Contribution ID : **93** Type : **Poster**

Crystal structure of pig kidney Fructose 1,6-biphosphatase with sulfate has a quaternary state between the canonical R- and T-states.

Wednesday, 12 August 2015 17:30 (1:00)

Abstract content

Fructose 1,6-biphosphatase (FBPase) governs a key step in gluconeogenesis. Catalyzes the hydrolysis of fructose 1,6-biphosphate to fructose 6-phosphate and inorganic phosphate in presence of divalent cations such as Mg2+ or Mn2+. In mammals, AMP and fructose 2,6-biphosphate (Fru-2,6-P2) synergistically inhibit FBPase. Fru-2,6-P2, the concentration of which is subject to hormonal control, directly inhibits FBPase by binding to its active site, whereas AMP binds to an allosteric site and induces a conformational change, converting the enzyme from an active quaternary conformation (R-state) to an inactive form (T-state). FBPase has been a target for potential drugs in the treatment of Type II diabetes. Novel inhibitors have been developed, and in one case, knowledge of structure and mechanism contributed to the rational design of a new inhibitor. Here, we report the crystal structure of pig kidney FBPase in complex with sulfate ions. The three-dimensional structure has been determined by molecular replacement method. Pig kidney FBPase crystallized in the cubic space group I23 with two subunits of the tetramer in the asymmetric unit. The structure contains several sulfate ions. In the active site of each subunit there are three sulfates, one of them found at the position normally occupied by the 6-phosphate group of the substrate. Other sulfate is present at the phosphate place of the allosteric inhibitor AMP. The fifth sulfate is on the crystallographic 2-fold axis that relates subunits C1 and C2 (and subunits C3 and C4). Although a sulfate bound at the C1-C4 interface was not found, a difference with respect Escherichia coli FBPase-SO4 complex. However, the binding of sulfate anions to porcine FBPase generates a conformational change in quaternary state of the enzyme, a rotation of C1-C2 subunit pair respect to the C3-C4 subunit pair about the vertical 2-fold axis. FBPase rotates about 6 degrees from the R-state, then the enzyme is in an intermediate quaternary state relative to the canonical R- and T-state. This results suggest a role of sulfate in FBPase activation.

Summary

Primary author(s) : Dr. DÍAZ, Adelaida (Instituto de Biotecnología, UNAM)

Co-author(s) : Dr. RUDIÑO-PIÑERA, Enrique (Instituto de Biotecnología, UNAM)

Presenter(s) : Dr. DÍAZ, Adelaida (Instituto de Biotecnología, UNAM)

Session Classification : Posters I