Identification of Protein Abundance Changes in Hepatocellular Carcinoma Tissues Using PCT–SWATH
PCT-SWATH检测肝癌组织蛋白质丰度变化

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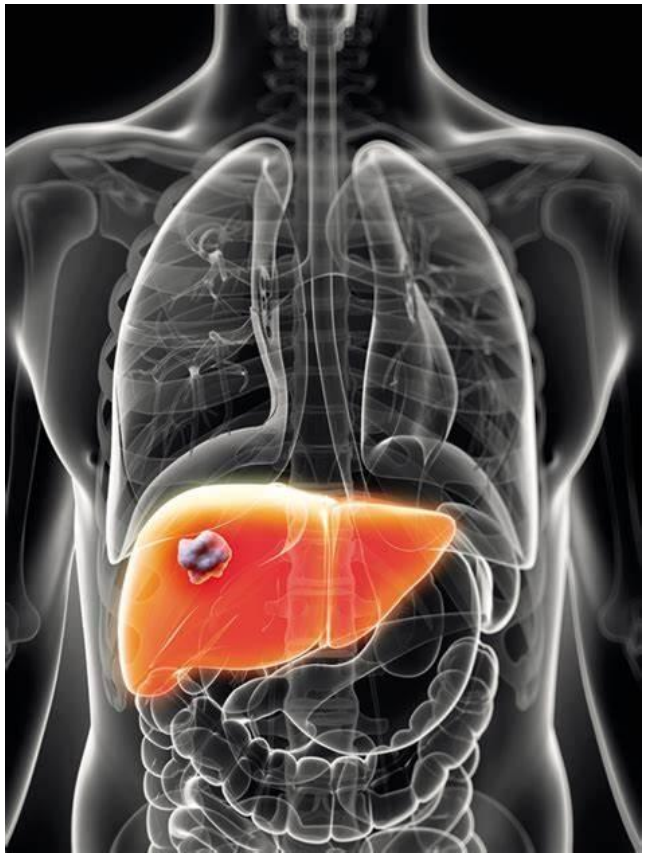
Background of thyroid nodules



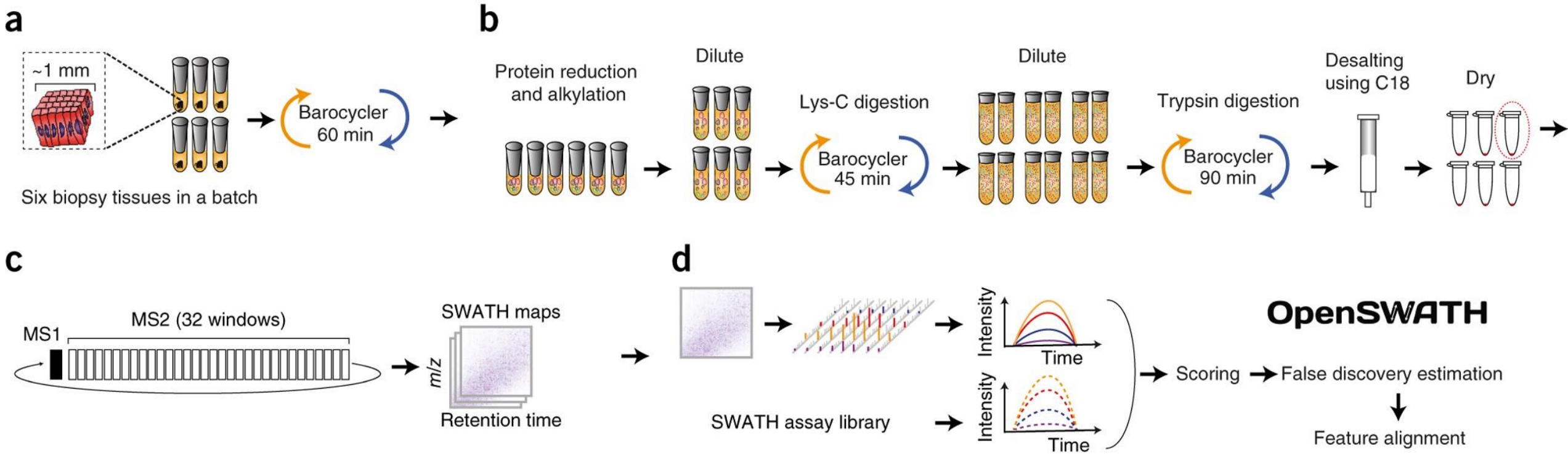
Hepatocellular carcinoma is the fifth frequent malignancy worldwide and ranks as the third leading cause of cancer-related mortality[1].

In China, HCC leads to more than 300 000 deaths every year [2].

Currently three FDA approved serum biomarkers and CT have low sensitivity and specificity[3]. Better biomarkers are needed for HCC.

