

A large scale proteogenomic atlas for precision oncology

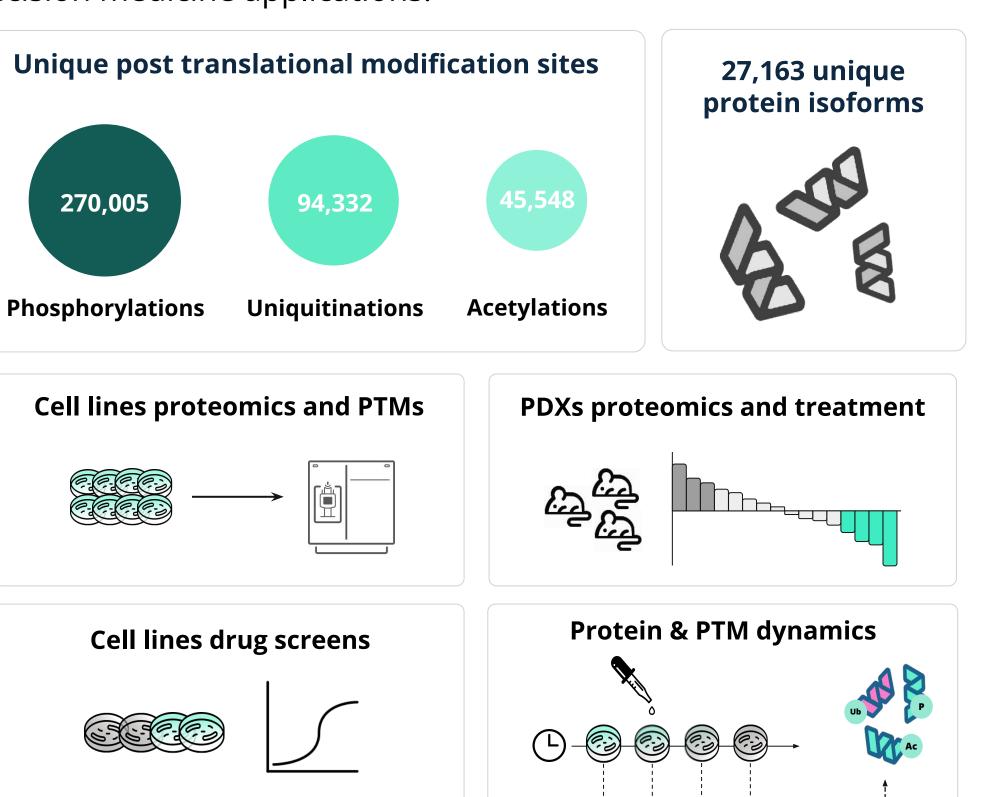
AACH American Association for Cancer Research

