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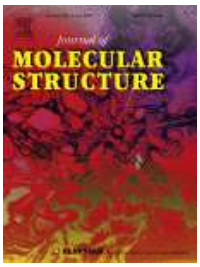

Identify the effect of As(III) on the structural stability of monomeric PKM2 and its carcinogenicity: A molecular dynamics and QM/MM based approach

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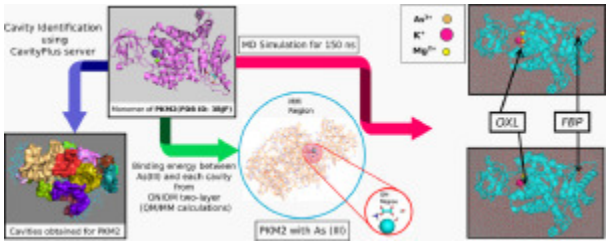
Abstract

Pyruvate Kinase M2 (PKM2) isozyme is categorized under the pyruvate kinase family, and it catalyzes the final step in the glycolysis process. PKM2 enzyme is highly expressed in tissues with anabolic functions like embryonic cells and cancer cells. Experimentalists have identified PKM2 as an arsenic binding protein. However, the exact binding site is still being debated. The findings in this study confirm the binding of As(III) with monomeric PKM2. It identifies the most favorable binding site of the enzyme for As(III) using quantum mechanics-molecular mechanics based calculations. And, the structural analysis based on trajectories of 150 ns molecular dynamic simulations shows that the monomeric PKM2 with As(III) is less stable than the free PKM2 enzyme. Therefore, this study suggests that the PKM2 monomer gets destabilize in the presence of As(III) and hence the destabilization of monomeric form does not cause cancer.

Graphical abstract



Keywords

Pyruvate kinase M2 isozyme
Molecular dynamics simulation
CavityPlus web server
ONIOM two-layer
Stride server