[1] H. B. El-Serag, K. L. Rudolph, *Gastroenterology* 2007
[2] T. Yau, V. Y. Tang, T. J. Yao, S. T. Fan, C. M. Lo, R. T. Poon, *Gastroenterology* 2014
[3] European Association For The Study Of The Liver, European Organisation For Research and Treatment of Cancer, *J. Hepatol.* 2012

PCT-SWATH



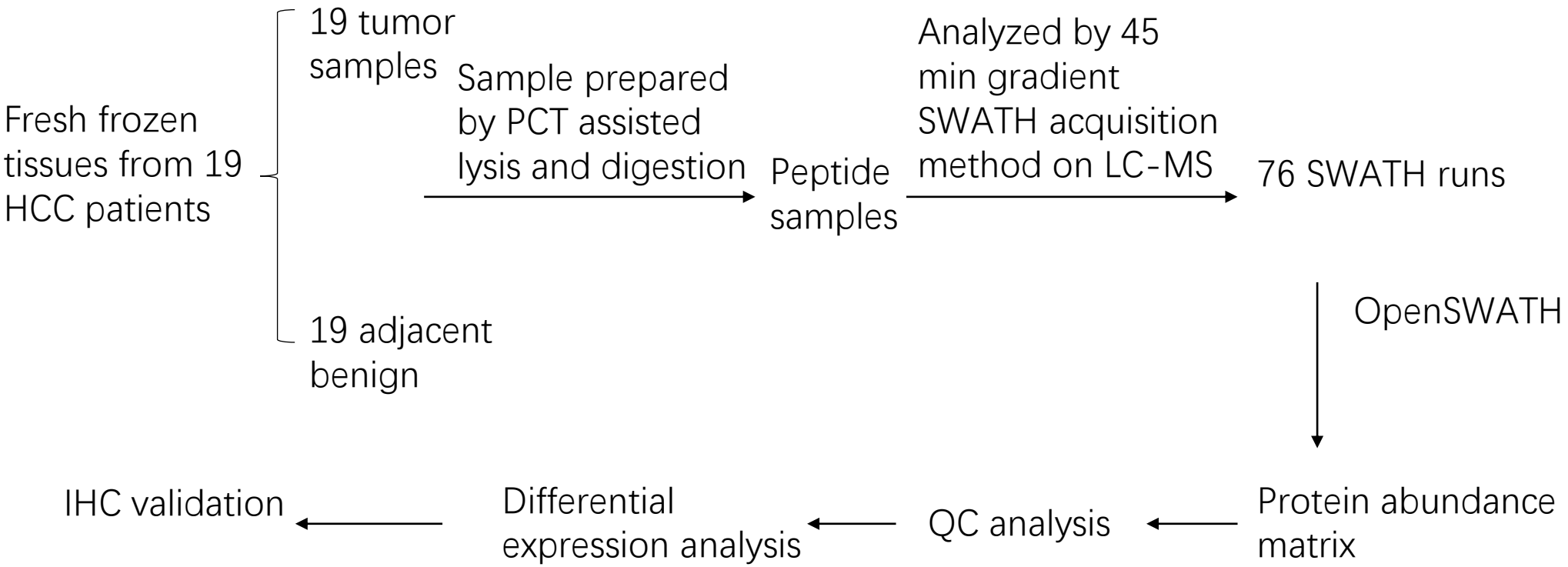
T. Guo, P. Kouvonen, C. et al. *Nat Med.* 2015

