frontiers | Frontiers in Physics

TYPE Editorial
PUBLISHED 08 July 2024
DOI 10.3389/fphy.2024.1439802

OPEN ACCESS

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RECEIVED 28 May 2024
ACCEPTED 19 June 2024
PUBLISHED 08 July 2024

CITATION
Arumugam MP, Vetrivel U, Jeyaraman J, Chauhan SC and Mannu J (2024), Editorial: Interaction and dynamics of biological molecules.
Front. Phys. 12:1439802.
doi: 10.3389/fphy.2024.1439802

Editorial: Interaction and dynamics of biological molecules

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KEYWORDS

molecular dynamics simulation, spike-hACE2, TOP2A, ovarian cancer, NARF, nutraceutical, glioma, D-alpha-Tocopherol acetate

Editorial on the Research Topic
Interaction and dynamics of biological molecules

Introduction

The investigation of molecular interactions and dynamics of biological macromolecules is a cornerstone of contemporary biomedical research, offering profound insights into the fundamental mechanisms of life and disease. This research delves into the critical role of protein-protein interactions and protein dynamics in cellular function, disease pathogenesis, and therapeutic development. By leveraging advanced computational techniques such as molecular dynamics (MD) simulations, docking studies, and *in silico* analyses, researchers can decode the complex behaviors of proteins and their interactions at an atomic level, facilitating the design of targeted and effective therapeutic strategies. This method is crucial for identifying potential drug candidates by predicting their binding affinity to target proteins, which is essential for their therapeutic efficacy. They facilitate the identification of deleterious mutations in TOP2A, evaluation of nutraceuticals for glioma treatment, design of a protein-based vaccine for breast cancer, and understanding temperature effects on SARS-CoV-2 interaction. By accurately predicting protein-drug interactions, these computational approaches guide the selection of promising candidates, enhance therapeutic efficacy, and accelerate the drug discovery process, ultimately contributing to the development of more targeted and effective treatments for various diseases. Understanding the precise manner in which a drug interacts with its target protein is crucial for optimizing its efficacy and minimizing off-target effects.

Evaluating the spike–hACE2 interactions in the wild type and variants of concern of SARS -CoV-2 at different temperatures (Mandal et al.).

This research examines the impact of temperature on the interaction between the SARS-CoV-2 Receptor Binding Domain (RBD) and the human Angiotensin Converting Enzyme 2 (ACE2) receptor using atomistic simulations. The study focused on both the wild-type and

variants of concern of SARS-CoV-2 at different temperatures. Findings revealed that while high temperatures did not cause significant conformational changes in the protein complexes, they did increase the proteins' dynamics, leading to a reduction in protein-protein contacts and interaction energies. Despite these changes, the protein-protein interaction remained relatively strong. These insights are valuable for understanding viral protein behavior and aiding the design of peptide-based vaccines and therapeutics.

Insights into the structure-function relationship of missense mutations in the human TOP2A protein in ovarian cancer (Kavitha et al.).

Topoisomerase 2-alpha (TOP2A) is crucial for maintaining DNA topology and is notably upregulated in ovarian cancer, with its copy number serving as a key prognostic indicator. An *in silico* analysis of 193 nonsynonymous SNPs in TOP2A identified four potentially damaging variants (Y481C, N7741, E922K, and R1514W), with Y481C and E922K being highly deleterious and destabilizing the protein. Structural modeling and molecular dynamics simulations showed that these mutants exhibit small structural variations and reduced stability. Molecular docking indicated that these mutations could confer resistance to etoposide, a TOP2A-targeted chemotherapeutic. qRT-PCR confirmed a threefold increase in TOP2A expression in ovarian adenoma cancer cells. These findings suggest that Y481C and E922K significantly impact TOP2A function and may contribute to ovarian cancer pathogenesis.

Tackling suppressive cancer microenvironment by NARF-derived immune modulatory vaccine and its validation using simulation strategies (Paranthaman et al.).

This research focuses on developing an immunotherapy targeting the tumor microenvironment in breast cancer stem cells (CSCs) by utilizing the nuclear prelamin A recognition factor (NARF). The study identified epitope regions in the NARF protein capable of stimulating T and B cells, which were then fused with adjuvants (RpfB and RpfE) and linkers (AAY, GPGPG, KK, and EAAAK) to construct a vaccine. The vaccine's physicochemical properties and population coverage were assessed, and its interactions with toll-like receptors (TLRs) were explored through computational studies. Docking studies, molecular dynamics, and immune simulation analyses were performed to understand the vaccine's mechanism of action, structural stability, and immune response. The vaccine was then back-translated, codon-optimized, and introduced into a pET-28 (+) vector. The findings suggest that the NARF protein-based vaccine could effectively provoke immune responses in the target organism via TLR-7 binding and MHC class-II mediated antigen presentation, presenting a promising approach for future immunotherapy development.

Exploring the potential of nutraceutical to combat gliomas: focus on mIDH2 protein (Murali et al.).

This study investigates the potential of nutraceuticals to enhance the efficacy of existing glioma treatments, particularly targeting mutations in the Isocitrate Dehydrogenase 2 (IDH2) enzyme, which is linked to various malignancies including glioma. Enasidenib, the current FDA-approved drug for IDH2, has limitations due to poor brain penetration and toxicity. The study evaluated the binding affinity and free energy of various nutraceuticals through molecular docking and MM-GBSA analysis, identifying 14 compounds for further assessment. Using machine learning-based rescoring, pharmacokinetic and toxicity analysis, and virtual cell line assays, DB14002 (D-alpha-Tocopherol acetate, a Vitamin E analog) emerged as a promising candidate. It demonstrated good binding affinity, brain penetration, and antineoplastic activity against glioma. Conformational stability and dynamic characteristics of DB14002 were confirmed over 250 ns, suggesting its potential as a synergistic drug-like candidate for mIDH2 inhibition in glioma treatment.

Conclusion

Molecular docking and molecular dynamics simulations are transforming the landscape of drug discovery and development. These techniques provide insights into the interactions and dynamics of biological macromolecules, enabling the design of more effective and safer therapeutic strategies. By leveraging the advantages of these computational methods, researchers can identify better drug candidates, optimize their binding modes, and reduce the likelihood of adverse effects. The integration of these techniques into drug discovery and development processes offers significant advantages, from identifying effective binding modes to developing drugs with greater efficacy and fewer side effects. This investigation emphasizes the critical role of these advanced techniques in modern biomedical research and their potential to significantly enhance the efficacy and safety of new therapeutics.

Author contributions

MA: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing–original draft, Writing–review and editing. UV: Data curation, Supervision, Visualization, Investigation, Writing–review and editing. JJ: Data curation, Investigation, Validation, Writing–review and editing. SC: Formal Analysis, Investigation, Visualization, Writing–review and editing. JM: Data curation, Investigation, Writing–review and editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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