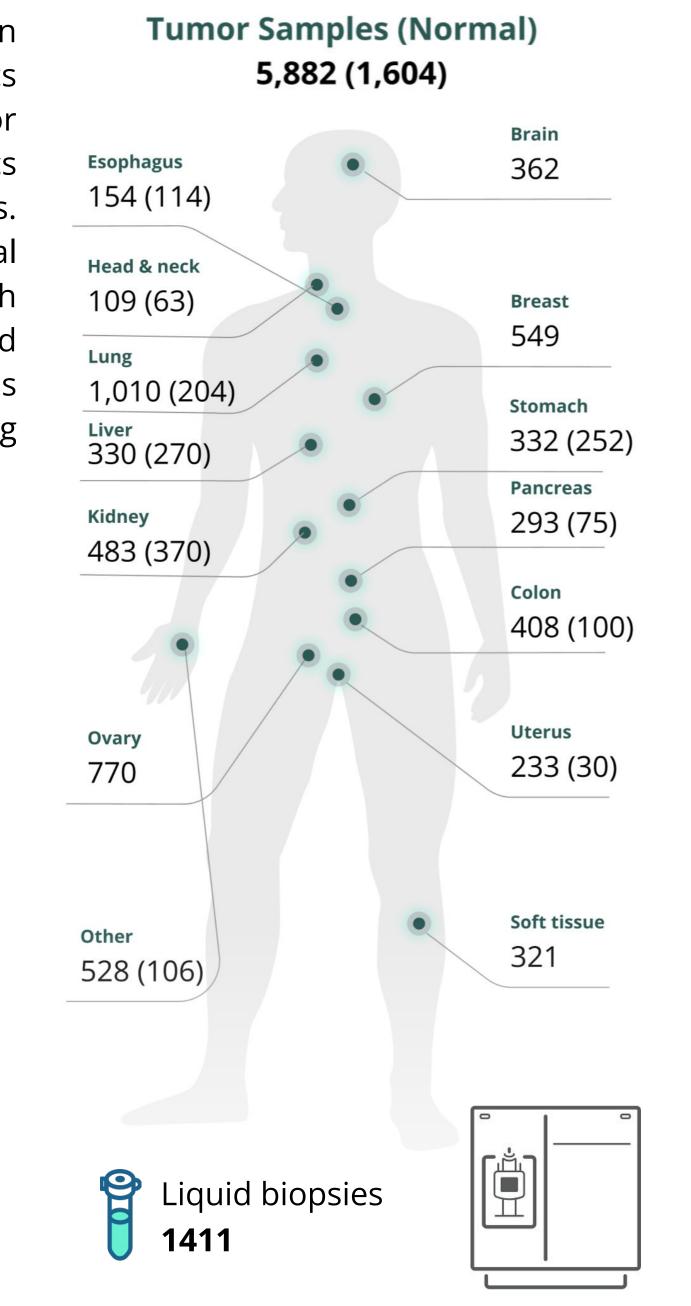
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Abstract number: 6241

Protai clinical atlas represents proteome of wide range of tumors

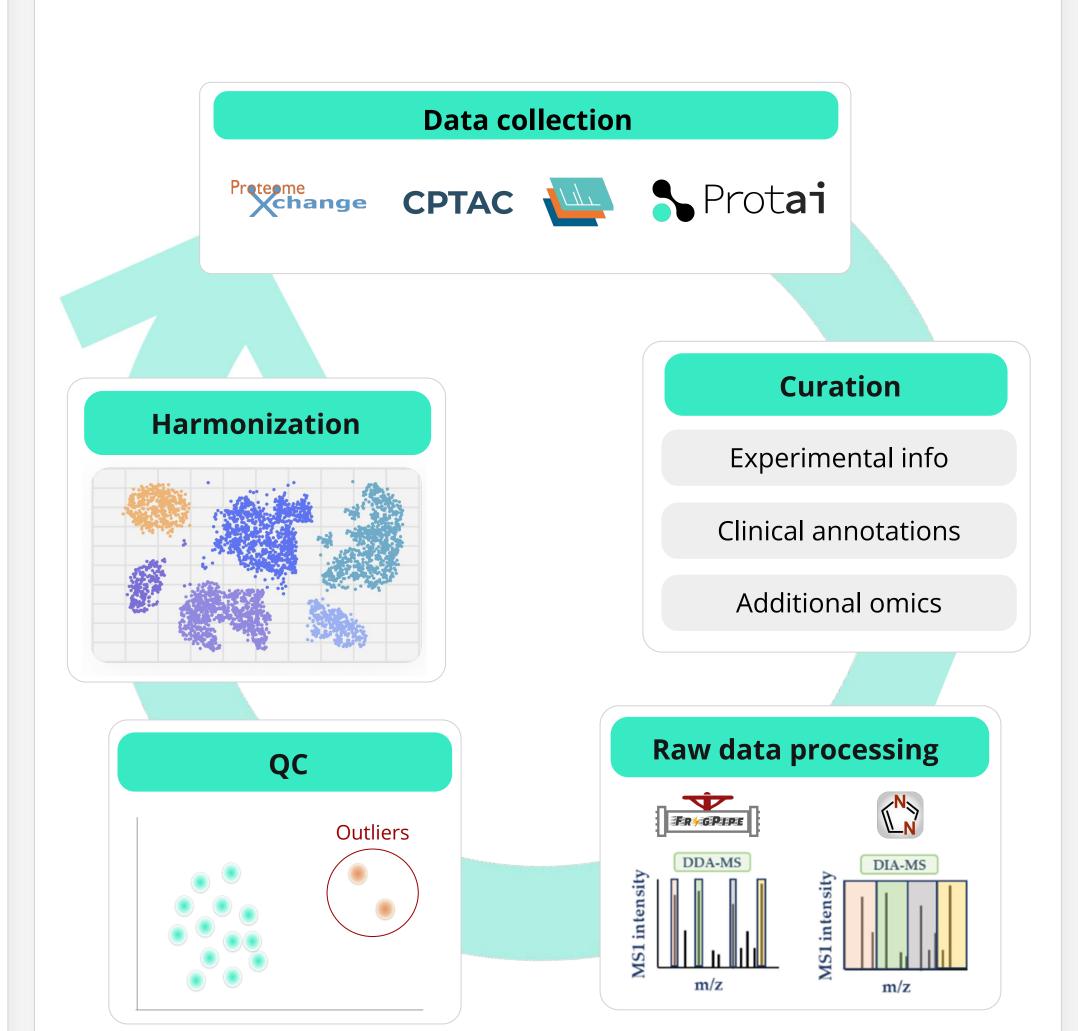
Biomarker and target discovery remain as unmet needs in precision medicine. The exponential growth in mass spectrometry proteomics presents both a significant challenge and a promising opportunity for breakthroughs. The AIMS™ platform transforms the vast proteomics datasets into a catalyst for novel drug and biomarker discoveries. AIMS™ integrates a broad range of preclinical and clinical proteogenomic data with detailed clinical annotations, together with deep post-translational modifications, from both public and proprietary sources. Our atlas offers insights into patient outcomes and drug sensitivities in tumor and normal samples, supporting precision medicine applications.





