SCoPE-MS: Quantifying Proteomes of Single Mammalian Cells

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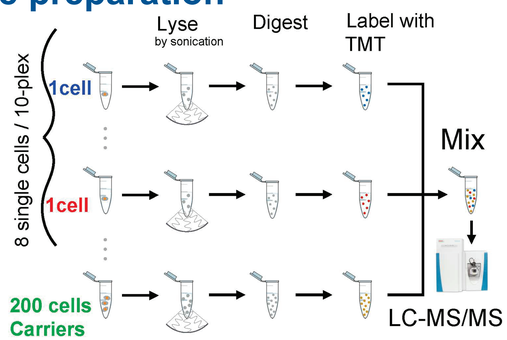
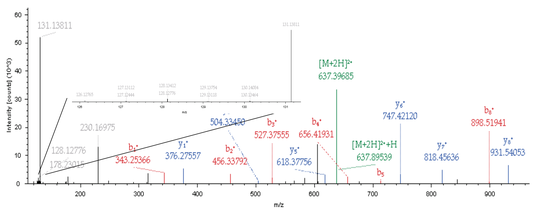
Summary

- Proteome heterogeneity is largely unexplored because of the limitations of existing methods for quantifying protein levels in single cells. Two major hurdles were:
  I. Delivering the proteome of single cell to mass spec with minimal losses
  II. Simultaneously identifying and quantifying peptides from single cell samples
- SCoPE-MS overcomes these hurdles and quantifies over 1000 proteins in single mammalian cells.
- Comparison with mRNA data indicates coordinated mRNA and protein covariation.

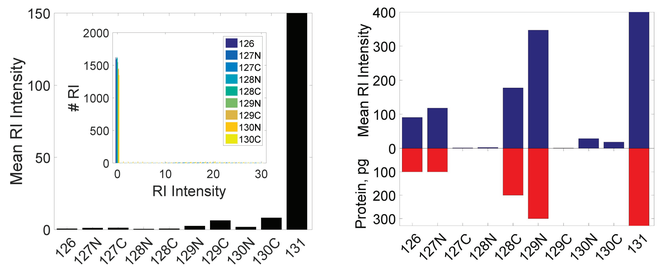
Carrier channel minimizes losses in sample preparation



TMT and carrier channel enable separation of peptide quantitation and identification

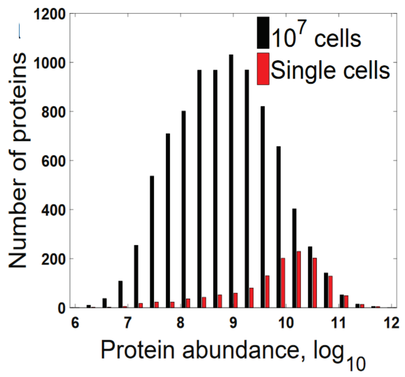


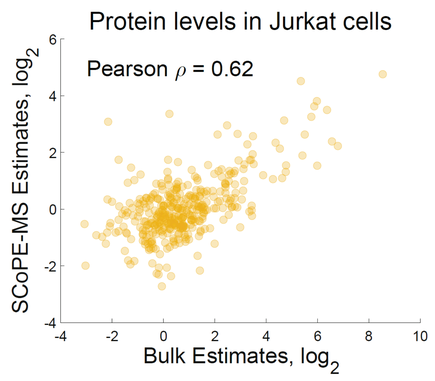
Background noise is low compared to signal from peptides



- (a) Reporter ion intensities in a SCoPE-MS set in which the single cells were omitted while all other steps were carried out.
- (b) Mean RI intensities for a TMT set corresponding to 100, 100, 200, and 300 picograms of cellular proteome.

Comparison to bulk proteomic measurements



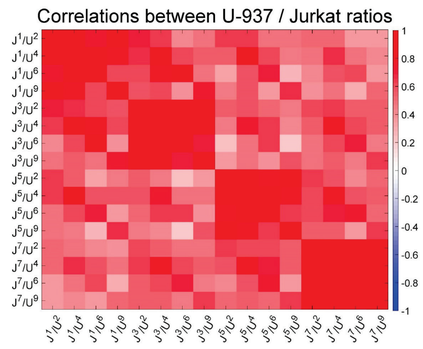


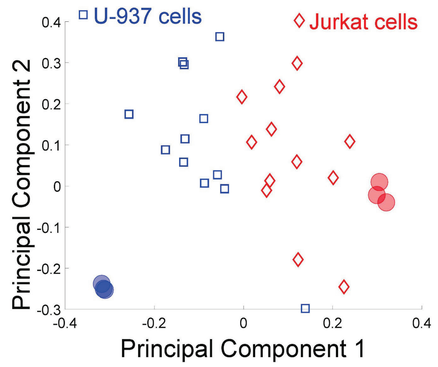
- Probability of quantifying a protein by SCoPE is close to 100 % for the most abundant proteins quantified in bulk samples and decreases with protein abundance.
- SCoPE-MS estimates are the average from 12 Jurkat cells from the experiments described in the figure below.

