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LETTER

Critical Response to Article "Network Pharmacology and Experimental Validation to Explore the Effect and Mechanism of Kanglaite Injection Against Triple-Negative Breast Cancer" [Letter]

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Dear editor

We reviewed the work by Zhao et al[1] about the potential therapy of Kanglaite from the perspective of in silico and in vitro studies. However, given numerous bioactive compounds in herbal medicine with their potential targets, interaction and effects, we noticed that critical points regarding methodology should be addressed properly.

First, the use of term "injection" in the title is quite misleading for readers since there was no Kanglaite administration via injection route in this study. Secondly, dosage standardization should be described in order to get an overview that the experiment had been conducted in reproducible manner.[2] Then, databases other than GEO, ie, DisGeNET should be included so that wider range of candidates for triple-negative breast cancer can be obtained.[3] We tried to re-analyze the GEO dataset and found at least more than 1800 unique gene targets after normalization in GEO2R option (please see the Supplementary File, Suppl_1.xlsx in the sheet norm1 for the unique and normalized targets as well as the sheet not_norm1 for the non-normalized; the remaining sheets, sig_norm denotes the raw list of most significantly expressed genes retrieved from the Volcano Plot exploration window in GEO2R, Annotated_norm for target list with clear gene names and Duplicates_norm for the gene list with duplicate annotation. The sheet for the non-normalized counterparts was provided with the suffix _not_norm). Please note that the non-normalized ones yield higher numbers while in the paper, it is mentioned that 228 plus 53 overlapping targets were retrieved from GEO, making total of only 281 targets. Moreover, we note that around 1500 gene targets were found by using TNBC terms from DisGeNET only, as shown in the Supplementary File, Suppl_1.xlsx in sheet TNBC and TNBCa. Fourth, since this network involved many protein targets and multiple compounds, their interaction prediction could use such designated tools such as STITCH (http://stitch.embl.de/). Fifth, other centrality parameters such as betweenness and closeness should be included when building the network as these may contribute to different ranking of potential nodes.[4]

Lastly, the docking protocol should be validated with native ligand corresponding to its protein target as control and comparison is applied not only to their binding affinity, but also key residues implicated in their interaction at the same binding pocket.[5] Since the results of this study are very promising, we hope that our suggestion can be considered in the future to optimize its findings.

Acknowledgments

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Disclosure

All authors declare that they have no conflicts of interest in this communication.

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