Comparative Analysis of the Subtypes of Esophageal Cancer

Analysing the Tumor Microenvironment of Adenocarcinoma and Squamous Cell Carcinoma using Single-Cell Transcriptomic

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1. INTRODUCTION

Background: Esophageal cancer is a pernicious disease with early recurrence (post-treatment) and a low five-year survival rate[1]. It has two dominant sub-types: Adenocarcinoma (EAC) and Squamous Cell Carcinoma (ESCC) [1].

Problem: ESCC is more susceptible to novel methods like immunotherapy and radiotherapy[1,2].

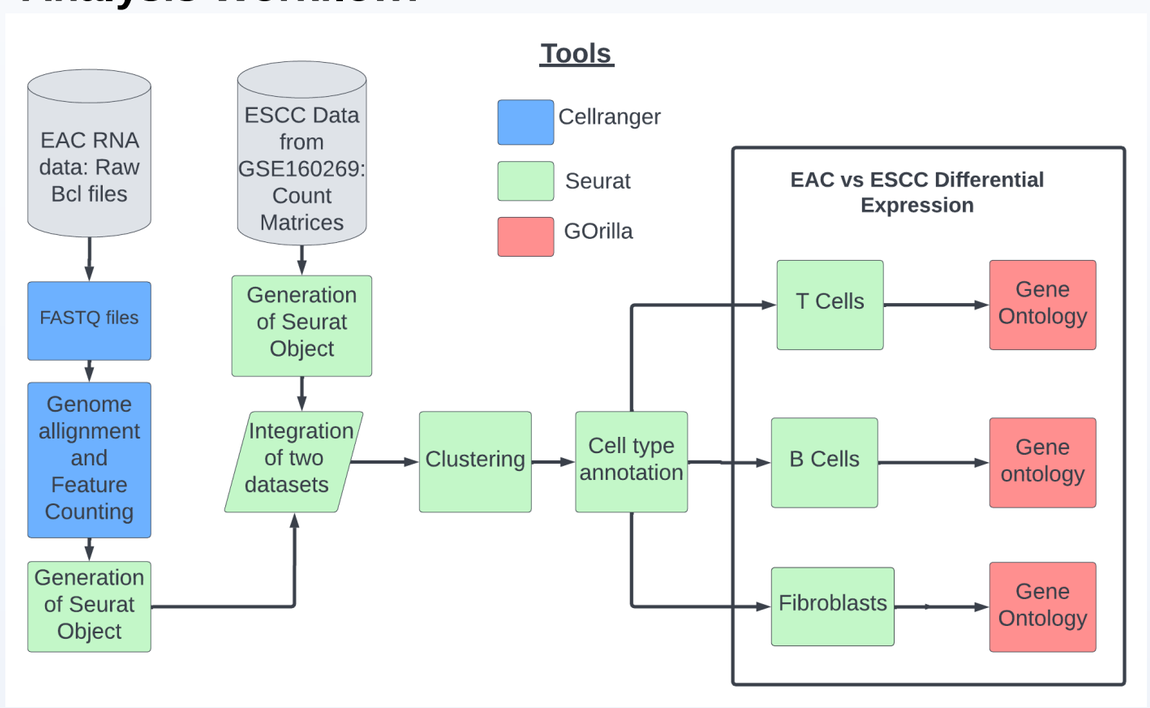
Objective: Find key differences in the cell-type contexture in the tumour microenvironment between EAC and ESCC to identify possible targets for new immunotherapy to offer evidence for ongoing clinical studies.

2. METHODS

Dataset:

- EAC – 65,368 single-cell transcriptomes from Illumina platform derived from 8 tumor samples and 2 adjacent normal tissue samples from 8 patients generated by the Moss Group at the University of Birmingham.
- ESCC - A total of 208,659 single-cell transcriptomes derived from 60 tumor samples and 4 adjacent normal tissue samples from 60 patients published by Zhang et al.[2].

