

Peer Review

Review of: "New Approach for Targeting Small Molecule Candidates for Intrinsically Disordered Proteins"

Hany Akeel Al-hussaniy¹

1. University of Baghdad, Iraq

This study presents an innovative computational strategy employing the Informational Spectrum Method for Small Molecules (ISM-SM) to identify potential modulators of intrinsically disordered proteins, particularly the tau protein associated with Alzheimer's disease. The manuscript addresses a critical challenge in modern drug discovery, as IDPs lack stable binding pockets and remain difficult targets for conventional structure-based screening approaches. The integration of spectral compatibility analysis with large database screening, including DrugBank and COCONUT, represents a creative and scientifically relevant methodology that successfully identified both known and novel candidate compounds such as bryostatin-14. The manuscript is generally well-structured and demonstrates strong theoretical and computational foundations; however, several areas could be strengthened. In particular, clearer justification of frequency selection criteria, expanded methodological transparency regarding scoring thresholds and database filtering, and improved discussion of the biological relevance and mechanistic implications of identified hits would enhance interpretability. Additionally, while the *in silico* findings are promising, the absence of experimental or independent computational validation limits translational confidence. Inclusion of docking studies, molecular dynamics simulations, or preliminary biochemical validation would substantially reinforce the study's impact. Overall, this work provides a valuable conceptual contribution to IDP-targeted drug discovery and highlights ISM-SM as a potentially complementary tool within integrated therapeutic discovery pipelines.

Declarations

Potential competing interests: No potential competing interests to declare.