Transforming public patient omic data into precision oncology targets: A comprehensive pan-cancer approach

MOLECULAR ANALYSIS FOR PRECISION ONCOLOGY CONGRESS 2024 MAP

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Introduction

- The shift toward precision oncology requires the identification of **novel, highly specific drug targets**.
- Publicly available transcriptomic data offer a rich resource for identifying such targets, yet they remain largely underutilized.
- To address this, we present a **scalable, data-driven platform for pan-cancer antigen target discovery** leveraging the **untapped potential of public transcriptomic data,** along with extensive biological and pharmaceutical knowledge.
- This approach was systemically applied to **cohorts of patients spanning 18 indications**, which were all stratified and analyzed.

Methods

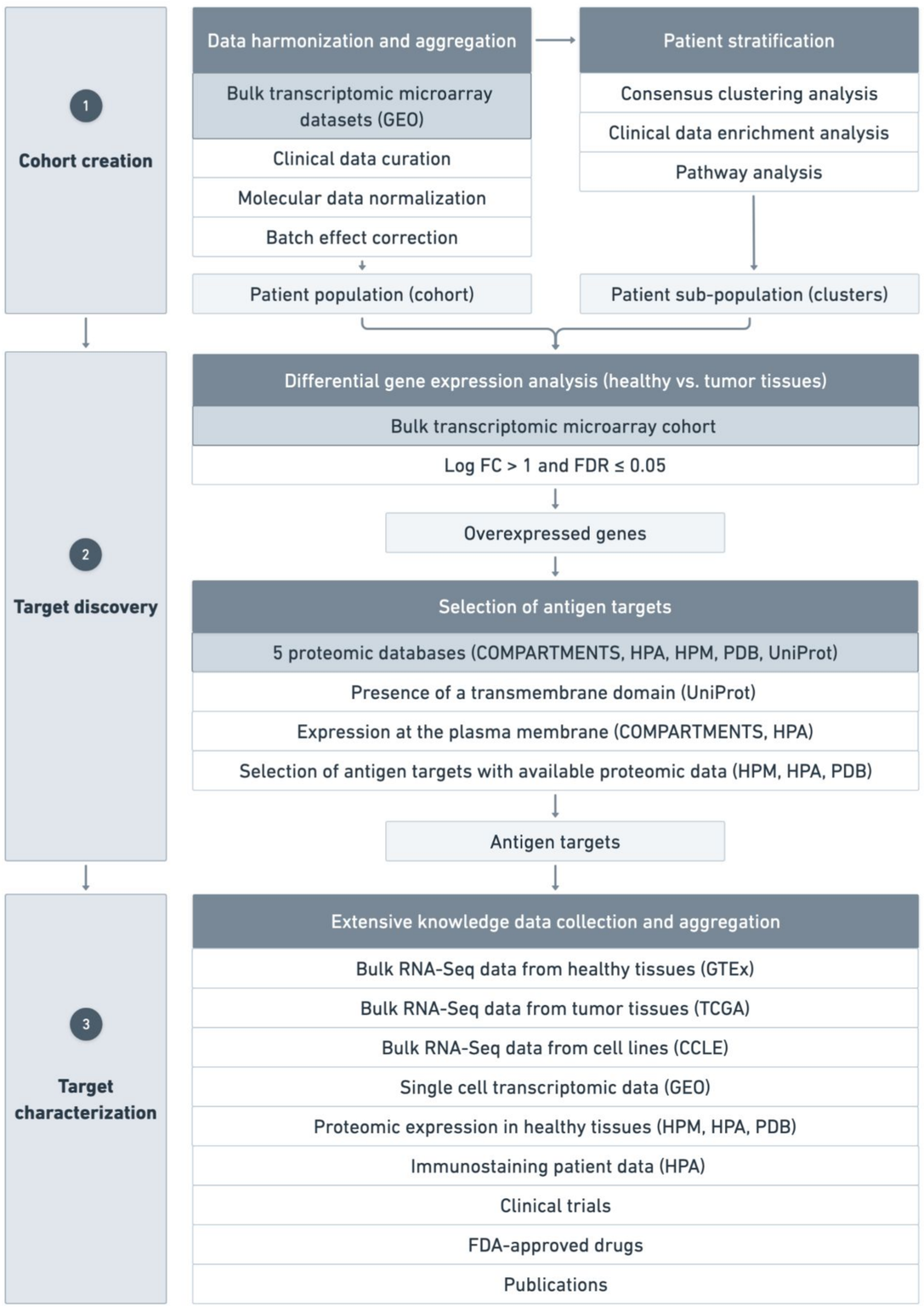

Figure 1: Epigene Labs' antigen target discovery platform
(Log FC = Log Fold Change, FDR = False Discovery Rate, HPA = Human Protein Atlas, HPM = Human Proteome Map, PDB = Protein Data Bank, GTex = Genotype-Tissue Expression, TCGA = The Cancer Genome Atlas , GEO = Genome Expression Omnibus, CCLE = Cancer Cell Line Encyclopedia, FDA = Food and Drug Administration)

Conclusion

- Our target discovery pipeline **re-discovered FDA-approved and clinically investigated targets** alongside **novel targets** with promising profiles.
