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TRANSCRIPTOMIC PROFILING OF SQUAMOUS CELL LUNG CANCER

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Objective:

Lung cancer is the leading cause of cancer-related death worldwide. Squamous cell lung cancer (LUSC) accounts for 25-30% of all diagnosed lung cancer cases. It is known that interactions between cancer, immune and stromal cells can impact tumor proliferation and progression, however immune microenvironment of LUSC is still not well characterized. Omics approaches to cancer research started a new era of precision medicine, allowing analysis of large pools of available data. Identification of new predictive and prognostic biomarkers for LUSC using this approach could help optimize therapy decision, since only few targeted therapies were approved for treatment of LUSC specifically so far.

In this study we examined mRNA expression profiles of 23 treatment naive patients diagnosed with primary LUSC and 3 healthy controls using RNA-sequencing approach. We determined total of 1535 differentially expressed genes between patients and controls and interrogated the role of those genes with Gene Ontology analysis. Gene Set Enrichment Analysis (GSEA) was used for further characterization of dysregulated genes. To characterize tumor microenvironment of LUSC, we used ESTIMATE package in R. Both immune and stromal scores, that represent the infiltration level of immune cells and presence of stroma in tumor tissue, showed different patterns in our samples. To elucidate this further we used GSVA (Gene Set Variation Analysis) to test enrichment of 17 immune-related gene sets in our samples.

Our results show that upregulated genes in tumor samples are associated with DNA replication, DNA repair, mitotic cell-cycle process activity and signaling activity. Downregulated genes are associated with signal transduction, immune response activity, cell adhesion and migration activity. GSVA analysis coupled with hierarchical clustering showed four distinct patients subgroups (immune-subtypes) based on levels of immune cells infiltration. Identified immune-subtypes showed significantly different infiltration levels of macrophages, NK bright, NK dim cells, central memory T cells, effective memory T cells, $CD8^+$ T cells and eosinophils. Additionally, in early stage cancer patients upregulation of inflammation-related genes was identified (e.g. CXCL13, CXCR5, IL36G, CXCR3, CCL19, CCR5, IRAK1, CXCL10).