Continuously expanding atlas

The atlas is continuously updated by integrating data from diverse sources, including our proprietary datasets. This data is processed in our cloud-based pipeline, subjected to stringent quality control and harmonization, ensuring it remains the largest reported proteomic atlas enabling oncology research of multiple tumor types and sub-groups



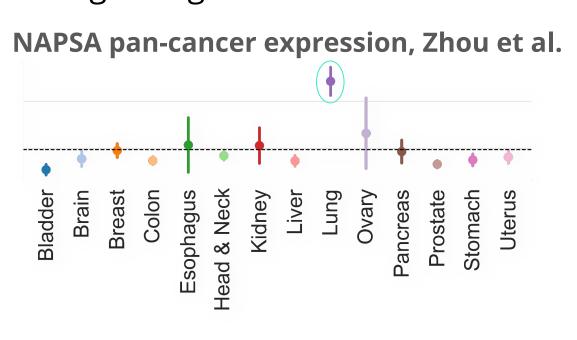
Novel benchmarked harmonization

Two benchmarks are presented, illustrating significant improvements in biological signal post-harmonization, affirming our data's enhanced quality.

Tissue Overexpression Score =

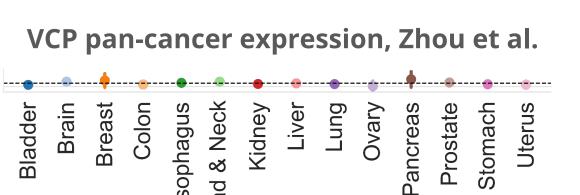
Tissue markers benchmark

50 literature validated tissue specific cancer markers were collected from 2 pan-cancer datasets (8, 9). These 0.4 to evaluate the 0.3 harmonized enhancement of tissue biological signal.