- Developing scalable pipelines remains instrumental in the advent of precision oncology.
- Combining **unbiased data-driven tools with cancer biology-driven** approaches, our state-of-the-art platform can be used for **any cancer type and antigen-targeting modality**, including antibody-based therapies.
- The present study illustrates the potential of our platform to leverage our 18 large and unique patient cohorts.
- We are not only able to **detect relevant subgroups of patients, but also identify novel antigen target candidates** for these specific populations exemplifying its potential to accelerate oncology drug discovery.

References

1. A. Talbot et al. Integrating Transcriptomics and Proteomics for the Discovery of Novel Antigen Targets on Surface of Malignant Plasma Cells Amenable for Chimeric Antigen Receptor-T (CAR-T) Cell Approach in the Treatment of Patients with Relapsed/Refractory Multiple Myeloma. Blood 2022; 140 (Supplement 1): 7094–7095.
2. **Poster #1915 -** E. Fox, L. Meunier et al. A scalable pan-cancer antigen target discovery platform for precision oncology. **AACR 2024.**
3. **Poster #6209** - L. Meunier et al. From data disparity to data harmony: A comprehensive pan-cancer omic data collection. **AACR 2024.**

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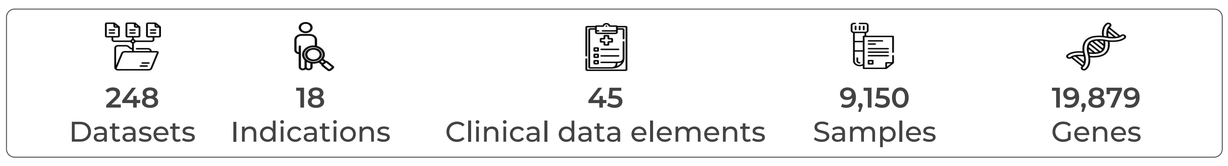
The authors have no conflict of interest to declare.

