Lab 6- Amino Acid Substitutions of STAT2 in Cancer

STAT2 is a transcription factor in the type I interferon pathway. When an individual is exposed to a virus, inflammatory cytokines called type-I interferons stimulate the cell and set off an intracellular signaling cascade. STAT2 is one of the proteins involved in this cascade and is responsible for binding to DNA and initiating the transcription of interferon stimulated genes in response to infection.

STAT2 expression is found to be altered in inflammatory bowel disease as well as several types of cancer suggesting it plays a role in additional, and perhaps, unknown biochemical pathways. The data analyzed in this figure was collected (by myself under the supervision of Ana Gamero, PhD) from the cBioPortal for Cancer Genomics and includes a list of all point mutations of STAT2 found in tumor tissue samples across all cancer types.

There are six characterized regions or domains of STAT2 which are associated with a particular protein function. These functions are often defined by the composition of amino acids in the region e.g. nonpolar amino acids participate in nonpolar interactions, charged amino acids participate in ionic interactions. The objective of this analysis was to determine 1) if any of the amino acid substitutions found in cancer were significant i.e. changes from one class of amino acid to another and 2) what kind of substitutions those were i.e. polar to nonpolar, charged to uncharged, special* amino acid to any other amino acid.

There appears to be a large number of ‘change in polarity’ substitutions in the DNA-binding domain (DBD). This is the region of STAT2 which associates with other proteins in order to bind DNA. Perhaps amino acid substitutions in this region alter the efficacy of DNA-binding of STAT2. Additionally, there is a large number of substitutions in Src-homology 2 domain (SH2), many of which are a change in charge. As this domain is named for its genetic similarity to other STAT proteins, a high frequency of substitution could indicate a deviation of mutant STAT2 from its ancestral function.

*Special amino acids refer to cysteine (C), glycine (G), and proline (P) which are often important to secondary structure and protein folding. These are excluded from the other amino acid classes due to their unique structures.

cBioPortal query where mutation data was extracted from:
https://www.cbioportal.org/results/mutations?tab_index=tab_visualize&Action=Submit&session_id=6219519604dc35387468addd&plots_horz_selection=%7B%7D&plots_vert_selection=%7B%7D&plots_coloring_selection=%7B%7D