Poster Presentation

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

Kon Ho Lee[1], Killivalavan Asaithambi[2], Young-Shik Park[3]

[1]Department Of Microbiology School Of Medicine Gyeongsang National University, Jinju, Korea, Rep., [2]Department of Convergence medical science Graduate school Gyeongsang National University, Jinju, Korea, Rep., [3]School 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