# Proteotypic features of NCI-60 cancer cells obtained by SWATH-MS predicts phenotypes

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** Equal contribution*

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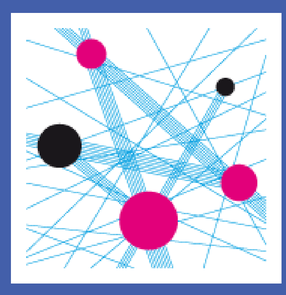


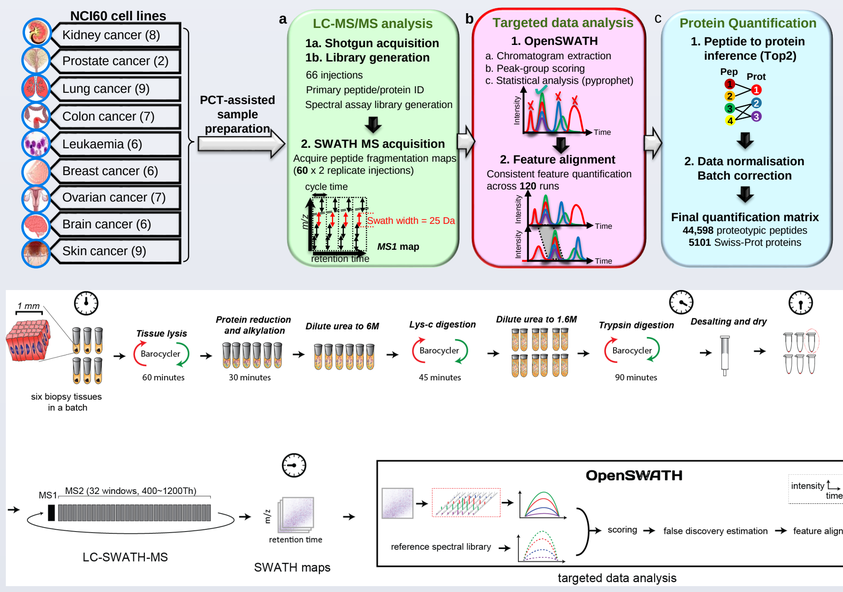
## Research Goal

One of the central hypotheses underlying the personalised/precision medicine and emerging omics fields dictates that specific molecular make-up of a cell or a tissue determines its (clinical) phenotypes. To date, mainly owing to the maturity and accessibility of DNA- and RNA- based techniques, forays into the molecular landscapes of diseases, in particular cancer, have primarily focused on the genomics, transcriptomics and epigenomics levels.

Proteins drive and catalyse essentially all biochemical reactions in a cell. Conceivably, the proteotype – the precisely quantified acute state of the cellular proteome – represents more closely the physiological, phenotypical and mechanistic states of a cell at a given time compared to its DNA signatures or RNA transcripts (levels).

Here we explored the link between the proteotype and phenotype.

