Reviewer’s report

Title: Computational analysis of receptor tyrosine kinase inhibitors and cancer metabolism: Implications for treatment and discovery of potential therapeutic signatures

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Reviewer: Mohammad Aziz

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In this manuscript, authors have tried to explore the metabolism related mechanism and pathways that could help understand RTK inhibitors. While at the

1. While authors claimed that "The results reveal the strength of multiple-cancer analysis over conventional signature-based analysis on a single cancer type", there is no convincing clear data to substantiate that claim. They still focused on individual cancers like breast citing the higher incidence.

2. Authors have suggested to better understand the cross talk between signaling and metabolic pathways. It is unclear how this study helps in that direction. Computational metabolic models have been developed to integrate information but have not been discussed here.

3. Claim to discover 'metabolic therapeutic signature; is not well supported by the results. How are the two figures useful in therapy of breast and CNS cancer?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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