Objectives

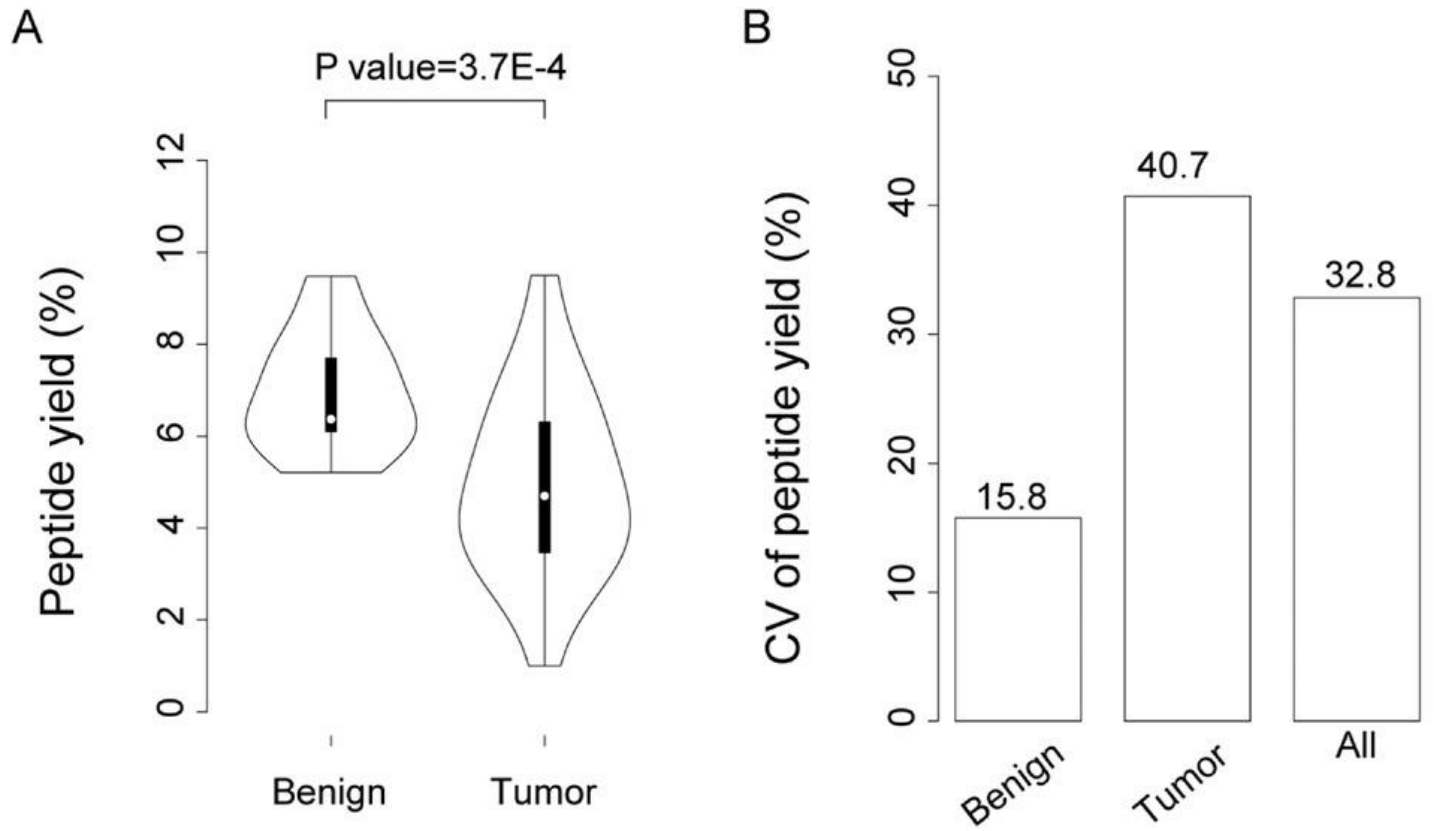
Combining PCT and shorter gradient of SWATH to improve throughput while keep the reproducibility and enough proteome depth of proteomic analysis of clinical tissue biopsies.

Find potential protein biomarkers of HCC.

