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| Book Name: | [**Medical Science: Trends and Innovations**](https://www.bookpi.org/bookstore/product/medical-science-trends-and-innovations-vol-1/) |
| Manuscript Number: | **Ms\_BPR\_4559** |
| Title of the Manuscript:  | **Impact of TP53 Gain-of-Function Mutations on Metabolic Reprogramming in Prostate Cancer Progression** |
| Type of the Article | **Book Chapter** |

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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 *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **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 addresses a critical gap in understanding how TP53 gain-of-function mutations drive metabolic reprogramming in prostate cancer. Which is a major factor in therapy resistance. This work provides potential biomarkers for prognosis and therapeutic targets by identifying specific metabolic alterations linked to R175H and R273H mutants. These could improve treatment strategies for aggressive, castration-resistant prostate cancer. These findings are relevant to researchers and clinicians aiming to combat metabolic adaptation in advanced prostate cancer. |  |
| **Is the title of the article suitable?****(If not please suggest an alternative title)** | The title is suitable but could be more precise. Suggested revision:**"Impact of *TP53 R175H* and *R273H* Gain-of-Function Mutations on Metabolic Reprogramming in Prostate Cancer Progression"** |  |
| 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 is well-structured but could be enhanced by:1. Briefly mentioning the methodology (e.g., LC-MS metabolomics in PC3 cell models) and stating the clinical implications of identifying pseudouridine/spermidine as biomarkers.
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| **Is the manuscript scientifically, correct? Please write here.**  | The study is scientifically rigorous, but the following should be addressed:1. **Figures**: Ensure all referenced figures (e.g., heatmaps, volcano plots) are included and clearly labeled in the final submission.
2. **Claims**: Some statements in the discussion (e.g., NADP+ downregulation increasing oxidative stress) need direct experimental validation in this study.
3. **Clarify**: Specify whether metabolite changes are causal or correlative to TP53 mutations.
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| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.****-** | References are mostly up-to-date |  |
| Is the language/English quality of the article suitable for scholarly communications? | The language is scholarly but requires minor edits |  |
| Optional/General comments | 1. **Limitations**: Acknowledge limitations, such as the use of a single cell line (PC3) and lack of in vivo validation.
2. **Clinical Relevance**: Expand on how pseudouridine/spermidine could be translated into clinical biomarkers or therapeutic targets.

The manuscript is well-written and addresses an important topic in prostate cancer research. It provides valuable insights into the metabolic consequences of TP53 gain-of-function mutations, with potential implications for therapeutic targeting. However, minor revisions are required to improve clarity, address methodological details, and strengthen the discussion. Specifically:1. Ensure all figures are included and clearly labeled.
2. Clarify the causal vs. correlative nature of metabolite changes.
3. Update references marked as "In-press" and include additional relevant literature.
4. Simplify complex sentences and correct minor grammatical errors.

With these revisions, the manuscript will be suitable for publication. |  |

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| **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)* |  |

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| **Reviewer Details:** |
| Name: | **Kanwal Shabir** |
| Department, University & Country | **GCU, Pakistan** |