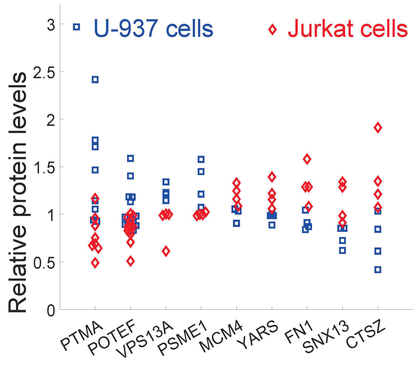
Reproducible relative quantitation allows separation of mammalian cell types

Experimental Design Table

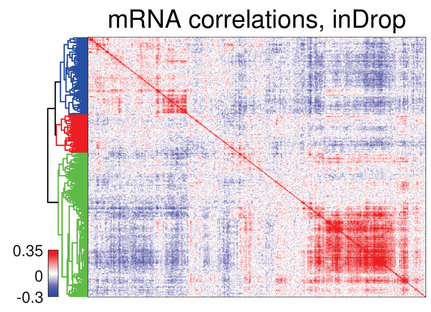
Label	Set 1	Set 2	Set 3
126	U-937	Jurkat	Jurkat
127N	Jurkat	U-937	Jurkat
127C	U-937	Jurkat	Jurkat
128N	Jurkat	U-937	Jurkat
128C	U-937	Jurkat	U-937
129N	Jurkat	U-937	U-937
129C	U-937	Jurkat	U-937
130N	*empty*	*empty*	*empty*
130C	Jurkat	U-937	U-937
131 Carriers	100 Jurkat 100 U-937	100 Jurkat 100 U-937	100 Jurkat 100 U-937

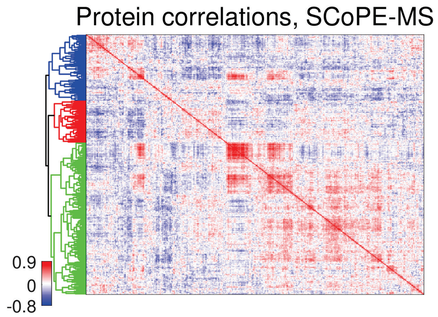


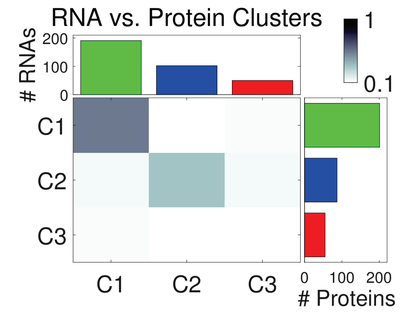




Comparison between mRNA and protein clusters

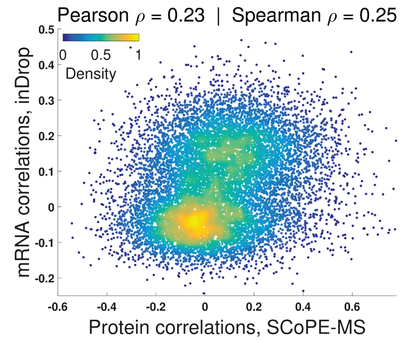


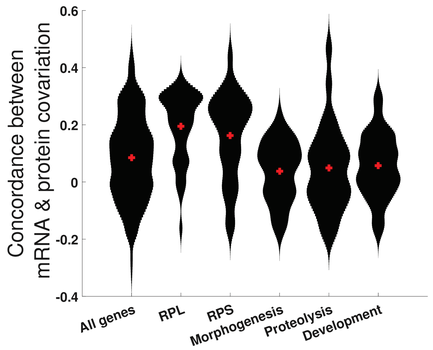




- Clustergrams of pairwise correlations between mRNAs with 2.5 or more reads per cell as quantified by inDrop and proteins quantified by SCoPE-MS in 12 or more single mouse embryoid body cells.
- Overlap between mRNA and protein clusters indicates similar clustering patterns.

Concordance between single cell mRNA and protein correlations suggests covariation for certain cellular functions





Conclusion

SCoPE-MS is broadly applicable to measuring proteome configurations of single cells and linking them to functional phenotypes, such as cell type and differentiation potentials.

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Budnik B., Levy E., Slavov N. (2017) Mass-spectrometry of single mammalian cells quantifies proteome heterogeneity during cell differentiation, bioRxiv, DOI: 10.1101/102681