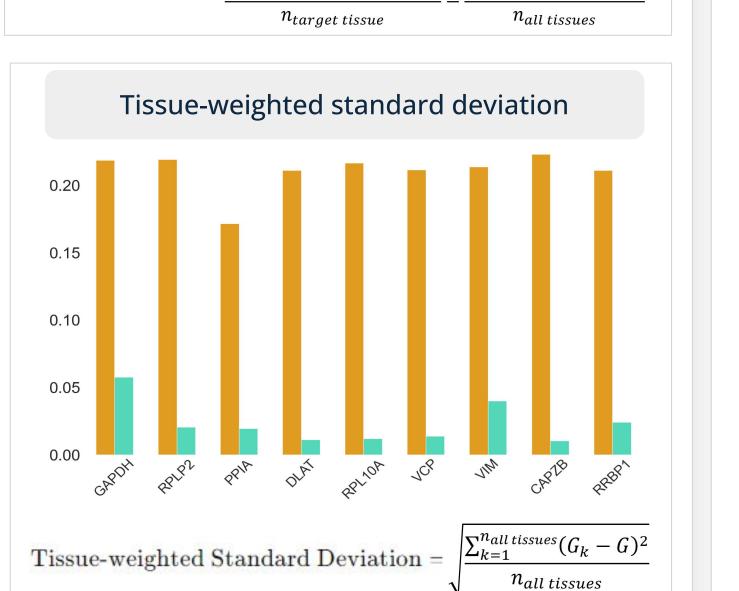


Housekeeping genes benchmark

To ensure consistent quality and comparability within our datasets different indications is measured and expected to be minimized.



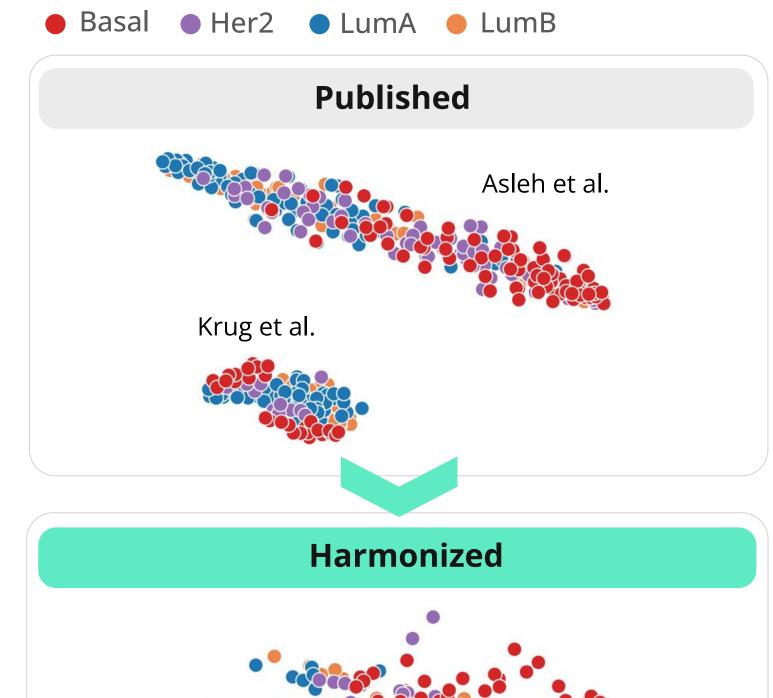
Tissue overexpression score TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA TESTIGIA