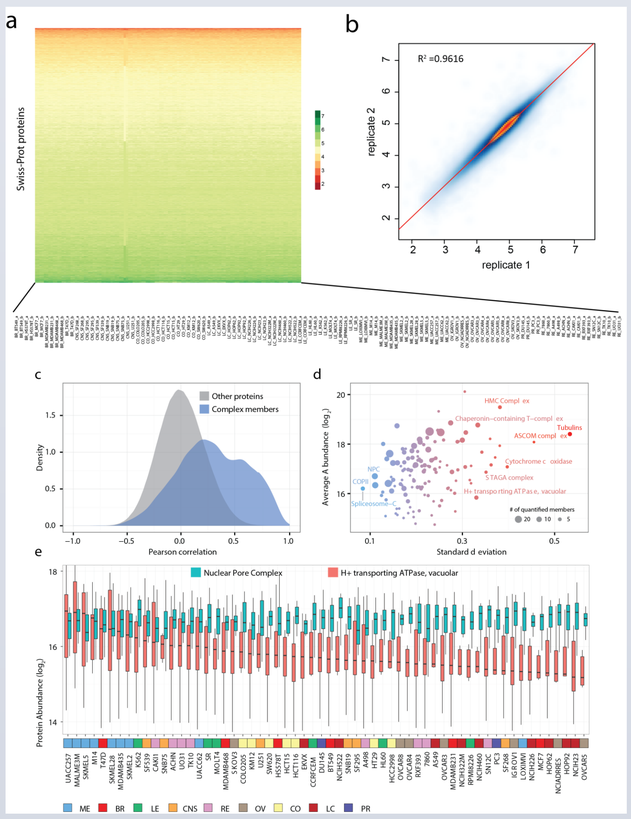
## NCI-60 cells and PCT-SWATH




PCT: pressure cycling technology

SWATH: sequential window acquisition of all theoretical fragment-ion spectra

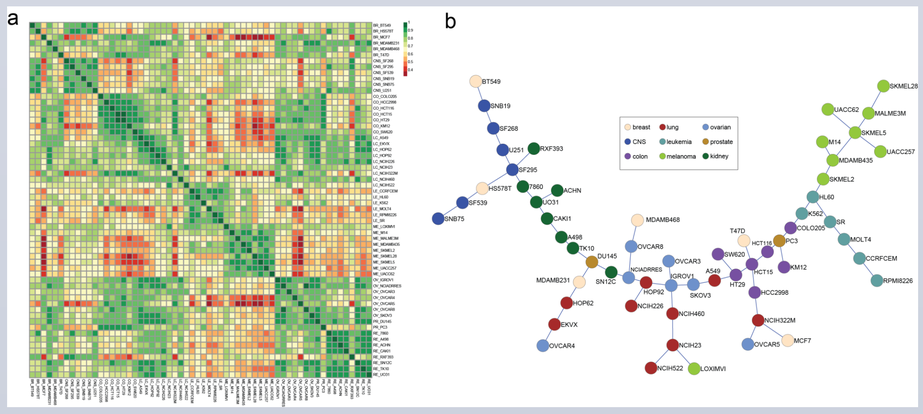
## Benchmarking of NCI60 proteotypes.



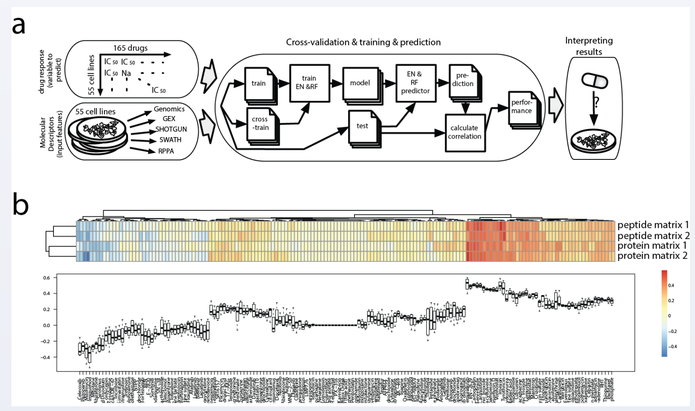

(**a**) Overview of NCI-60 proteotype. 5101 Swiss-Prot proteins were quantified in 120 SWATH runs corresponding to technical replicated measurement of NCI-60 cells. (**b**) Technical reproducibility of NCI-60 proteotype. (**c**) 561 proteins from 133 complexes were quantified across NCI60 cell lines. Distributions of Pearson correlation coefficients were plotted for pairwise comparisons between members of the same complex (blue) and between proteins from different complexes (grey). (**d**) A scatter plot of average abundance versus average standard deviation of protein complexes calculated across cell lines. (**e**) Variation of the relative abundance of the Nuclear Pore Complex (green, n=13 members) and the vacuolar $H^+$ transporting ATPase (orange, n=6 members) is shown as boxplots across the NCI60 cell lines (colored according to tissue of origin).

## Proteotypes for stratification of cancers.

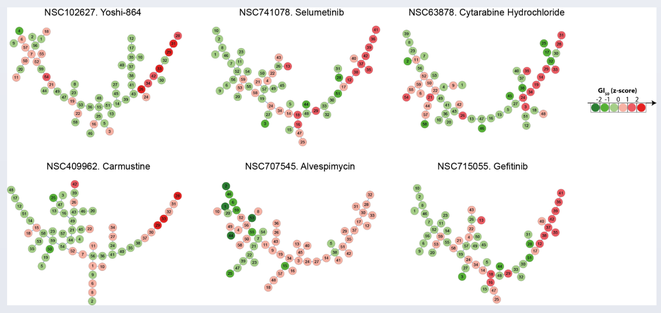
(a) distance map of 60 cells based on 252 selected protein features. (b) Tree analysis of 60 cells based on selected protein features.




