Review of: "A single-cell transcriptomic landscape of innate and adaptive intratumoral immunity in triple negative breast cancer during chemo- and immunotherapies"

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Last year, Falvo and colleagues published in *Cancer Research* a comprehensive study on the effects of chemotherapy and immunotherapy on triple-negative breast cancer (TNBC) murine models, revealing that combinatorial therapy promoted tumor immune response through checkpoint inhibition, antigen presentation, and stem-like CD8+T activation. Based on single-cell transcriptome data in the research, Carpen et al. made further analysis on the transcriptomic features of the tumor immune microenvironment derived from murine breast cancer with different drug efficacies.

This sequencing was based on massive data sequencing two murine models (two cell lines: 4T1 and EMT6) under 17 conditions before and after treatment, including two single-agent group (cyclophosphamide, □PD-1), and six groups with different drug combinations (cyclophosphamide + vinorelbine, cyclophosphamide + □PD-1, cyclophosphamide + vinorelbine + □PD-1, doxorubicin + □PD-1, cisplatin + □PD-1, and paclitaxel + □PD-1). The bioinformatics analysis was based on a total of 48,648 cells and identified several main cellular components in the tumor microenvironment including CD4+ T cells, CD8+ T cells, B cells, and macrophages. However, this research is still a shallow one with shortcomings in integrity, logical precision, and clinical significance.

First, the study seems like a piling-up of results from standard bioinformatics pipelines. Subclustering of cell types was based on automatic assignment, followed by a plain listing of several biomarkers. Indeed, this is an observational study based on data published previously, yet important biomarkers or differentially expressed genes should be focused on with more background information explained, and newly found biomarkers or transcriptomic features should be testified. Secondly, more detailed information is needed to clarify and consolidate the analysis. Dealing with massive data requires accurate thresholds and proper filtering. Usually, not all primary results are meaningful for follow-up research, and tiny adjustments could result in quite different results. Therefore, necessary parameters are required for a comprehensive manuscript. Moreover, since single-cell transcriptomics analysis is mostly based on observational study, many other factors such as post-transcriptional regulation also affect the phenotypes of certain cell clusters, which requires mechanistic studies to validate the biological functions of certain transcriptomic features. Last but not least, the clinical significance of this research is challenged.

Combination therapy and tumor microenvironment have risen to be the hottest topics of oncology, arousing great concerns recently. With the development of second-generation sequencing and public database construction, more attention should be paid to solving problems in clinical practice. Excessive subclusering of cell types is truly valuable only when the biomarkers and biological functions are fully explained. Deep-sequencing provides mountains of data, yet merely presenting and describing is not enough, further filtering, together with a more detailed examination, is desperately desired in the familiar yet unknown field of oncology.

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