Reduced technical noise and enhanced biological signal enabled by harmonization

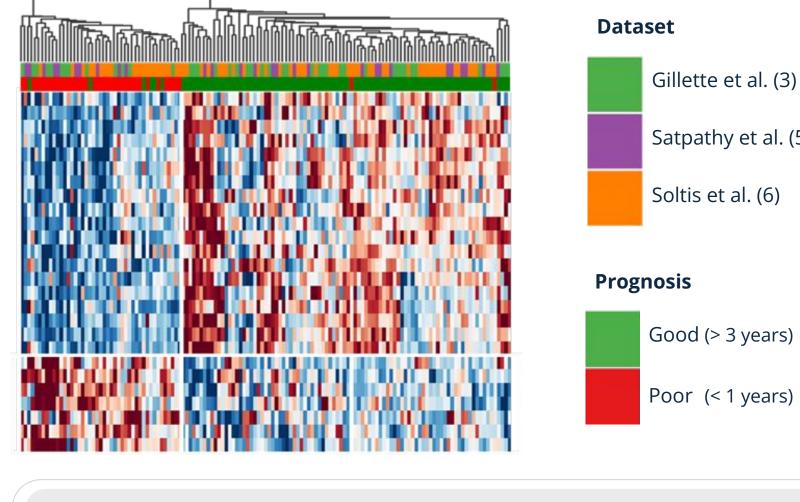
From batch to breast cancer subtypes

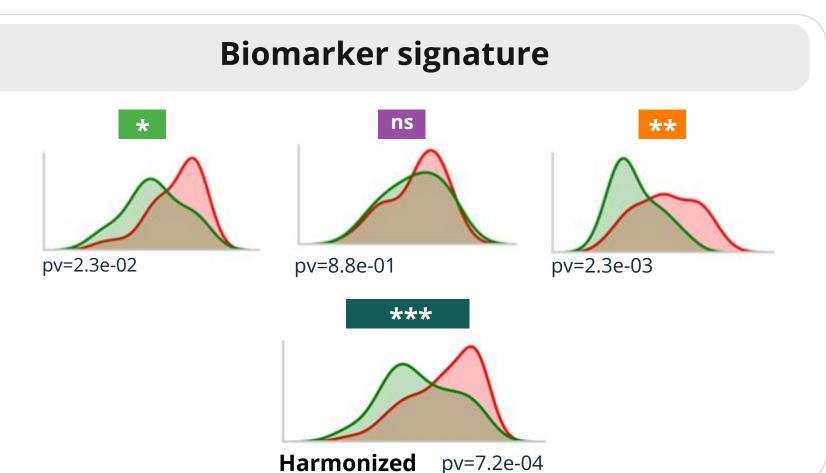
Protai harmonization overcomes batch effects between different labs, studies, methods and protocols. In this case, breast subtypes from two different studies of different labs are presented, showing that the biological signal is preserved while the dataset batch effect is removed.



Amplifying prognostic signal in Lung

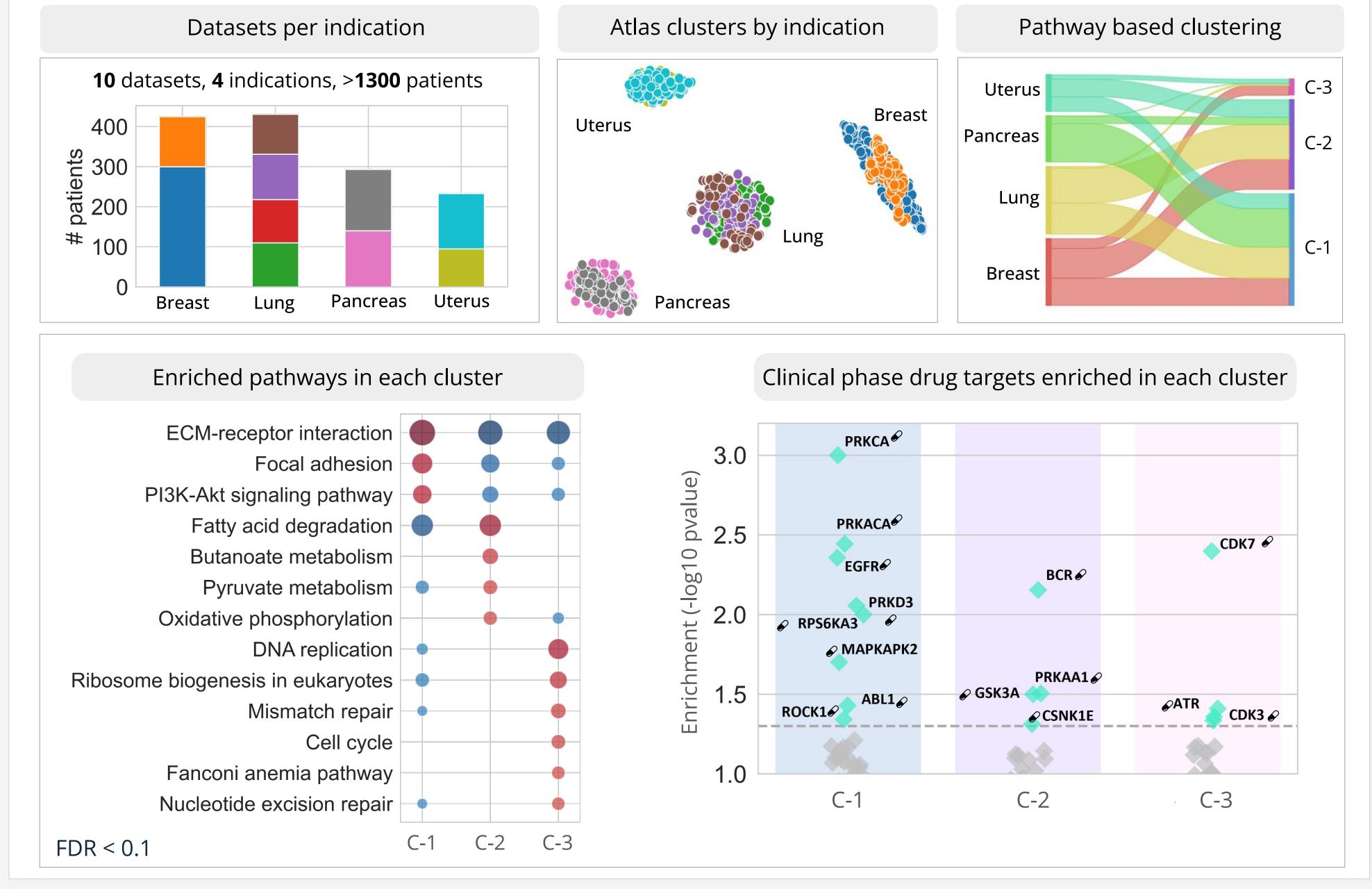
By leveraging a larger sample size, this approach enables identification of a biomarker that remained undetected when analyzing each dataset separately. This finding highlights the importance of harmonization for revealing previously undiscovered insights, and its applicability extends to other applications.