Analysis Workflow:



3. RESULTS

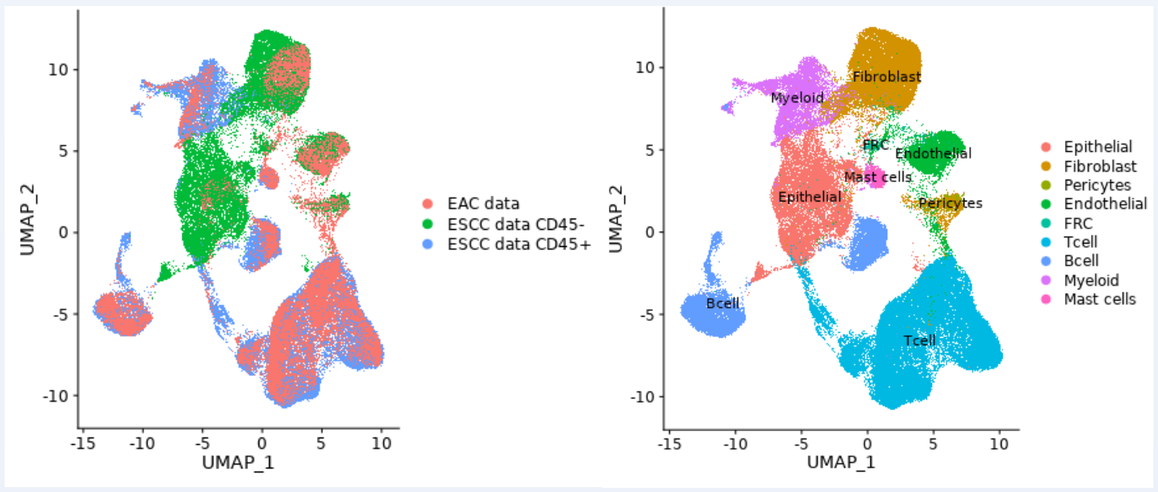
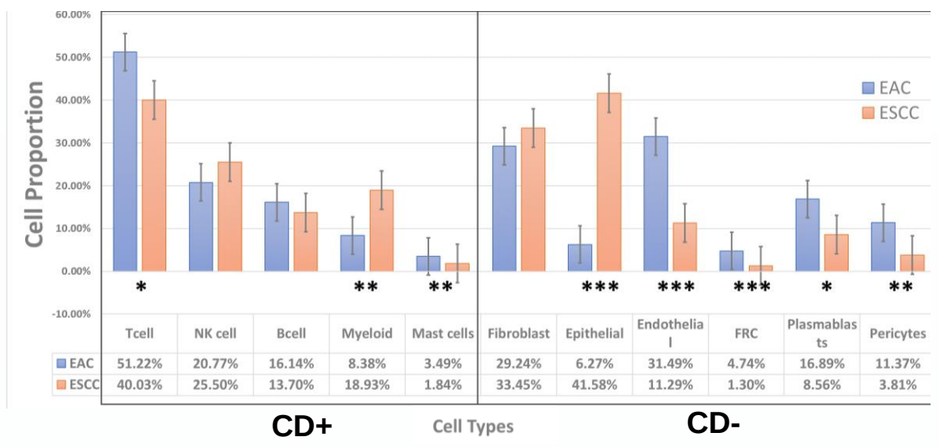


Fig. 1: UMAP embedding overlaid with cancer type and high-level cell type

CD45+ includes B-cells, T-cells, Myeloid, and Mast Cells.
CD45- includes Epithelial cells, Fibroblasts, Endothelial cells, Fibroblastic Reticular cells (FRC), and Pericytes.

3. RESULTS (contd.)



p > 0.05 ** 0.001 < p < 0.01
* 0.01< p< 0.05 *** p < 0.001

Fig. 2: Percentages of Cell Types: EAC vs ESCC in CD+ and CD- clusters
Significant differences in the proportions of cell types in CD+ and CD- clusters between EAC and ESCC

