The Pan-Cancer Proteome Atlas, a mass spectrometry-based landscape for discovering tumor biology, biomarkers and therapeutic targets

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As proteins are key to virtually everything happening in cells, comprehensive and quantitative protein measurements are of high interest for phenotypic characterization. Mass spectrometry (MS)-based proteomics provides a powerful approach to directly measure protein abundance and modification. Most cancer proteomics studies to date have focused on a single cancer type.
We report The Pan-Cancer Proteome Atlas (TPCPA) based on data-independent acquisition mass spectrometry, to better understand cancer biology and identify therapeutic targets and biomarkers. TPCPA includes 9670 proteins derived from 999 primary tumors representing 22 cancer types. We describe pan-cancer and cancer type-enriched proteins with extensive external annotation, prioritizing candidate drug targets and biomarkers. Relevant for proteolysis-targeting chimeras, we identify E3-ubiquitin ligases highly expressed in specific tumor types, including HERC5 (esophageal cancer) and RNF5 (liver cancer). Co-expression analysis reveals 13 modules, including unexpected hub proteins as potential drug targets (e.g., GFPT1, LRPPRC, PINK1, DOCK2, PTPN6). Analysis of 195 colorectal cancers identifies protein markers for RNA-based CMS subtypes and two immune subtypes with prognostic value. We report a cancer type classifier for identification of cancers of unknown primary origin. A queryable TPCPA data resource is available at http://r2platform.com/TPCPA.

Highlights:

- Pan-cancer proteome across 18 solid and 4 liquid cancers from 999 human samples
- Tissue type biology influences, but does not fully determine, tumor classification
- Co-expressed pan-cancer proteins and biology with potential therapeutic utility
- Cancer (sub)type enrichment reveals new proteins with biomarker potential
- CMS proteins and immune subtypes with prognostic value in colorectal cancer
- Multi-cancer classifier for identification of metastasis of unknown primary origin

References

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Brief biography of Prof. dr. Connie R. Jimenez

Connie Jimenez is full Professor of Translational OncoProteomics, Principle Investigator of the OncoProteomics Laboratory and Director of the Proteomics Core Resource, all at Amsterdam University Medical Center, Amsterdam, The Netherlands.
She is a biologist who pioneered neuropeptide profiling of single neurons by mass spectrometry during her PhD studies in the early 90s at the Vrije Universiteit in Amsterdam. Since her postdoc at UCSF, San Francisco in the laboratory of Prof. Al Burlingame, she has been working on biological and biomedical applications of proteomics.
In 2006, she founded the OncoProteomics Laboratory (www.oncoproteomics.nl) with a start-up grant of the Cancer Center Amsterdam. Her lab applies innovative mass spectrometry-based proteomics and data analysis to obtain systems biology insights into disease and to improve early diagnostics and treatment, most notably of cancer and neurodegenerative disease.
Dr. Jimenez founded the Netherlands Proteomics Platform in 2001 and since then serves as a member of the steering group. She was elected HUPO Council member from 2013-2016 and is co-chair of the HUPO Cancer Initiative. Furthermore, she is currently re-elected Vice-President of EuPA (2024-2026) and chair of the EuPA Mentoring Committee. She (co-) authored over 250 peer-reviewed scientific papers and is editorial board member of five major proteomics journals. She won the HUPO Translational Proteome Science award in 2022 and the EuPA Juan Pablo Albar Proteome Pioneer award in 2025.