POSTER - RNA AND TRANSCRIPTOMICS

COMPARATIVE ANALYSIS OF GENE EXPRESSION IN CACHEXIA AND NON-CACHEXIA MICE MODELS OF COLORECTAL CANCER USING SINGLE-CELL RNA SEQUENCING

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Cancer-associated cachexia (CC) is a multifactorial syndrome characterized by weight loss and is marked by skeletal muscle and adipose tissue wasting and systemic inflammation. Cachexia is responsible for the death of at least 20% of all cancer patients and is prevalent in 50-61% of colorectal cancer patients. The use of colorectal cancer mouse models is an indispensable approach for investigating treatments for cancer cachexia. The literature has established the CT26 tumor model, derived from colon carcinoma cells, as one of the most used and well-established models for studying cachexia. This model promotes a pro-inflammatory response, which plays a critical role in muscle and adipose tissue wasting, and the tumor secretes cachexia-inducing factors (CIFs) as

those found in humans. Emerging technologies like single-cell RNA sequencing (scRNA-seq) have enabled us to gain a more comprehensive and in-depth understanding of the cellular makeup of tumor microenvironments, providing novel insights into regulatory mechanisms. In this study, we used scRNA-seq data (GSE121861) to compare the gene expression profiles of malignant single cells from two mouse models: CT26 (4,479 cells, 2 samples), which induces cachexia, and MC38 (1,310 cells, 2 samples), a non-cachexia model. The scRNA-seq data were processed in Seurat 4.3.0 package (R 4.2.1), including quality control, PCA, clustering, cell type annotation, selection of malignant cells, integration of malignant cells and gene expression analysis. Cell markers from literature were used to annotate malignant cells. The malignant cells from both CT26 and MC38 models were integrated and re-clustered. Next, we identified genes that marked each cluster and differentially expressed genes between each cluster compared to all other cluster were analyzed using the EnrichR online tool (https://maayanlab.cloud/Enrichr/) for ontology (GO Biological Process 2021) and pathways (Reactome 2022). We found that out of the eight clusters examined, clusters 3 and 7 had a predominance of CT26 cells, while the other clusters had a homogeneous cell distribution between the models. Interestingly, cluster 7 showed enrichment for the inflammatory response and activation of the innate immune system pathway, which may be related to cachexia in CT26 model. In conclusion, we found that the gene expression profiles of malignant cells from CT26 and MC38 cell lines, derived from the same tissue, are similar. However, the CT26 model promotes a greater pro-inflammatory response pathway that may be linked to cachexia. Future research into tumor microenvironment and CIFs can provide further insight into the interaction between malignant and immune cells in cancer cachexia models, leading to the development of more effective therapies to combat this debilitating condition.