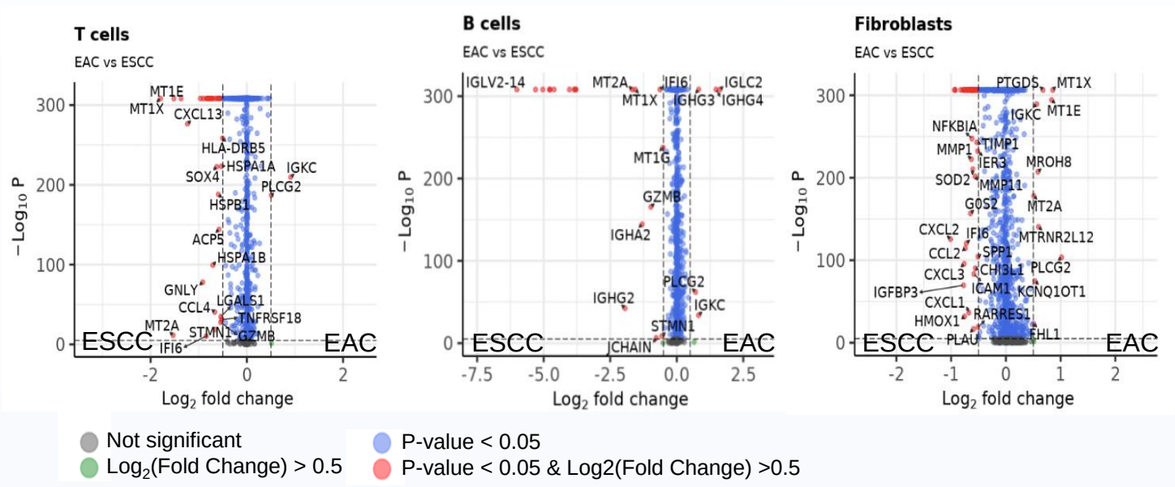


Fig. 3: Differentially Expressed Genes (DEGs) between EAC and ESCC.
Red points represent genes differentially expressed with p-value < 0.05 and $\log_2$(Fold Change) > 0.5.
T-cells have 27 DEGs in ESCC and 2 in EAC.B-cells have 17 DEGs in ESCC and 5 in EAC. Fibroblasts have 39 DEGs in ESCC and 9 in EAC.

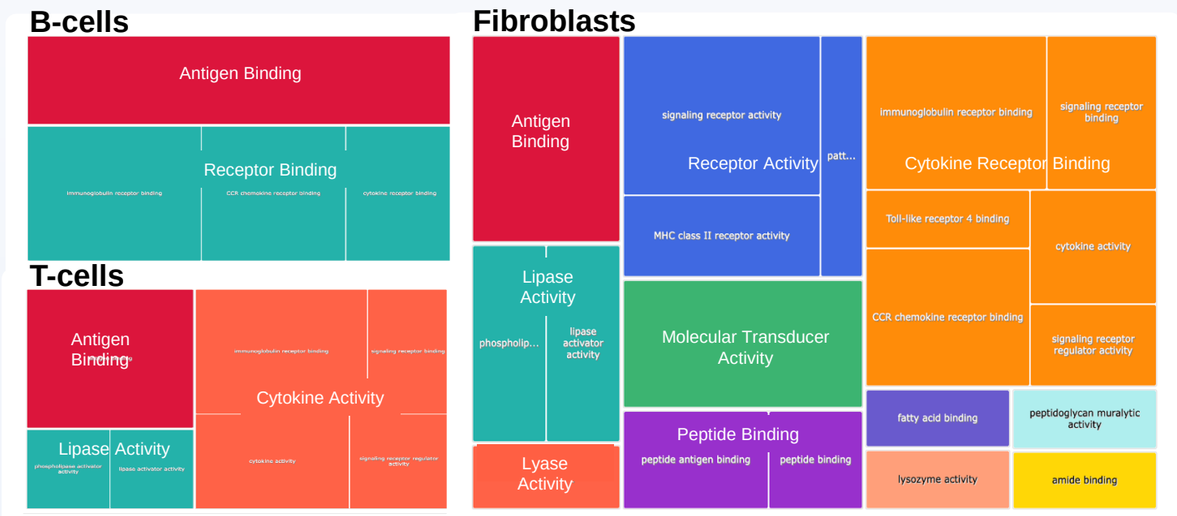


Fig. 4: Gene Ontology Treemap. Terms enriched within differentially expressed genes. Color indicates terms strongly linked and size shows significance of the term.

4. CONCLUSIONS

Cell Proportions: EAC has a greater proportion of T-cells and B-cells with a fold change of 1.84 and 1.69 respectively. While for Fibroblasts, ESCC has a greater proportion with a fold change of 2.07. This suggests that EAC is more immunogenic than ESCC.

Differential Gene Expression: T-cells, B-cells and Fibroblasts showed unique sets of differentially expressed genes that are potential targets for evolving studies.

Gene Ontology Enrichment Analysis: Enriched clusters for DEGs are mostly represented by cytokine activity for T-cells and Fibroblasts.

5. REFERENCES

1. Kelly RJ, Ajani JA, Kuzdzal J, et al. Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer. *New England Journal of Medicine*. 2021;384(13):1191-1203. doi:10.1056/nejmoa2032125

2. Zhang X, Peng L, Luo Y, et al. Dissecting esophageal squamous-cell carcinoma ecosystem by single-cell transcriptomic analysis. *Nature Communications*. 2021;12(1):5291. doi:10.1038/s41467-021-25539-x

6. ACKNOWLEDGEMENTS

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