Results

1. Cohort creation



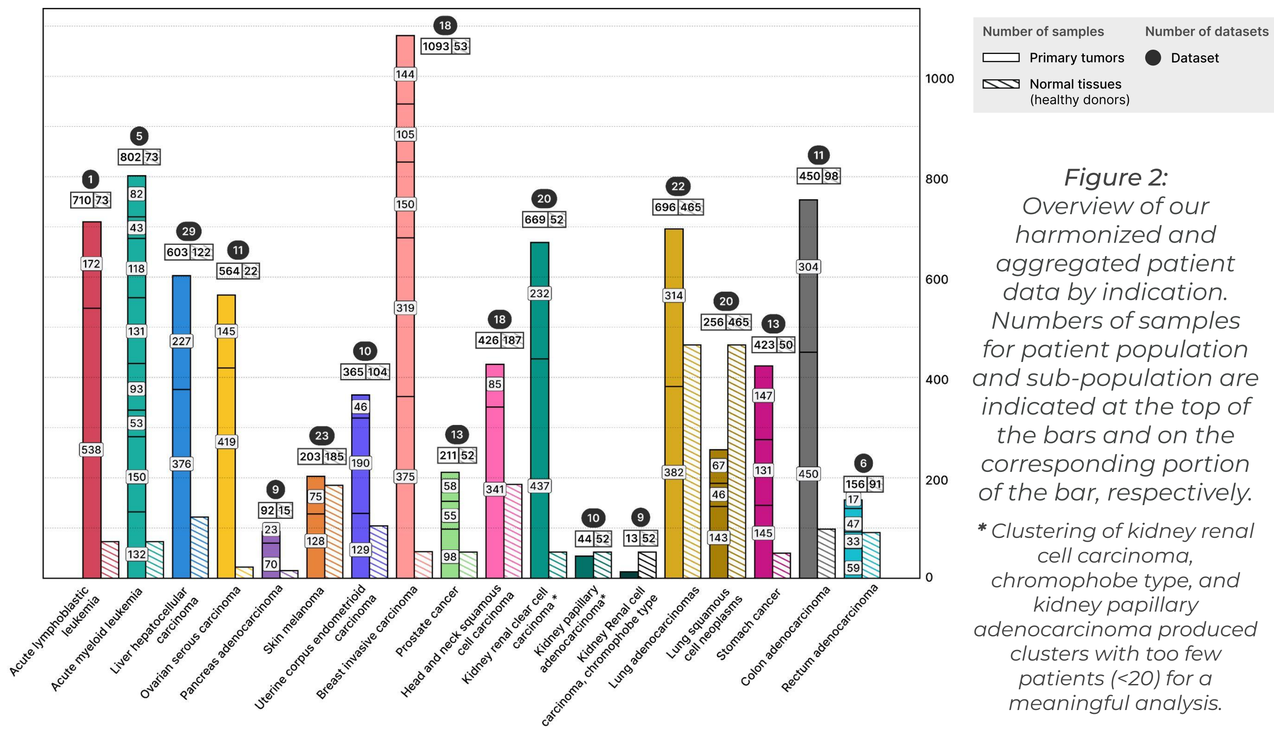


Figure 2: Overview of our harmonized and aggregated patient data by indication. Numbers of samples for patient population and sub-population are indicated at the top of the bars and on the corresponding portion of the bar, respectively.

** Clustering of kidney renal cell carcinoma, chromophobe type, and kidney papillary adenocarcinoma produced clusters with too few patients (<20) for a meaningful analysis.*

2. Target discovery

- An average of **204 potential antigen targets** identified across all indications.
- A total of **935 targets** matched to 2+ indications demonstrating the **tissue-agnostic potential** of certain antigen targets.
- All clusters found to be **associated with at least one clinical data element and/or one relevant biological pathway** (*e.g.* poor overall survival, molecular subtypes, translocations).
- In all indications, stratification resulted in **higher target counts**, ranging from **1.7x to 21x**, with an average of **3 clusters** and **160 potential targets** per cluster → reducing the cohort heterogeneity increases the potential antigen target discovery rate.
- Successful identification of **7 FDA-approved antigen targets**, including **ERBB2** and **TACSTD2** in breast invasive carcinoma, **CD19** and **CD22** in acute lymphoblastic leukemia, **CD33** in acute myeloid leukemia, **CD274** in skin melanoma, and **PSMA** in prostate cancer.

