Mass Spectrometry-based Omics Solutions

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LSMS

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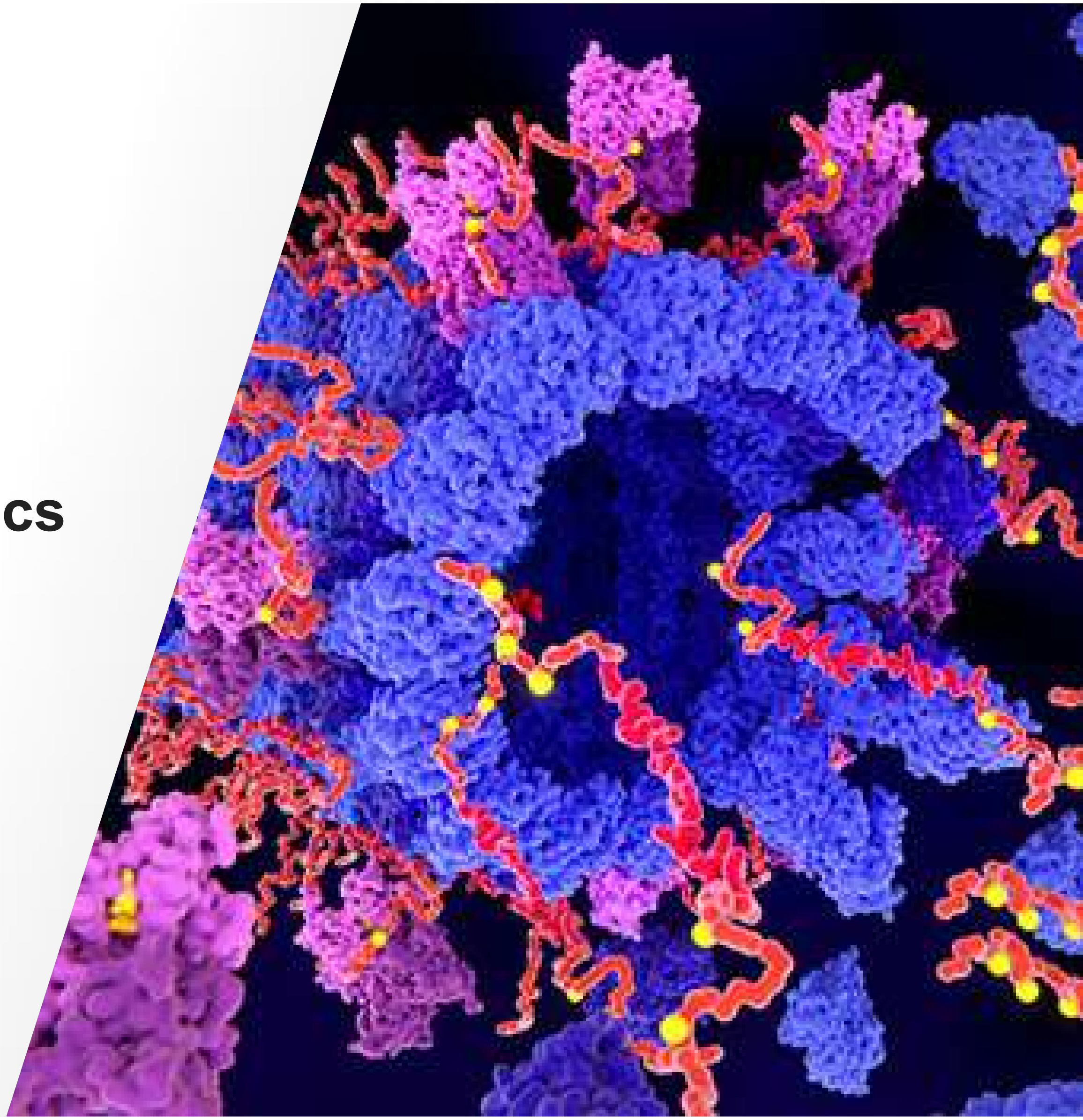
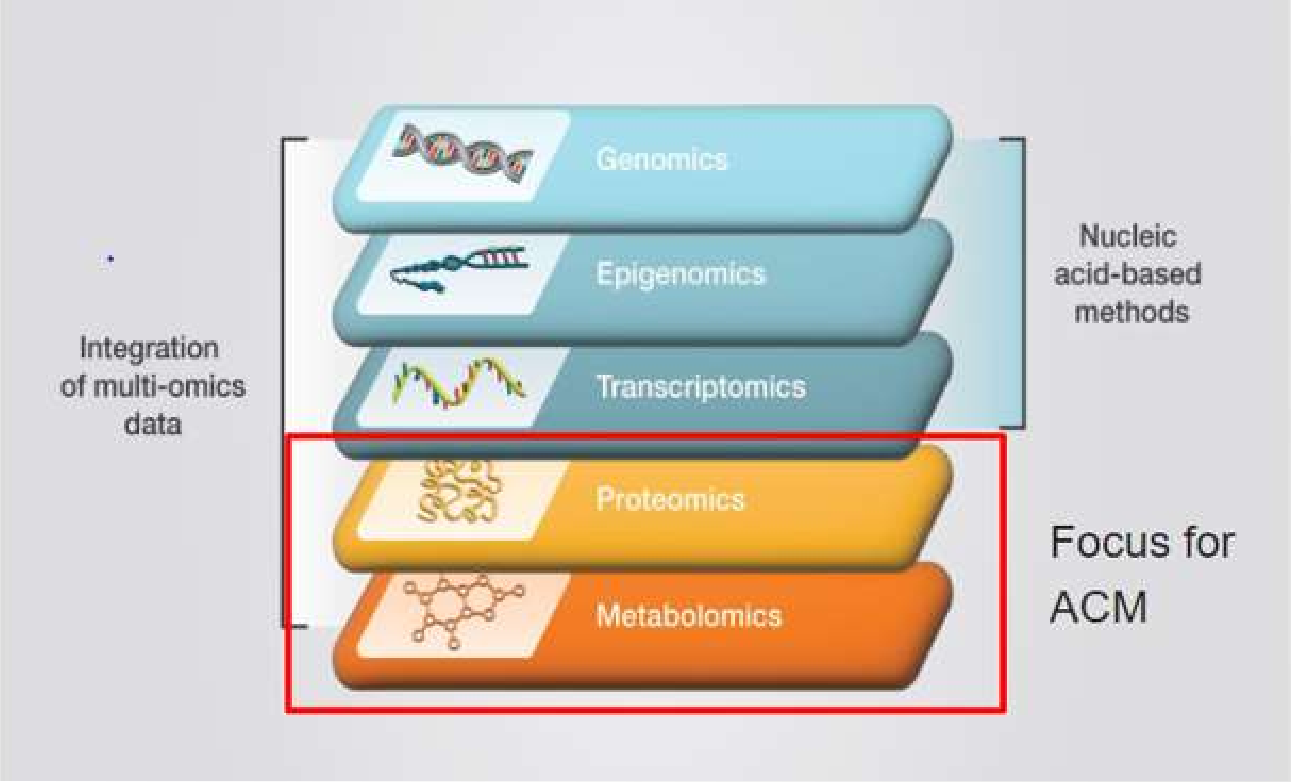
The world leader in serving science