Pan-cancer harmonization uncovers clusters with therapeutic potential

The following analysis encompasses a comprehensive pan-cancer dataset, integrating 10 distinct datasets across four different indications. By clustering patients based on pathways that show high expression in at least two indications, the patients are grouped into 3 clusters, pinpointing specific mechanisms that are upregulated within each cluster. Then, drug targets that are uniquely active in each cluster are suggested, suggesting a potential for indication expansion.



Enhancing patient selection for MEKi with phospho-proteomic signature of MEK activation

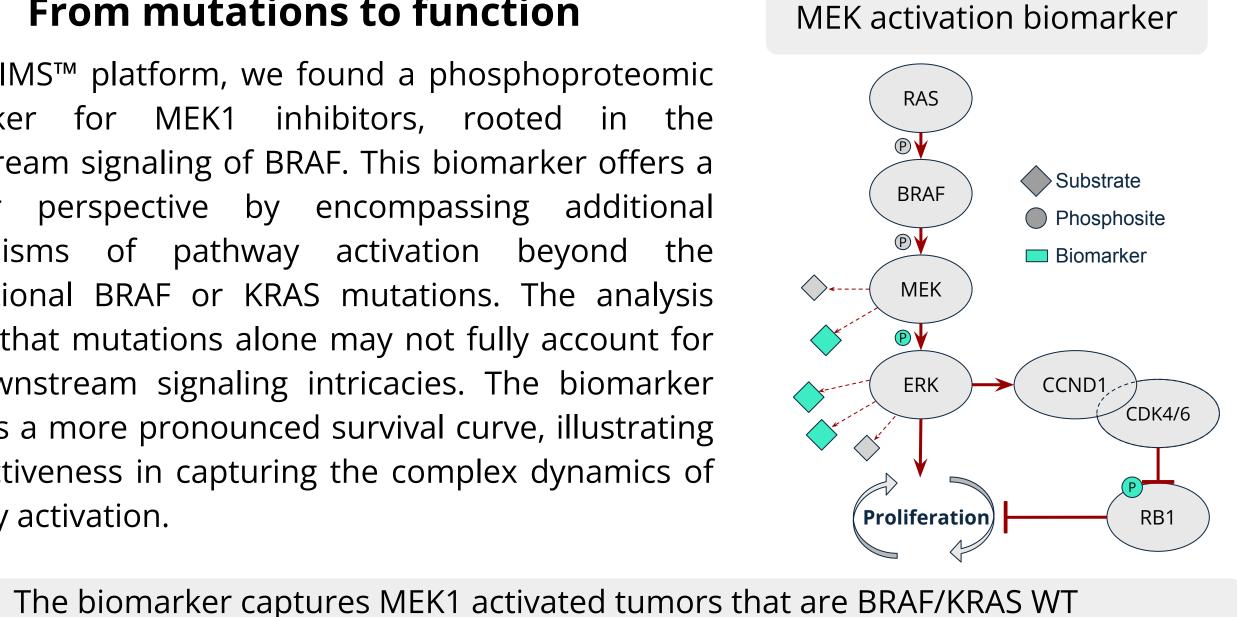
From mutations to function

Using AIMS™ platform, we found a phosphoproteomic biomarker for MEK1 inhibitors, rooted in the downstream signaling of BRAF. This biomarker offers a broader perspective by encompassing additional mechanisms of pathway activation beyond the conventional BRAF or KRAS mutations. The analysis reveals that mutations alone may not fully account for the downstream signaling intricacies. The biomarker achieves a more pronounced survival curve, illustrating its effectiveness in capturing the complex dynamics of pathway activation.

