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**F1L Internship Emulator – Week 1 – 7/15/2024 – Key Scientific Question and Memorandum**

**Paraphrase of Key Scientific Question in my own words:**

The goal of week one of the figure one lab internship simulator is to understand the key scientific question of the internship emulator and create a memo about our understanding of it. The key scientific question of the emulator is as follows: given data in the form of single cell RNA sequencing, how might I as the intern explore the usage of FDA-approved antibody therapies outside of their prescribed approval? This is to say, how might I explore their (Trastuzumab & Bevacizumab) monoclonal antibody therapies in other cancers for which they are not also approved?

**Current Understanding:**

My current understanding: it is my current understanding that in order to target a given cancer with a given monoclonal antibody therapeutic, the cancer must express the target gene as a cell surface protein to facilitate binding. As in the figure one lab information, “Trastuzumab targets HER2 and is used in the treatment of HER2-positive breast and gastric cancers.” It would therefore be inappropriate to treat HER2 negative cancers with this antibody therapy, as the antibody could not bind to the tumor cell, and the anti-tumor mechanism of action is lost.

Investigations into targeting of other cancers therefore, will involve confirming that HER2 (Trastuzumab) and/or VEGF (Bevacizumab) are indeed expressed by these cancer types. Cancer is complex in that among the same type of cancer, certain tumors will express a given gene while others may not (e.g. via some deletion or mutation). It is for this reason that certain therapeutics may not be prescribed without first completing tumor genotyping.

**Helpful Resources:**

[**https://sites.broadinstitute.org/ccle/**](https://sites.broadinstitute.org/ccle/)

(from F1L resources)

[**https://www.sc-best-practices.org/preamble.html**](https://www.sc-best-practices.org/preamble.html)

(not from F1L resources)

**Elements of the KSQ which are still unclear:**

A bit outside the scope of this but I’m going to use this section to “thought dump” here and explore some interesting questions (or perhaps shortcomings in my own knowledge):

1. Let’s say for example we have a known cell surface protein of interest. Is the protein’s presence, as measured via its precursor molecule mRNA, synonymous with finding it as a cell surface protein? Is this an assumption or is it axiomatic?
2. Are there cell surface proteins which are also secreted from the cell?