What is OMICS in general?

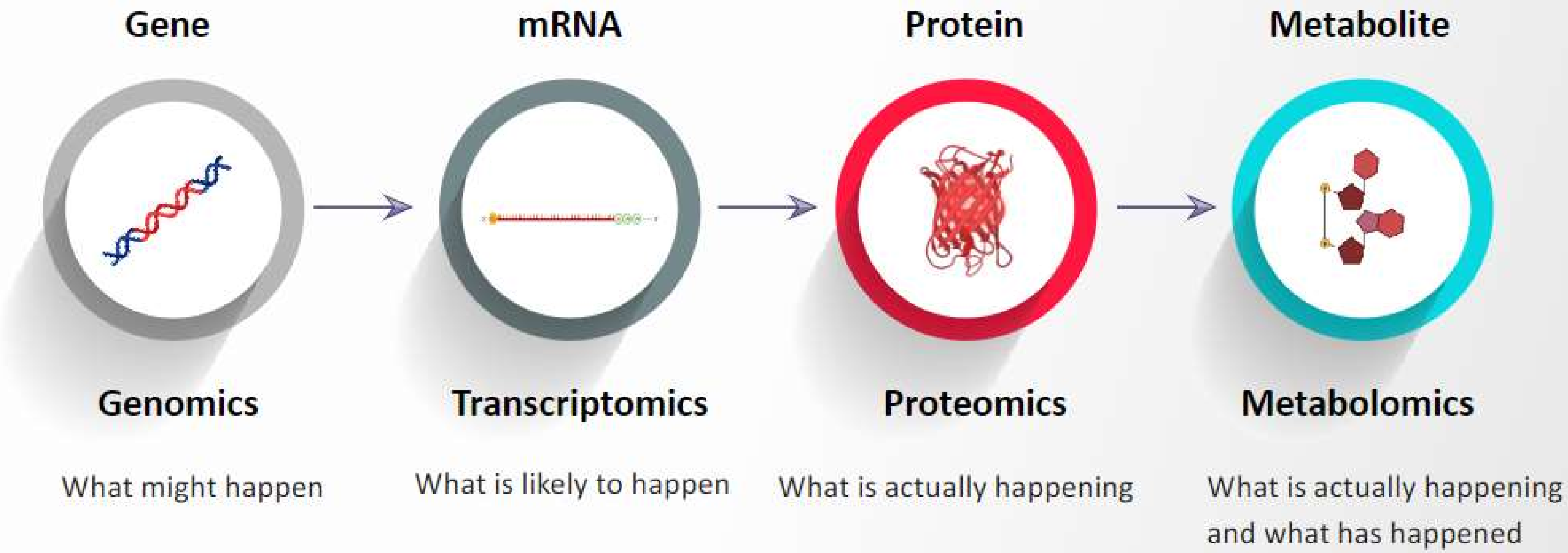
…. *Omics sciences aim to characterize and quantify pools of biological molecules that translate into the structure, function, and dynamics of an organism or organisms…..*