Study Design



Performance of PCT-assisted peptide preparation



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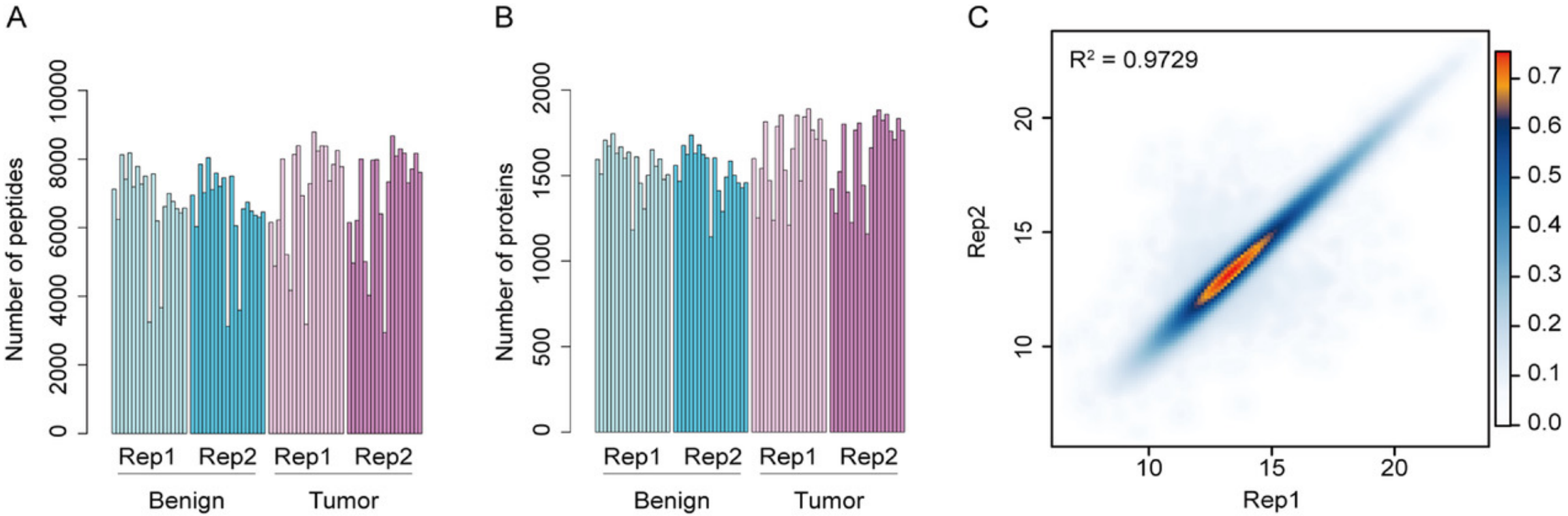
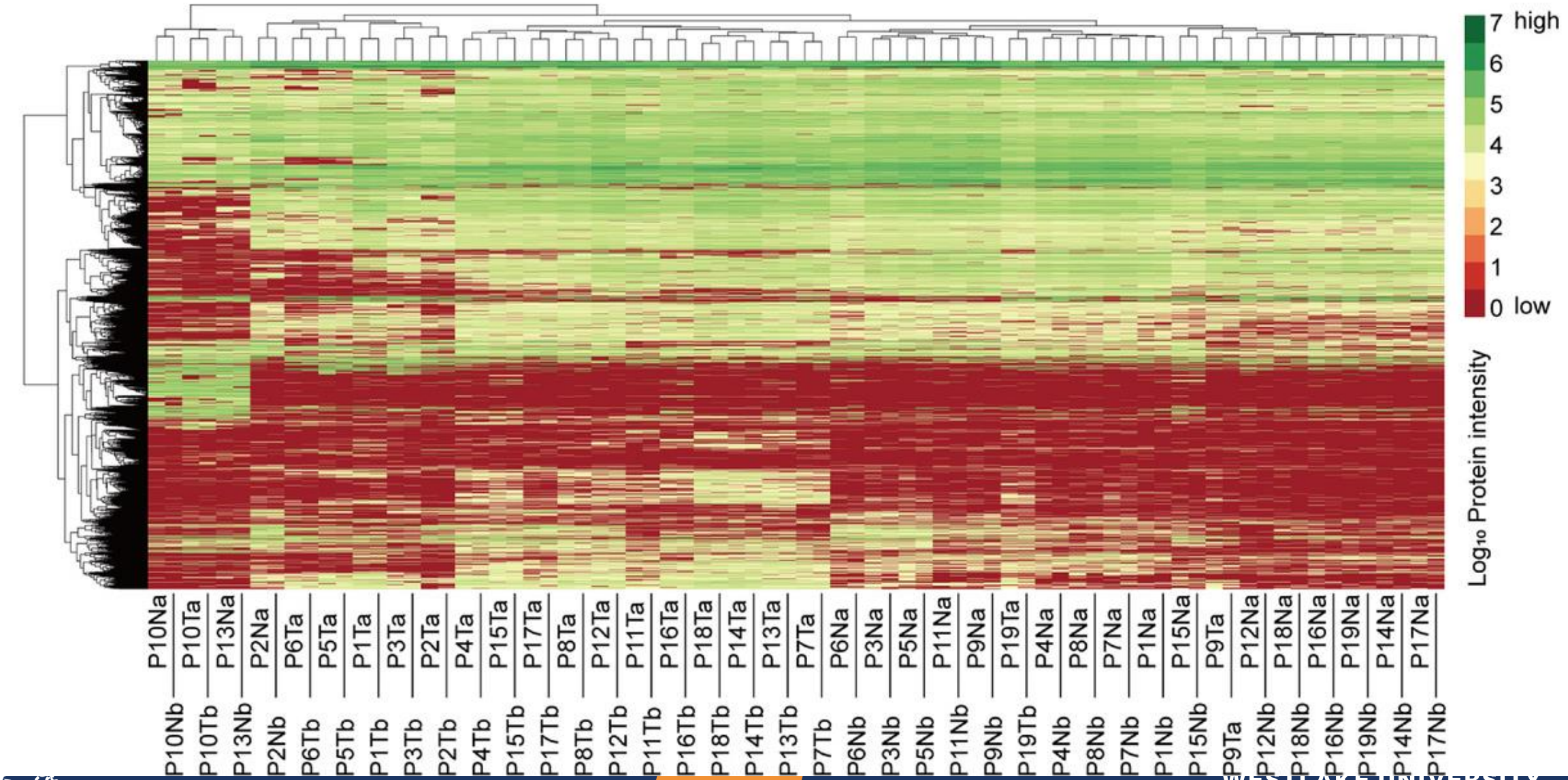
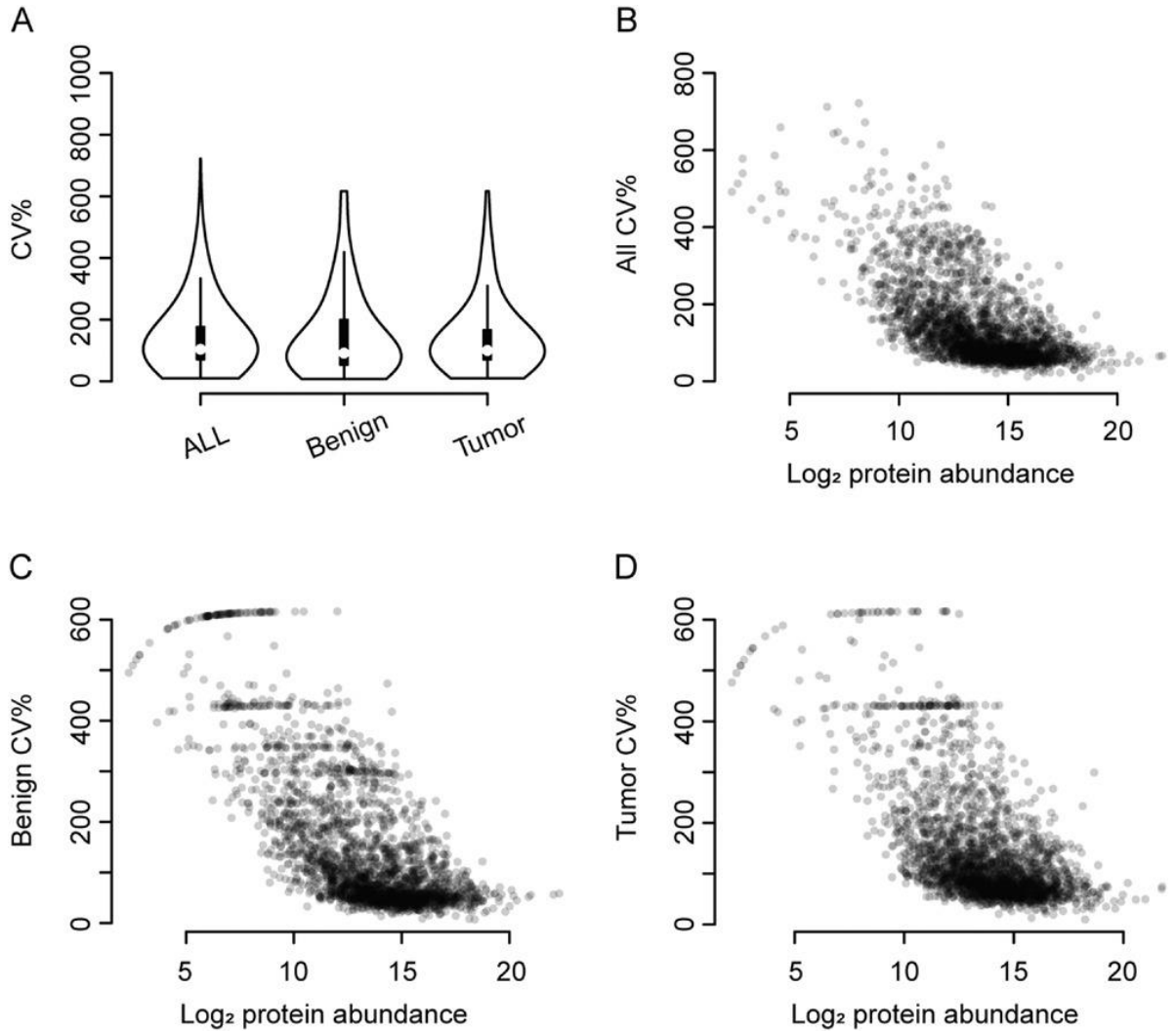


