

Crystal Structure of Escherichia Coli Thiamine Pyrophosphate- Sensing Riboswitch in The Apo State

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The thiamine pyrophosphate (TPP)-sensing riboswitch is one of the earliest discovered and most widespread riboswitches. Numerous structural studies have been reported for this riboswitch bound with various ligands. However, the ligand-free (apo) structure remains unknown. Here, we report a 3.1-Å resolution crystal structure of E. coli TPP riboswitch in the apo state, which exhibits an extended, Y-shaped conformation further supported by small-angle X-ray scattering data and driven molecular dynamics simulations. The loss of ligand interactions results in helical uncoiling of P5 and disruption of the key tertiary interaction between the sensory domains. Opening of the aptamer propagates to the gene-regulatory P1 helix and generates the key conformational flexibility needed for the switching behavior. Much of the ligand-binding site at the three-way junction is unaltered, thereby maintaining a partially preformed pocket. Together, these results paint a dynamic picture of the ligand-induced conformational changes in TPP riboswitches that confer conditional gene regulation.