EN.585. 788: Foundations of Computational Biology and Bioinformatics – Project Proposal
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Cancer cells produce cytokines and chemokines that attract a diverse population of immune cells, including macrophages, neutrophils, and lymphocytes, although other cell types may also be present. However, persistent activation of the immune system and failure of the inflammatory response to resolve can lead to chronic inflammation, which promotes tumor growth.

The intricate interplay between tumor and immune cells in the microenvironment leads to the production of a wide variety of cytokines and growth factors that foster tumor cell proliferation, survival, and metastasis. The complex nature of this communication highlights the significant impact that immune cells have on the tumor microenvironment, with both pro-tumoral and anti-cancer roles.

Recent studies have shown that accounting for the heterogeneity of immune cell infiltration can result in more sensitive survival analyses and more accurate tumor subtype predictions [2,3]. Ongoing research is focused on the role of infiltrating lymphocytes and other immune cells in the tumor microenvironment.

Myeloid cells such as macrophages, monocytes, dendritic cells, neutrophils, basophils, and eosinophils are frequently found in the tissue of various tumors. In malignant tumors, levels of infiltrating immune cells are associated with tumor growth, and cancer progression [6, 8].

Advances in single-cell RNA sequencing and flow cytometry have enabled the identification of various immune cell populations. As a result, numerous methodologies have been proposed to infer the proportions, or deconvolve, individual cell types from bulk RNA-seq samples [1,4,7,8,11].

Our objective is to examine whether the proportions of different cell types are associated with *BRCA*-associated breast cancer and outcome. To investigate this, we will correlate the proportions of each immune cell type with patient-matched overall survival, as profiled by The Cancer Genome Atlas (TCGA). We will control variables such as tumor stage, race, gender, and age, to ensure that immune cell proportions, specifically macrophages, Neutrophils, B lymphocytes, T lymphocytes, and natural killer cells are analyzed as independent prognostic factors for overall survival. Furthermore, we may additionally explore the relationship between somatic mutations, such as single-nucleotide variants (SNVs), mutation clusters, and copy number variations (CNVs) [12] in immune cells and immune cell proportions and cancer subtypes [3].

Our approach will start by identifying relevant single-cell RNA-seq datasets to extract cell-type-specific expression values and cell-type proportions. We will search for these datasets on platforms such as Gene Expression Omnibus (GEO) [9], The Single Cell Portal [13], or in specific past research articles. Alternatively, we plan to use the deconvolution tool, MuSiC [2], which provides both single-cell and bulk RNA-seq datasets. We will compare these single-cell RNA-seq datasets to bulk tumor data for *BRCA*-associated breast cancer from the TCGA. Accurately determining immune cell-type proportions in bulk samples can be challenging, so we will generate pseudo-bulk mixtures with known compositions.

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