis, or splitting, of one molecule of glucose into two molecules of pyruvate, producing a net gain of two ATP molecules. Pyruvate can then be used in anaerobicor aerobicmetabolism. The glycolysis pathway and the genes involved are illustrated here.Phosphofructokinase is a hetero-oligomeric enzyme composed of four alpha and four beta subunits, arranged as four heterodimers of alpha-beta. Electron microscopy studies at 2 nm resolution revealed that the three-dimensional structure consists of two quasi-equivalent tetramers in which four alpha subunits form the central core of the octamer. The amino acid sequences of Pfk1p and Pfk2p exhibit 20% homology between the N- and the C-terminal halves for each subunit and 55% homology between the two subunits overall. Although biochemical analysis indicated that the beta subunits contain binding sites for the substrate fructose 6-phosphate and hence confer the catalytic activity of the enzyme, more recent mutant studies have shown that each subunithas both a catalytic and a regulatory function. Studies on the regulation of glycolytic genes indicate that glucose strongly induces PFK2 and PFK1 mRNA synthesis. This induction facilitates production of phosphofructokinase during a shift from gluconeogenesis to glycolysis. Phosphofructokinase activity is also subject to allosteric control, with ATP inhibiting the enzyme and AMP, as well as fructose 2,6-bisphosphate, reversing the inhibition. Allosteric control is abolished by a single point mutation in either subunit, which impairs growth on gluconeogenic carbon sources but does not affect growth on glucose. This suggests that the main function of the allosteric regulation is to facilitate growth in changing environments.PFK1 and PFK2 show significant homology to PFK subunits from mammals and bacteria. Analysis of these PFK sequences has led to the hypothesis that two gene duplication events occurred in the evolution of the yeast PFK genes: the first event occurred soon after the separation of prokaryotic and eukaryotic lineage, and the second took place in Saccharomyces later. Although Pfk protein sequences are conserved, the oligomeric structure of the functional enzyme varies among organisms, with homotetramers found in bacteria and mammals, homooctamers in S. pombe, and heterooctamers in S. cerevsiae and K. lactis. In humans, mutation in the muscle isoenzyme of Pfk causes glycogen storage disease VII, also called Tarui disease. Note: PFK1 and PFK2 nomenclature is reversed in some earlier studiesrelative to that used now.