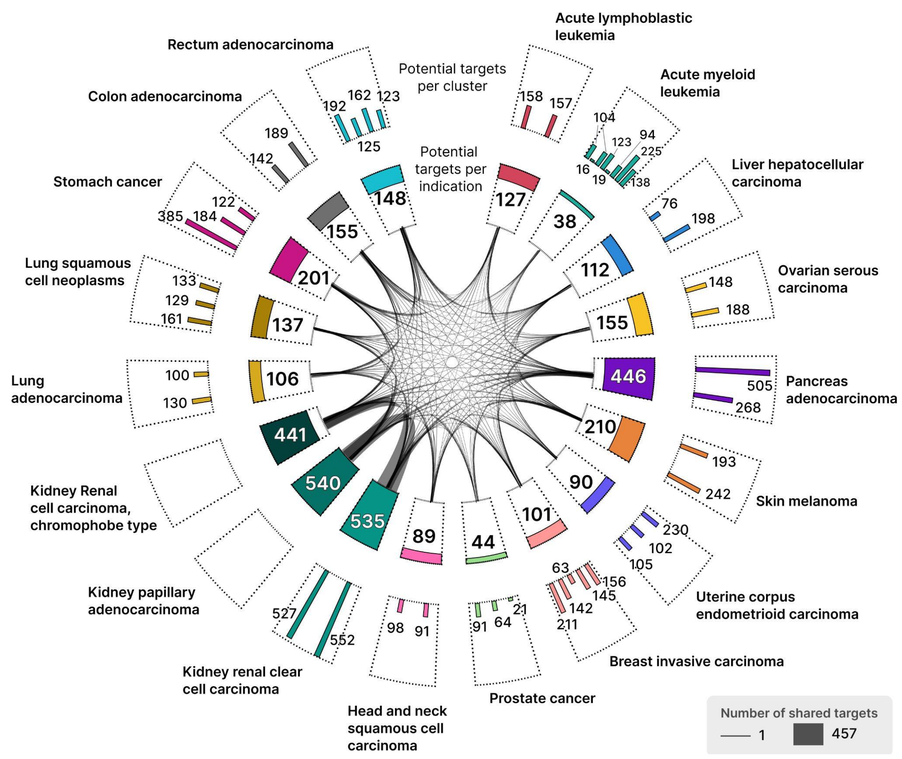


Figure 3: Overview of our pan-cancer antigen target discovery analysis in 18 indications. Numbers of targets for each cohort and cluster are represented, respectively, by the inner circle and outer bar plot. Numbers of targets shared between indications 2 by 2 are represented by the inner links.

3. Target characterization of breast invasive carcinoma

- Of the **412 potential targets** identified in breast invasive carcinoma, 2 corresponded to FDA-approved antigen targets and **8 were investigated in clinical trials**, including MUC1.
- Among the discovered targets, 392 cited in literature as targets, and 172 specifically mentioned in **breast cancer-related research papers.**
- This characterization process allows to identify targets with favorable safety and/or efficacy profiles, with for example **113 targets** having **limited or absent expression in healthy brain tissues**, or the **110 targets** that exhibit a **particularly high expression** in primary tumors (> 50 nTPM in corresponding TCGA).
- Our pipeline's flexibility allows for a focus on specific therapeutic modalities, such as CAR-T cells, identifying 100 potential targets with **no detectable expression in healthy T-cells**.

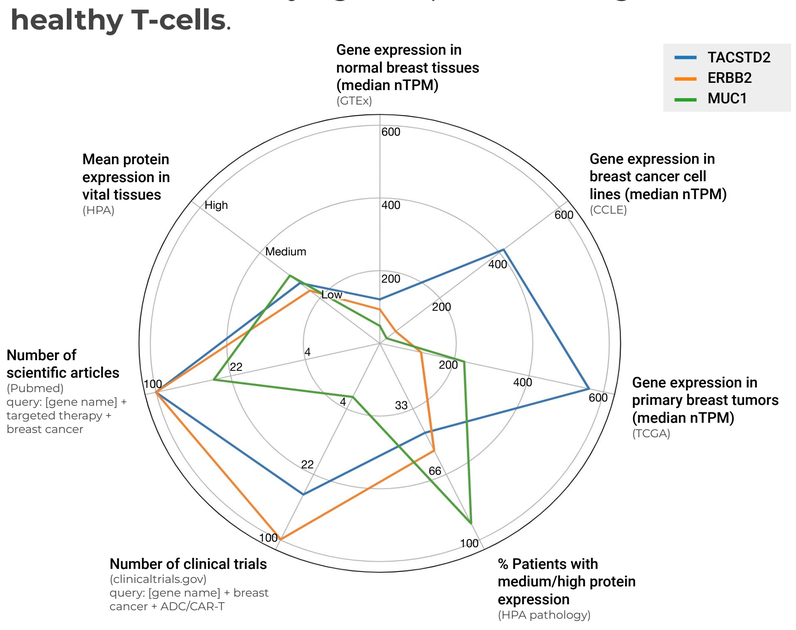


Figure 4: Target characterization profiles of breast cancer targets. Radar plot showcasing the diverse data integrated into our target characterization framework, applied to well-characterized breast cancer antigen targets.
(nTPM = normalized Transcript Per Million)