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Structural Insights into kinase domain of RIP1

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Abstract

The receptor-interacting protein kinase 1 (RIP1) plays a crucial role in cellular signaling pathways, particularly in regulating apoptosis and necroptosis [1]. Understanding the structural dynamics of kinase domain of RIP1 is essential for elucidating its functional mechanisms and therapeutic potential [2, 3]. This study aims to compare the structural characteristics of the native RIP1 kinase domain with the S166A mutant variant, utilizing molecular dynamics simulations (Gromacs-2019.2) to analyze key biophysical properties.

Results reveal significant differences in the root mean square deviation (RMSD), radius of gyration (R_g), and root mean square fluctuation (RMSF) between the native and mutant forms. The RMSD analysis indicates a more stable conformation for the native kinase domain, while the S166A mutant exhibits increased fluctuations, suggesting a potential loss of structural integrity. The S166A mutation results in decreased hydrogen bond numbers (H-bonds) and a lower R_g value, suggesting a more compact and stable conformation than the native structure. Additionally, the analysis of the solvent-accessible surface area (SASA) further corroborates these findings, indicating enhanced exposure of hydrophobic regions in the mutant.

In conclusion, our findings provide valuable insights into the structural implications of the S166A mutation in the kinase domain of RIP1. These results underscore the importance of specific residues in maintaining the stability and functionality of the kinase domain, offering potential avenues for targeted therapeutic strategies in diseases associated with dysregulated RIP1 activity.

Key words: RIP1, Kinase Domain, Mutant^{S166A}, MD simulation

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