

Review Form 3

Journal Name:	Archives of Current Research International
Manuscript Number:	Ms_ACRI_131281
Title of the Manuscript:	A Computational Approach to Identify Small Molecules Interact with the Crystal Structure of Programmed Cell Death Protein 1 as Potential Therapeutics for Cancer Immunotherapy
Type of the Article	Original Research Article

General guidelines for the Peer Review process:

Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guidelines for the Peer Review process, reviewers are requested to visit this link:

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PART 1: Comments

	Reviewer's comment Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.	Author's Feedback <i>(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.	This manuscript is relevant to the field of cancer immunotherapy as it addresses the growing need for small-molecule inhibitors targeting the PD-1/PD-L1 pathway. Given the limitations of monoclonal antibody therapies—such as cost, immune-related adverse effects, and limited administration routes—the study provides a computational workflow that could expedite the discovery of novel small-molecule inhibitors. The integration of pharmacophore-based screening, molecular docking, and ADMET predictions strengthens the study's reliability. However, as an entirely in silico study, the findings require validation through experimental assays.	Agree
Is the title of the article suitable? (If not please suggest an alternative title)	The title is somewhat awkward and grammatically incorrect. A suggested revision is: "A Computational Approach to Identifying Small Molecules Targeting the Crystal Structure of PD-1 as Potential Cancer Immunotherapy Agents." This revision enhances clarity, conciseness, and grammatical correctness.	Agree. Title changed.

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Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.	The abstract provides a well-structured summary of the study, but it could be improved by: <ul style="list-style-type: none">Clarifying that this is a fully in silico study early in the abstract.Clearly stating the significance of computational methods in accelerating drug discovery.Avoiding redundancy; for example, "Further evaluation through in vitro and in vivo studies is necessary" is implied and can be more concisely stated.Improving grammar, particularly in "Discovering a new therapeutic drug is a complex, costly and lengthy process," which could be rewritten as "The discovery of new therapeutic drugs is complex, costly, and time-consuming."	Agree. Changed.
Is the manuscript scientifically, correct? Please write here.	The manuscript is scientifically sound in its use of computational methods such as pharmacophore-based virtual screening and molecular docking. However, the following concerns should be addressed: <ul style="list-style-type: none">The docking results should include a comparative analysis with known PD-1 inhibitors to benchmark binding affinities.A discussion of the limitations of virtual screening and docking (e.g., potential false positives) should be included.The study does not confirm that the identified compounds will exhibit strong binding in biological systems; experimental validation is essential.	Agree. Changed. To our knowledge, no small molecule PD-1 inhibitors have been approved so far.
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.	The manuscript references a sufficient number of recent studies, particularly in the field of computational drug discovery and PD-1/PD-L1 inhibition. However, additional references discussing previous attempts at small-molecule inhibitors for PD-1/PD-L1 should be included to provide broader context.	To our knowledge, no small molecule PD-1 inhibitors have been approved so far. The introduction section covers previous efforts to develop small-molecule inhibitors targeting the PD-1/PD-L1.
Is the language/English quality of the article suitable for scholarly communications?	The manuscript requires grammatical corrections to enhance readability. Examples of awkward phrasing include: <ul style="list-style-type: none">"To date, immune checkpoint inhibitors are monoclonal antibodies that cover various cancer indications as monotherapy or in combination, have revealed remarkable clinical success..." (This sentence is convoluted and should be rewritten for clarity.)"Due to the inherent limitations of antibodies, it is reasonable to consider discovering orally bioavailable small molecule inhibitors..." (Consider rewording to: "Given the limitations of antibody therapies, orally bioavailable small-molecule inhibitors present a viable alternative.") A thorough proofreading and revision for fluency and coherence are recommended.	Agree. Changed. Editors can further edit for proofreading.
Optional/General comments	Figures should be better labeled and referenced in the text to ensure clarity. The discussion should include potential next steps for experimental validation. Consideration should be given to the selectivity of identified compounds for PD-1 over other immune checkpoints.	Agree.

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	(If yes, Kindly please write down the ethical issues here in details)	NO