SUMOylation of LKB1: Computational Insights towards Cell Growth Regulation

Bita Amiri Hazaveh
Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Maryam Azimzadeh Irani *
Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Mahdieh Alamdari
Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Abstract

SUMOylation, a reversible post-translational modification in which SUMO (Small Ubiquitin-Like Modifier) covalently attaches to substrate proteins, modulates diverse cellular functions. LKB1 (also known as STK11), a tumor suppressor kinase, plays a critical role in cell polarity, energy metabolism, and growth regulation. In this study, we performed a computational analysis to investigate the structural and functional impact of SUMOylation of LKB1 on its interaction with key partners MO25 and STRADα. Structural models of LKB1, SUMO1, MO25, and STRADα were obtained from the PDB, and SUMOylation was modeled by linking SUMO1 to lysine 178 of LKB1. Molecular docking revealed that SUMOylation significantly reduced the binding affinity and stability of the LKB1-MO25 and LKB1-STRADα complexes, as indicated by increased RMSD and decreased buried surface area. Residue-level interaction analysis further confirmed altered binding interfaces upon SUMOylation. These findings suggest that SUMOylation of LKB1 may regulate its activity by modulating complex stability and partner interactions.

Keywords

LKB1, molecular modeling, post-translational modification, SUMOylation.