Stratification of prostate cancer tissue biopsy samples using PCT-SWATH

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INTRODUCTION

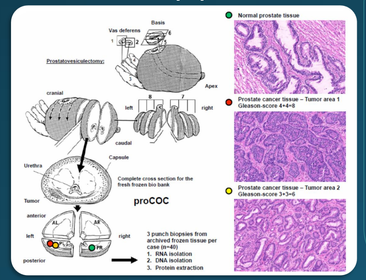
Prostate cancer (PC) patients are conventionally classified into three histological groups, *i.e.* low-grade, intermediate-grade and high-grade. The intermediate-grade group contains patients of mixed clinical outcomes that cannot be better classified using established diagnostic routines.

Here, we hypothesize that the quantitative proteomic analysis of tissue biopsy samples could be used to stratify intermediate-grade PC patients.

To obtain accurate quantitative proteotypes (the acute state of the proteome) of tissue biopsy samples, we used the recently developed combination of PCT (pressure cycling technology) and SWATH-MS (reference 1), which permits relative quantification of thousands of proteins from tissue biopsies with reproducibility and quantitative accuracy comparable to SRM, the gold standard quantitative MS method.

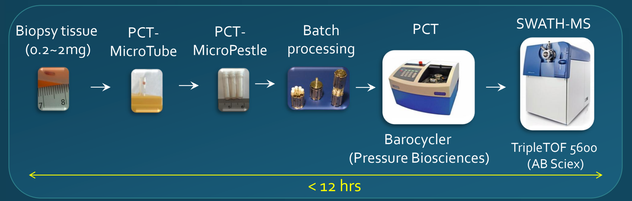
MATERIALS AND METHODS

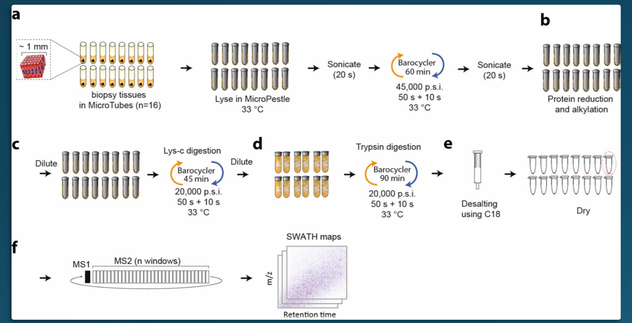
Fresh frozen biopsy tissues



We collected prostate tissues from low-grade, intermediate-grade and high-grade prostate cancer patients (n=39). Multiple biopsy samples were punched out from different histological regions using a 1-mm needle (2 or 3 per patient). Altogether we analyzed 105 biopsy samples.

PCT-SWATH





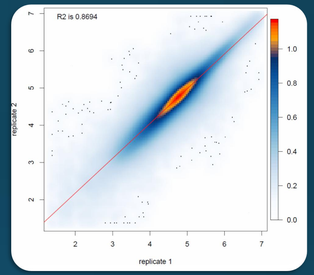
RESULTS

Build a SWATH assay library for prostate tissues

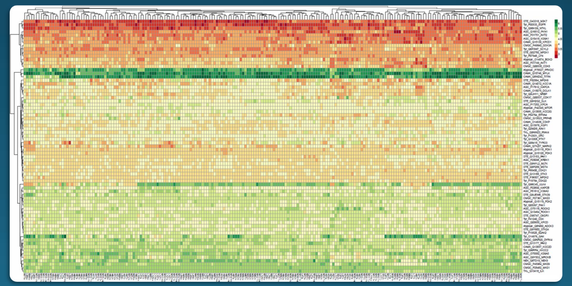
We analyzed 79 out of the 105 PCT-processed biopsy samples using data-dependent acquisition (DDA) mode in TripleTOF, and build a SWATH assay library for prostate tissues (reference 2).
The library contains 70,981 precursors from 59,017 proteotypic peptides in 6,686 SwissProt proteins, of which 4,991 proteins contain at least 2 peptides. 1,695 proteins contain only one peptide.

SWATH analysis of 105 prostate tissues in duplicates

Overall technical reproducibility.
3,812 SwissProt proteins quantified using OpenSWATH in duplicate are plotted against each other.

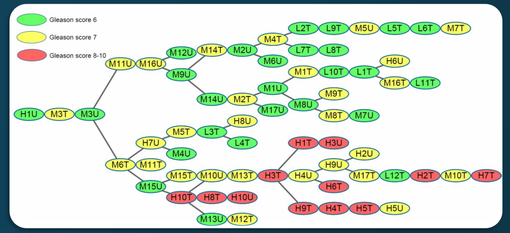


73 of 507 human protein kinases quantified in 105 PC tissues.



Expression of 73 protein kinases in 105 prostate tissue samples. Color indicates log 10 scaled protein intensity.

Stratification of prostate tissues



Each node represents a prostate tissue. Distance between samples based on 13 selected protein markers are displayed in a minimal spanning tree.

CONCLUSIONS

1. PCT-SWATH permits high-throughput, reproducible quantitative proteomic profiling of biopsy tissues.
2, The thus obtained proteotypes separated histologically indistinguishable tissue biopsy samples.
3, New protein biomarkers candidates for precise stratification of prostate cancer were identified, awaiting for further validation in independent cohorts.

REFERENCES

1, Guo et al. Nature Medicine. 2015. 21:407
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ACKNOWLEDGEMENTS

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