**May 10, 2024**

**Dear Editor-in-Chief,**

Please find enclosed our manuscript entitled “**tigeR: Tumor Immunotherapy Gene Expression Data Analysis R package**”, which we wish to be considered for publication as an “original article” in **iMeta**.

Immunotherapy have yielded substantial therapeutic benefits in advanced cancers, while it shows highly heterogeneous response among various patients and cancer types. Identifying biomarkers and developing robust predictive models to screen out potential immunotherapeutic beneficiaries is of great importance. Advances in high-throughput sequencing technologies, particularly in the context of transcriptomics, have facilitated identification of tumor biomarkers and evaluation of the tumor microenvironment, and thus guiding the development of personalized diagnostic and therapeutic strategies. Numerous web servers, including TIDE, TIMER 2.0, TIRSF, and TIGER, have been developed to integrate high-throughput expression data to assist users in exploring molecular biomarkers related to immunotherapy. However, these tools come with several limitations, including limited flexibility in customizing analyses, potential concerns regarding data security and privacy, processing constraints due to reliance on server-side computational resources.

In this context, we have developed the **Tumor Immunotherapy Gene Expression R package (tigeR)** to address the increasing need for effective tools to **explore biomarkers and construct predictive models** via built-in or custom immunotherapy gene expression data. tigeR encompasses **four distinct yet closely interconnected modules**. The **Biomarker Evaluation module** enables researchers to evaluate whether the biomarkers of interest and **23** build-in signatures are associated with immunotherapy response The **Tumor Microenvironment Deconvolution module** integrates **10** open-source algorithms to investigate the association between immune cell populations and immunotherapy response. The **Prediction Model Construction module** enables users to construct sophisticated prediction models using **7** built-in machine learning algorithms. The **Response Prediction module** predict the immunotherapy response for the patients using pre-trained machine learning models or public gene expression signatures. The source code and example for the tigeR project can be accessed at <http://github.com/YuLab-SMU/tigeR> or http://github.com/canceromics/tigeR.

We believe tigeR, with comprehensive suite of functionalities, could empower users to delve into the intricacies of immunotherapy response by exploring biomarkers, dissecting the dynamics between immune cell populations and treatment outcomes, and constructing predictive models using state-of-the-art machine learning algorithms. tigeR not only streamlines the analysis process but also catalyzes discoveries in the realm of tumor immunotherapy, ultimately contributing to advancements in patient care and outcomes.

We confirm that the work described is original and has not been submitted elsewhere for publication, in whole or in part. All the authors listed have approved the manuscript that is enclosed and have no conflicts of interest.

We deeply appreciate your consideration of our manuscript, and we look forward to receiving comments from the reviewers.

Yours Sincerely,

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