## Correlation between SWATH data and sensitivity to 163 drugs

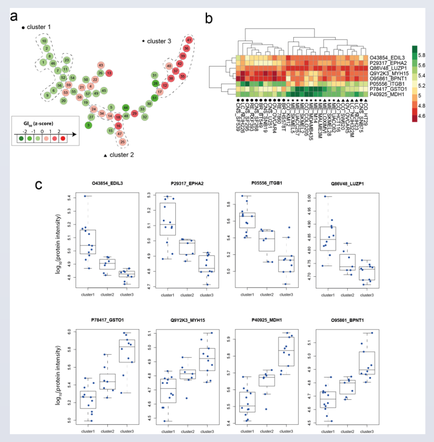



## Drug Response Tree (DRT) of representative chemotherapy and targeted drugs.

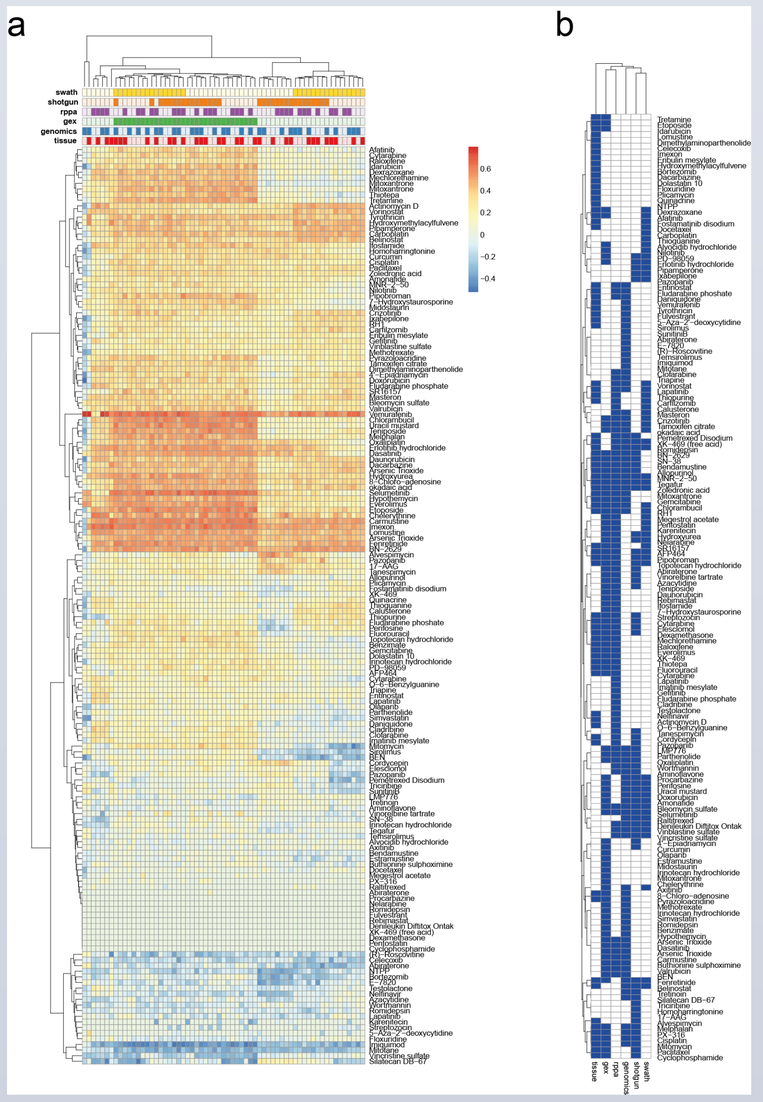



## Drug Response Tree (DRT) of MEK inhibitor selumetinib

(a) Drug response tree for MEK inhibitor selumetinib. Three clusters of sensitive and resistant cells are circled out. The number label of the node matches to the identity of the cell is shown in supplementary Fig. 6. (b) Eight proteins selected by Kruskal-Wallis test resolved the three clusters. (c) Expression of the 8 proteins in the 3 clusters of cancer cells.




## Integration of proteotypes and other features




(a) Overall performance of different feature lists and combinations. On the top of the heatmap, color bars indicate the presence of the 6 types of feature lists. Each column indicates a feature list or combination; each row represents a compound. The color indicates the predictive power of drug responsiveness. (b) Best model built on individual or combinatorial feature list(s) for each compound

## Conclusion

Proteotype obtained by PCT-SWATH provides unique insight to predict phenotypes

## Acknowledgements

Systems X