Heatmap overview of protein abundance patterns in 76 samples

D

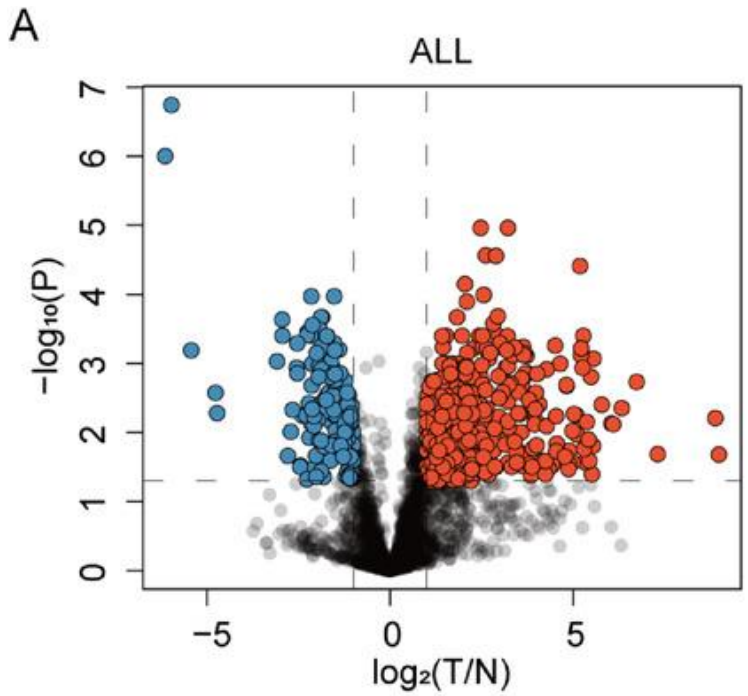


Variability of protein expression in liver tissues

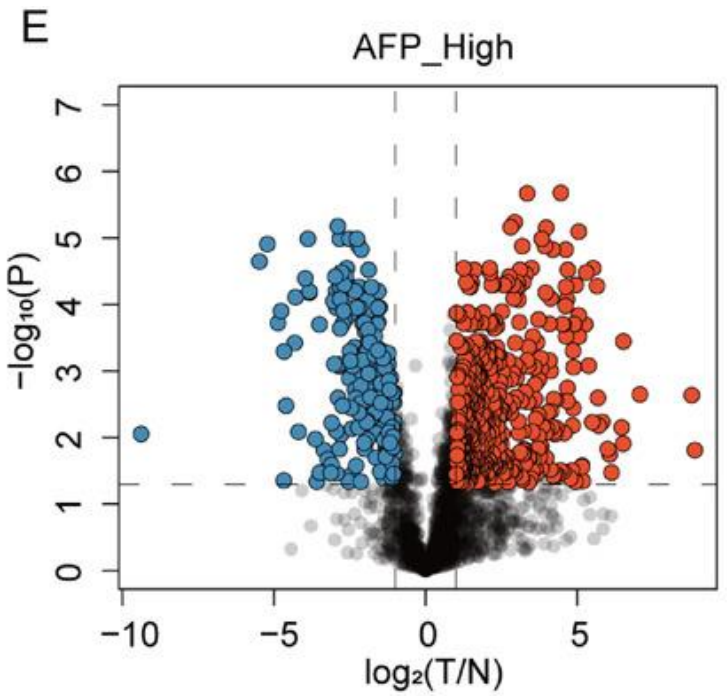


Tumor tissues have a slightly higher CV than benign

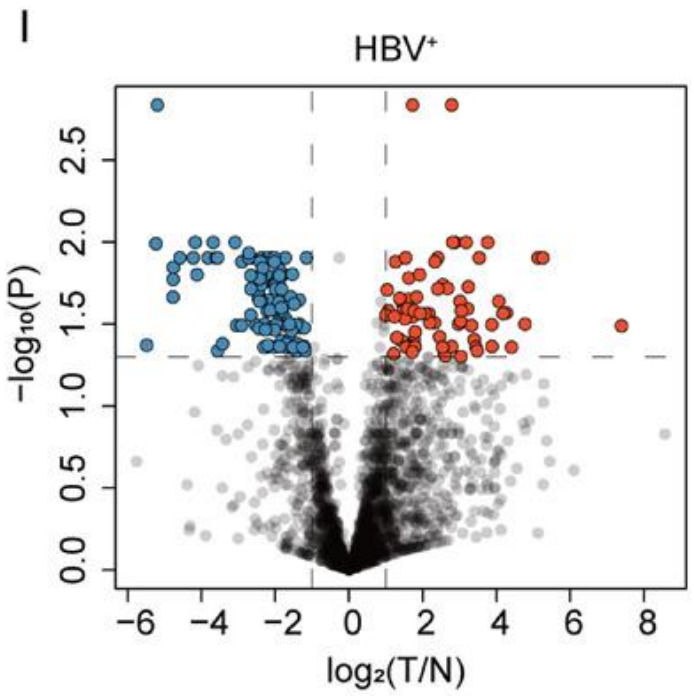
Differential regulated proteins in HCC



541 dysregulated proteins in all



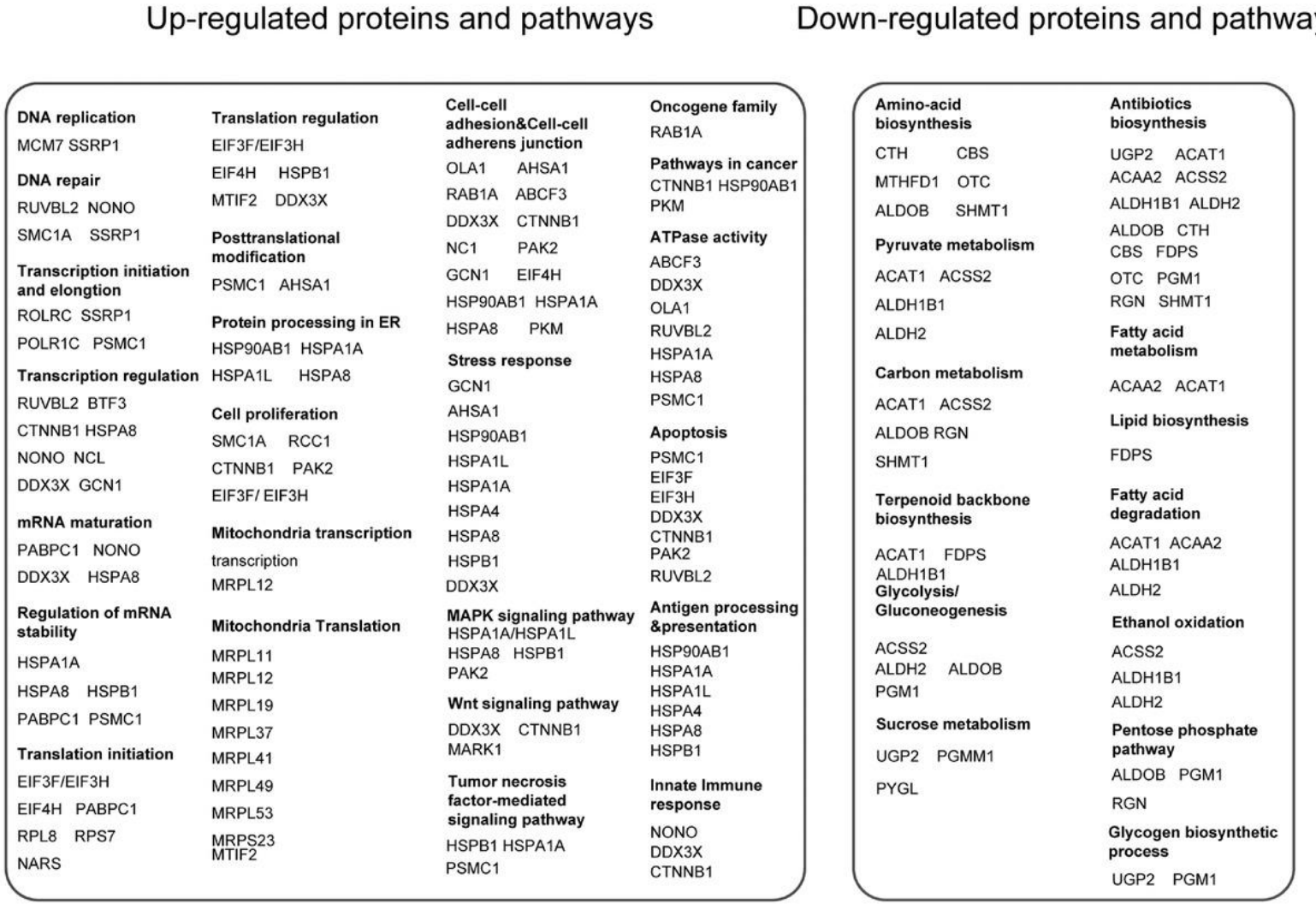
419 up-regulated
192 down-regulated



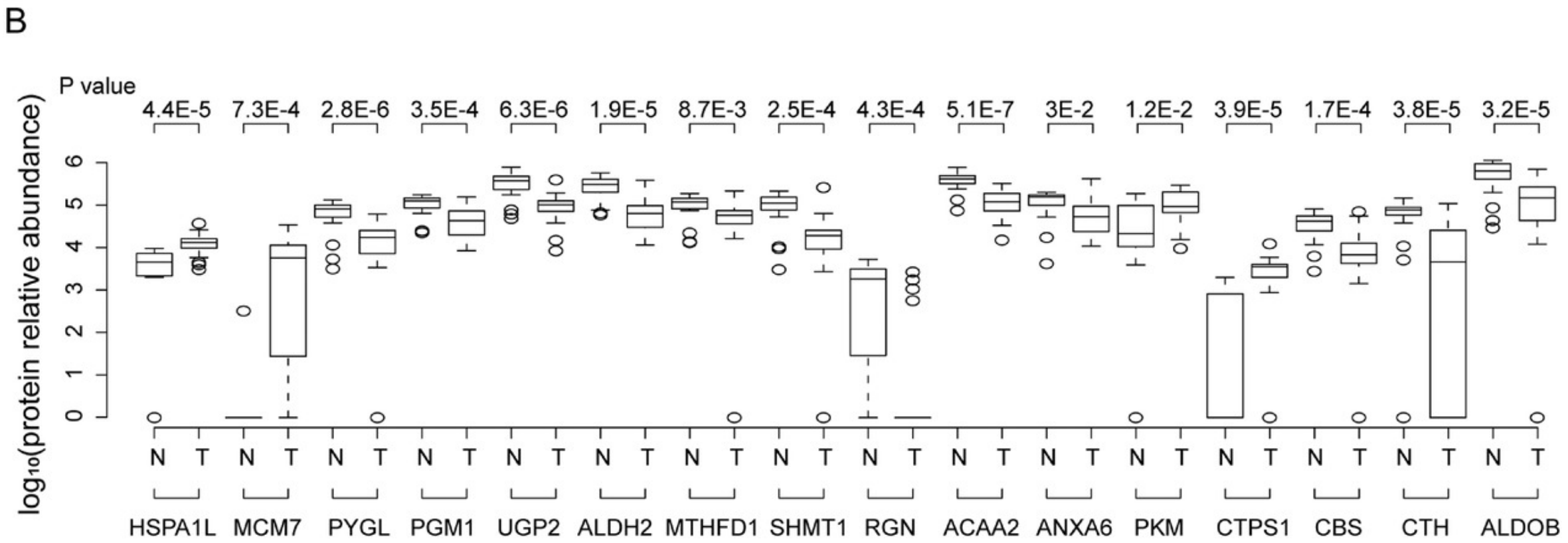
106 up-regulated
75 down-regulated

All proteins found regulated in HCC

A

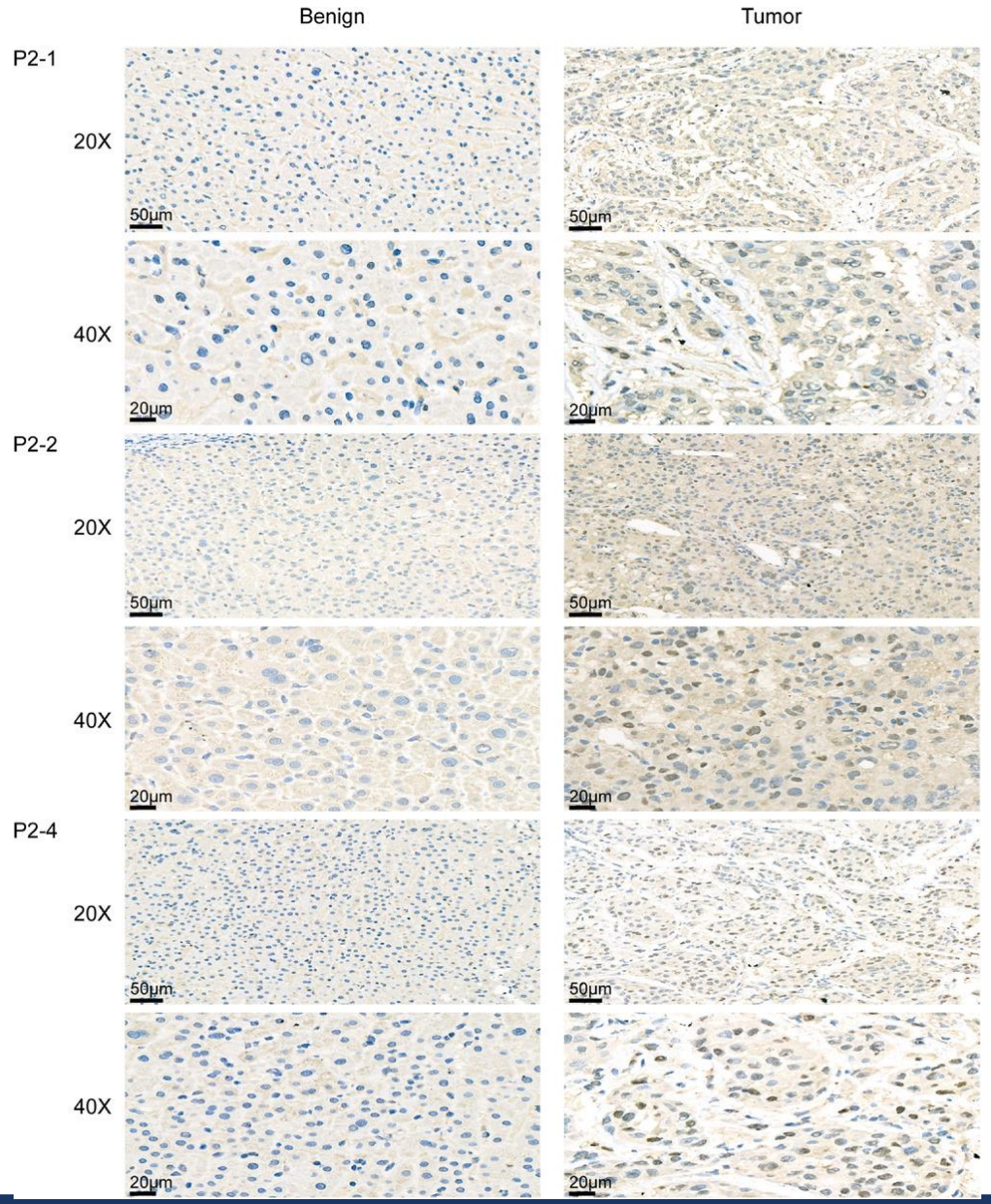


16 selected proteins significantly regulated in HCC tumors



