Structural analysis of UDP-glucose:tetrahydrobiopterin α-glycosyltransferase from cyanobacterium

Kon Ho Lee1, Killivalavan Asaithambi2, Young-Shik Park3

1Department Of Microbiology School Of Medicine Gyeongsang National University, Jinju, Korea, Rep., 2Department of Convergence medical science Graduate school Gyeongsang National University, Jinju, Korea, Rep., 3School of Biological Sciences, Inje University, Kimhae, Korea, Rep.
E-mail: lkh@gnu.ac.kr

The UDP-glucose:tetrahydrobiopterin α-glucosyltransferase (BGluT) enzyme has been discovered from cyanobacterium Synechococcus sp. PCC 7942. It transfers a glucose moiety from UDP-glucose to tetrahydrobiopterin (BH4), which forms a BH4-glucoside compound. The structures of apoBGluT and its complexes with UDP, BH2 and both UDP and BH2 were determined at resolution of 1.99, 2.03, 2.39 and 1.75 Å by using multi-wavelength anomalous diffraction (MAD) and molecular replacement. From the structures, BGluT protein consists of N-terminal and C-terminal domains, respectively with BH2 and UDP bound. There are large conformational changes in the binary and ternary complexes when compared with the apo structure. In the BGluT-BH2 structure a new squiggle conformation was formed due to the binding of BH2 in the N-terminal domain. In the BGluT-UDP-BH2 ternary complex the entire loop between β3 and α2 moved towards to BH2. In the BGluT-UDP structure helix α9 was shortened and part of the helix became a loop while in the BGluT-UDP-BH2 complex the helix α9 significantly moved closer to UDP binding site and a part of the loop after β7 reformed another α-helix (α7'). In addition, the residues R194, K199, E268 were identified to be important for catalysis by site directed mutagenesis. The structures and mutational analysis suggest that binding of UDP-glucose before BH4 binding is essential to produce a BH4–glucoside and Glu268 plays a role of nucleophilic base for cleavage of glucose from UDP-glucose and positive charged residues Arg194 and Lys199 in contact with the tail of UDP stabilize the glucose moiety in the catalytic process.

Keywords: glycosyltransferase, tetrahydrobiopterin, pteridine glucoside