RISE:2019 | Abstract ID: **2463**
Category: **Physical and Life Sciences Undergraduate**

Northeastern University

DART-ID Increases Single-Cell Proteome Coverage

Albert Tian Chen[1,2], **Alexander Franks**[3], **Nikolai Slavov**[1,2]

1 Department of Bioengineering, Northeastern University, Boston MA 02115, USA
2 Barnett Institute, Northeastern University, Boston MA 02115, USA
3 Department of Statistics and Applied Probability, UC Santa Barbara CA 93106, USA

Slavov Laboratory
Quantitative Biology

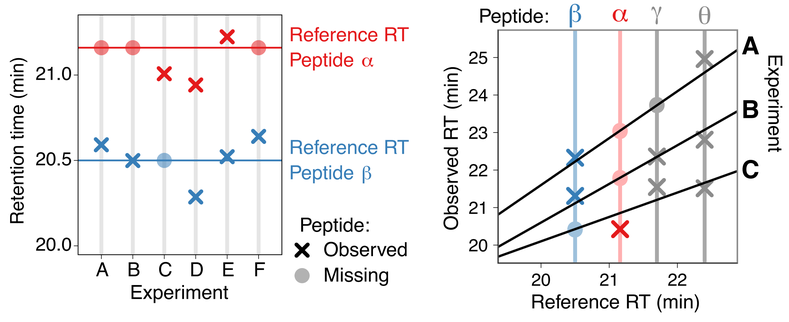
bioRχiv
THE PREPRINT SERVER FOR BIOLOGY
DOI: 10.1101/399121

Summary

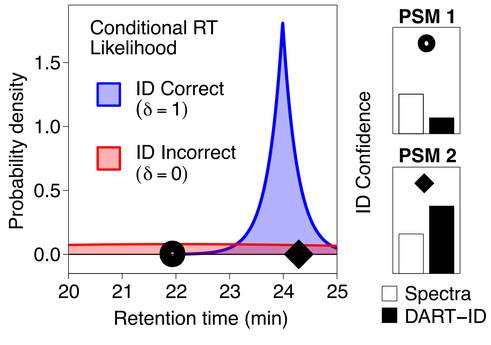
- Cells are unique; differences between single tumor cells can drive resistance to immune system, drugs, and targeted therapies
- Can quantify these differences with proteomics by mass-specrometry
- Single cell samples generate noisy peptide identifications, which reduce the amount of data available for downstream analyses
- Incorporating peptide retention time (RT) within a principled Bayesian framework increases ID confidence and proteome coverage.
- Global alignments of peptide RTs across experiments are more accurate and boost our results even further
- Manuscript: https://doi.org/10.1101/399121
- GitHub: https://github.com/SlavovLab/DART-ID

Approach

- Develop generative model to simultaneously align all experiments



- Incorporate accurate RT estimates with Bayes' Formula



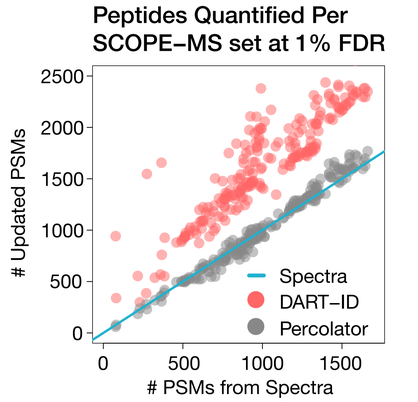
$$P(\text{ ID correct } | \text{ RT }) = \frac{P(\text{ RT } | \text{ ID correct }) \times P(\text{ ID correct })}{P(\text{ RT })}$$

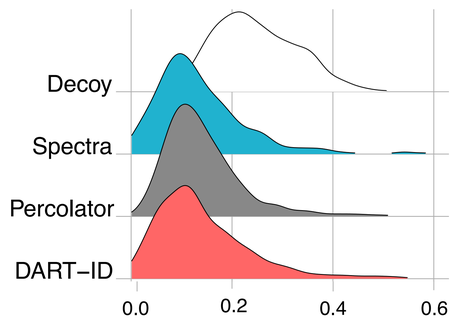
- PSM 1 - confidence downgraded
- PSM 2 - confidence upgraded

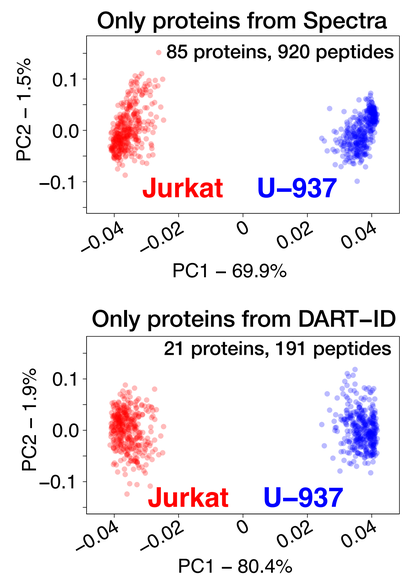
Thanks to members of the Slavov Lab for comments and feedback. This work was funded by the National Institute of Health to N.S. under Project Number 1DP2GM123497-01.

Results

- Increase number of confident peptide identifications by up to 50%
- New identifications are internally and biologically consistent

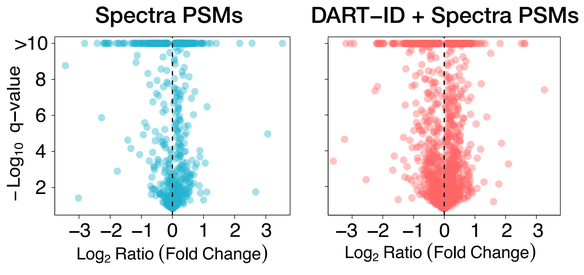


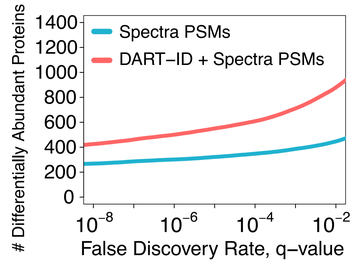


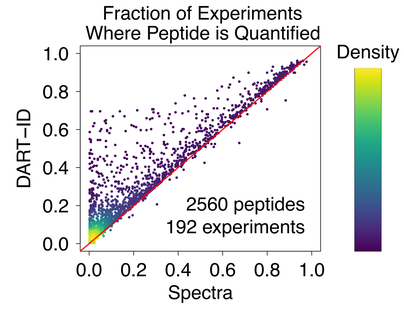


Impact

- Uncover new differentially abundant proteins, reduce amount of data imputation needed







- Boost quantitative coverage of single-cell proteomics experiments
- Improve understanding of individual regulation within single cells, uncover cool single-cell biology

Single cell analysis of differentiating mouse embryonic stem cells (Budnik et al 2019)