Detection of MCM7 in HCC Samples Using IHC

MCM7 IHC staining to three additional patients validated the upregulation of MCM7 in liver tumors



Take-home messages

- In conclusion, we report an optimized PCT–SWATH workflow enabling analysis of clinical tissue specimens with increased sample throughput without compromise of quantitative accuracy and proteomic coverage.
- Our study identified a few regulated proteins in this HCC cohort. Proteins with increased abundance are mainly related to mass production, oncogenic signaling, and immunity, whereas metabolic proteins are shown with lower expression.
- We identified 16 dysregulated proteins of reported clinical relevance to HCC. Upregulation of MCM7 in tumor tissue samples was observed using IHC in additional patients.
- The study demonstrates that the PCT–SWATH methodology has potential to be practically applied in clinical research to analyze tissue samples in high throughput.

Publications

Proteomics
Clinical Applications

Research Article | Full Access

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First published: 26 October 2018 | https://doi.org/10.1002/prca.201700179 | Citations: 16

Acknowledgements

西湖大學 WESTLAKE UNIVERSITY

西湖欧米 WESTLAKE OMICS

He Wang
Weigang Ge

UOMICS -since 2017

All labmates in Laboratory of Big Proteomic Data

ThermoFisher SCIENTIFIC

PBI Pressure BioSciences Inc.

THANK YOU

西湖大學
WESTLAKE UNIVERSITY