**Team 1: Joan, Adi, Aizhan, Gazie**

**Description of Step Four**

1. Compare results of pathway analysis from gene expression data and CIBERSORT analysis.

**a.** **Find pathways from Step 2 that are relevant to CIBERSORT results**

**b.** **Start with Reactome and proceed with Gene Ontology**

2. Generate a table with selected pathways and selected Gene Ontology categories.

**a.** **Explore the relevance of your findings to bladder cancer. Find relevant publications.**

**Table with Pathways**

**T.cells.CD4.memory.resting**

|  |  |  |
| --- | --- | --- |
| **Pathway** | **Description** | **Bladder Cancer Relation** |
| Positive Regulation Of Lymphocyte Differentiation (GO:0045621) | Activates or increases the frequency, rate or extent of lymphocyte differentiation and activated B cells or T cells become specialized immune cells | Lymphocytes as potential targets for immunotherapy, especially with the introduction of systemic immunotherapy that blocks immune checkpoints in bladder cancer |

**Macrophages.M2**

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| **Pathway** | **Description** | **Bladder Cancer Relation** |
| Positive Regulation Of Granulocyte Differentiation (GO:0030854) | The process in which a myeloid precursor cell acquires the specialized features of a granulocyte. Granulocytes are a class of leukocytes characterized by the presence of granules in their cytoplasm. These cells are active in allergic immune reactions such as arthritic inflammation and rashes. | Abnormal expression of cytokines and growth factors can influence the differentiation and function of granulocytes. Dysregulation of these factors may contribute to the tumor microenvironment and impact cancer progression. |
| Negative Regulation Of NF-kappaB Transcription Factor Activity (GO:0032088) | Process that stops/prevents transcription factor NF-kappaB (inflammatory and immune responses) | Interleukins regulate the immune response, crucial for recognizing and eliminating cancer cells. Also, some interleukins can influence cell proliferation and survival |

**T.cells.regulatory..Tregs.**

|  |  |  |
| --- | --- | --- |
| **Pathway** | **Description** | **Bladder Cancer Relation** |
| RUNX1 And FOXP3 Control Development Of Regulatory T Lymphocytes (Tregs) | T lymphocytes (Tregs) that suppress aberrant immune responses | Used by the tumors to aide in immune evasion |
| Transcriptional Regulation Of Granulopoiesis | Development and maturation of granulocytes, particularly neutrophils (type of white blood cell) | Chronic inflammation can recruit & activate immune cells, such as neutrophils |
| Negative Regulation Of CD4-positive, Alpha-Beta T Cell Activation | Process that stops/prevents CD4-positive, alpha-beta T cell activation | Tumors can inhibit T cell activation (immunosuppressive microenvironment) |

**Mast.cells.resting**

|  |  |  |
| --- | --- | --- |
| **Pathway** | **Description** | **Bladder Cancer Relation** |
| Negative Regulation Of NF-kappaB Transcription Factor Activity | Process that stops/prevents transcription factor NF-kappaB (inflammatory and immune responses) | Patients with bladder cancer experience a persistently active NF-κB pathway induced by pro-inflammatory cytokines, chemokines, and hypoxia. Contributes to the amplification of both the formation of cancer and its progression. |
| RUNX1 Regulates Transcription Of Genes Involved In Interleukin Signaling | signaling molecules in both the innate and adaptive immune systems, mediating inflammation in response to a wide range of stimuli | Interleukins regulate the immune response, crucial for recognizing and eliminating cancer cells. Also, some interleukins can influence cell proliferation and survival |

**T.cells.CD8**

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| --- | --- | --- |
| **Pathway** | **Description** | **Bladder Cancer Relation** |
| Positive Regulation Of CD8-positive, Alpha-Beta T Cell Activation (GO:2001187) | The activation of a CD8-positive, alpha-beta T cell upon encountering its specific antigen, mitogen, cytokine, chemokine, or cellular ligand. | In bladder cancer, both anti-tumor T cells (CD8+, cytotoxic CD4+, and Th1) and immunosuppressive Tregs infiltrate tumors concurrently in substantial numbers. |
| Positive Regulation Of CD8-positive, Alpha-Beta T Cell Differentiation (GO:0046638) | Any process that increases the frequency, rate, or extent of CD8-positive, alpha-beta T cell differentiation. This includes processes that promote the development and maturation of CD8-positive T cells from precursor cells. | Adequate positive regulation of CD8+ T cell differentiation is essential for generating a robust anti-tumor immune response in bladder cancer. Insufficient differentiation or functional impairment of CD8+ T cells can contribute to tumor progression and immune escape. |

3. Describe how you worked together as a team and the contributions of each member. We expect all team members to contribute equally so everyone has an opportunity to learn. Describe what challenges you faced and how you overcame them

**How we worked together**

**All -** Plotted cibersort graphs and compared

We researched the top 5 immune cell types and what pathways from reactome and GO BIO were relevant to these cells types. We split it up as follows

**Gazie: T.cells.CD4.memory.resting**

**Joan: T.cells.regulatory..Tregs. & Mast.cells.resting**

**Aizhan: Macrophages.M2**

**Adi: T.cells.CD8**

**All -** researched how the pathways connect to the cancer hallmarks

**Challenges**

* Understanding our stage of bladder cancer (how it differs from the other stages)
  + Overcame this through watching videos/reading articles provided to use as well as doing additional research
* Understanding how the hallmarks of cancer relate to the immune cell types
  + Researched the immune cells types and connected them back what we learned about cancer hallmarks in class