KRAS-MUT

KRAS-WT

Years



Lung SCC Protai biomarker score Protai biomarker score

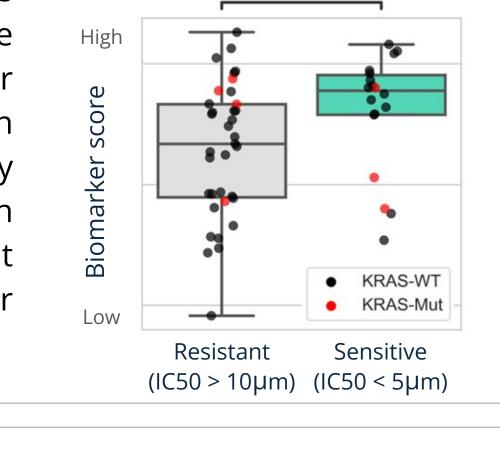
Positive

Negative

Years

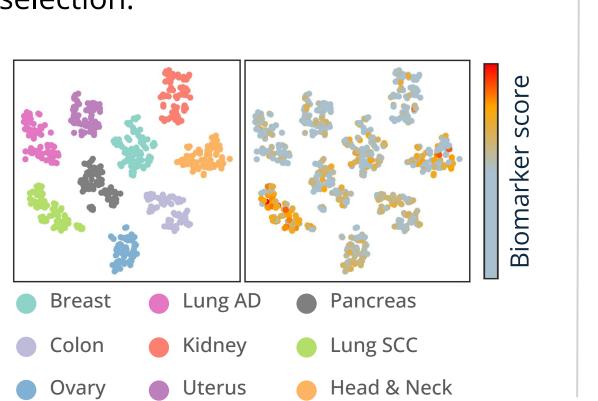
Improved biomarker for Selumetinib (MEK1i)

Validation of our novel biomarker is shown within a pan cancer cell line dataset, utilizing the MEK1 inhibitor Selumetinib. validation underscores the biomarkers efficacy distinguishing between Selumetinib sensitive and resistant cell lines, and shows potential for treatment in other indications.

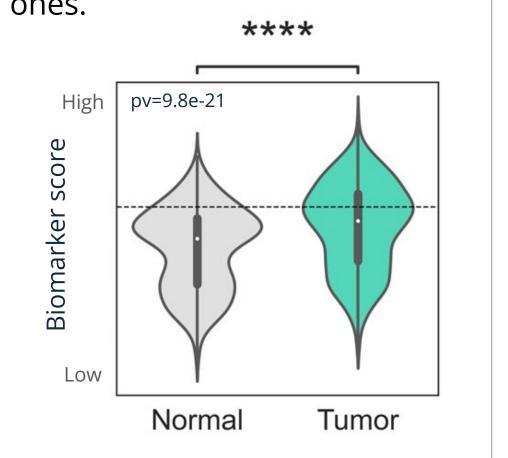


Indication expansion potential

Protai biomarker exhibits considerable potential in identifying LSCC patients who may benefit from MEKi therapy. Additionally, our analysis sheds light on patients from other indications where our biomarker suggests potential for therapeutic indication and improved patient expansion



clinical atlas of tumor and phospho-proteomic biomarker significantly in tumor samples compared to normal



Summary

- Protai has forged a high quality, routinely updated, clinical atlas of cancer proteomics and PTMs.
- AIMS™ harmonization method is validated and evaluated with two separate benchmarks.
- Increased sample size translates into qualitative improvement, offering unique precision oncology insights:
- Predictive and prognostic biomarker discovery.
- Indication expansion.
- Discovery of new therapeutic targets and combinations.

References

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