

The Atlas of Protein-Protein Interactions in Cancer

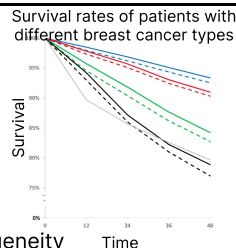
A web app to visualize & analyze cancer subtypes

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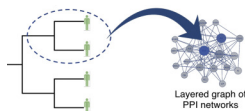
Patients within a shared cancer type display heterogeneity

- Patients affected by shared cancer type show differences in survival rates, genetic profiles, histology features¹
- Patients likely cluster into subgroups
 - Mechanisms may share traits, but likely have differences driving patient heterogeneity
- A need to understand cancer types at subtype level



Defining cancer subtypes using protein-protein interactions (PPI)

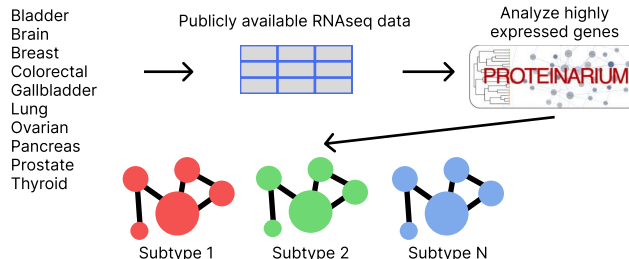
- GWAS is popular but not good enough: identify too many genes, each with little inheritance
- Proteinarium²
 - Uses patient RNAseq data, analyzes highly expressed genes
- clusters patients into subgroups & builds their shared protein-protein interaction (PPI) network



Objective

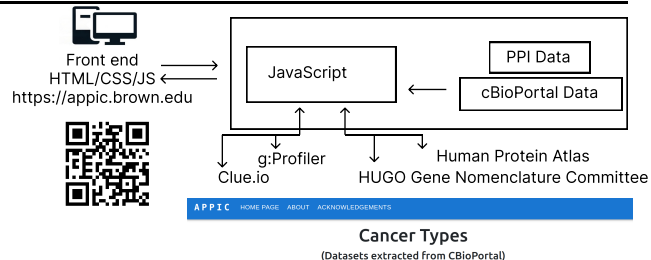
- Existing cancer database tools only aggregate data and fail to define cancer mechanisms³

Defining the protein-protein interactions of 26 subtypes across 10 tissue types

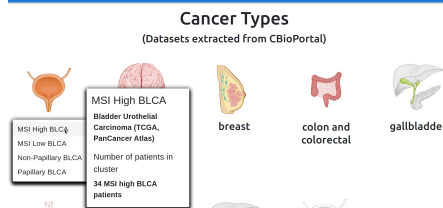


- Patients with similarly expressed genes are clustered into subtypes
- Final output for each subtype includes list of protein-protein interactions, gene names, patientIDs
- 10 tissue types; 26 total cancer subtypes

Developing a web app to display PPIs

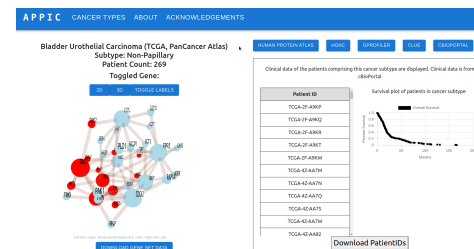


- Interacts with databases & PPI data in real time



Web app visualizes PPIs and aggregates relevant info from databases

- Visualization as 2/3D network diagram
- Integration of biological and clinical databases
 - Human Protein Atlas**: protein info
 - HUGO Gene Nomenclature Committee**: protein info
 - Clue.io**: drug repurposing
 - g:Profiler**: pathway analysis
 - cBioPortal**: clinical data



APPIC advances mechanistic understanding & therapy development of cancer subtypes

- PPIs identify **hub proteins** which could be key to understanding specific mechanisms driving cancer subtypes
- Clue.io uses a drug database with to **identify drugs with relevant gene/protein targets**
- cBioPortal enables analysis of survival rates & **clinical endpoints**
- Future work: expand the number of cancer subtypes

Citations

- Howlader, N., et al. (2018). Differences in Breast Cancer Survival by Molecular Subtypes in the United States. American Association for Cancer Research, 27(6), 619-626.
- Armanious, D., et al. (2020). Proteinarium: Multi-sample protein-protein interaction analysis and visualization tool. Genomics, 112(6), 4288-4296.
- Jensen, M. A., et al. (2017). The NCI Genomic Data Commons as an engine for precision medicine. Blood, 130(4), 453-459.

Gather patient RNAseq data of shared cancer type (cBioPortal)

Use Proteinarium to define cancer subtypes & PPIs

Program web app tool to visualize PPIs & analyze subtypes