Omics - Wikipedia



Focus for ACM

Why study Proteomics and Metabolomics



Gene

Genomics

What might happen

mRNA

Transcriptomics

What is likely to happen

Protein

Proteomics

What is actually happening

Metabolite

Metabolomics

What is actually happening
and what has happened

Research is often multi-omics

Metabolomics & Proteomics Platform

UNIVERSITY OF CALGARY

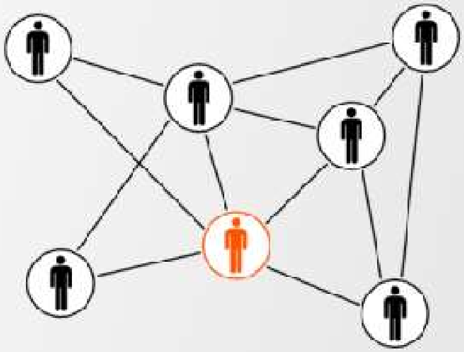
INTERNATIONAL MICROBIOME CENTRE

Proteomics & Metabolomics Core

Cedars Sinai

Proteomics & Metabolomics

Duke University School of Medicine



Mass Spectrometer (MS) main components

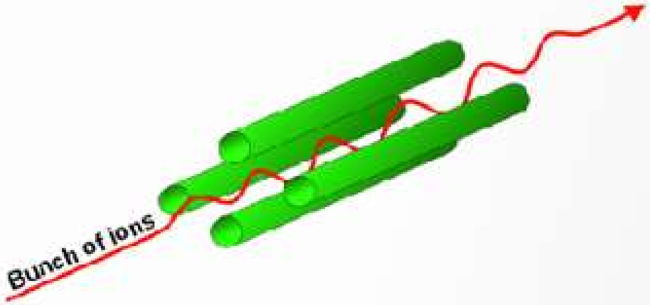
A mass spectrometer consists of three components

- Ion source
- Mass Analyzer
- Detector

Heated Electrospray Ionization (HESI-II) Probe

Soft Ionization techniques
- (ESI, CI, FAB, APCI, APPI, MALDI, DESI)

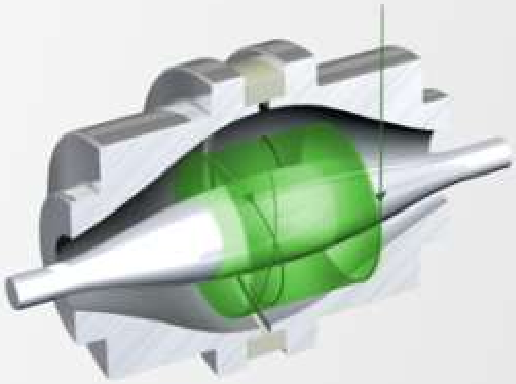
Hard Ionization techniques
- (EI)



Quadrupole mass analyzer

Low resolution
- Quadrupole mass filter
- Ion traps

High resolution
- Magnetic sector instruments
- Time-of-flight
- Orbitrap



Orbitrap Technology

Electron multiplier
    Faraday cups
Microchannel plate detectors
    TOF instruments
Orbitraps
    Both Detector and Analyzer

Mass Spectrometer partners and mass spectrum

Direct Injection coupling

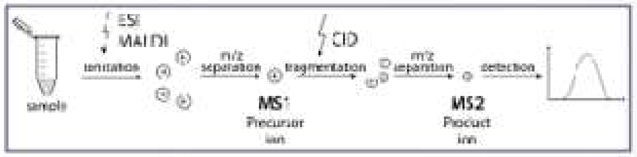
- FAIMS
- MALDI (AP-MALDI)
- LDTD
- DART
- ASAP

Separation techniques coupling

- **Liquid chromatography**
  - liquid chromatography (LC/MS or LC-MS) separates compounds chromatographically
- **Gas chromatography**
  - a gas chromatograph is used to separate different compounds
- **Capillary electrophoresis**
- **Ion mobility**
  - Ions are first separated by drift time through some neutral gas under an applied electrical potential gradient

Tandem Mass Spectrometry

Multiple rounds of MS separated by molecular fragmentation (MS/MS, or MS^n)



Methods for fragmenting molecules for tandem MS

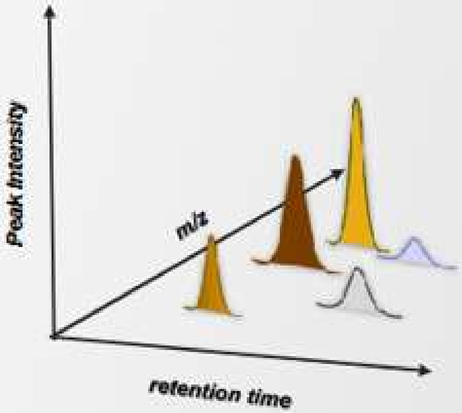
- collision-induced dissociation (CID)
- Higher-collision dissociation (HCD)
- electron capture dissociation (ECD)
- electron transfer dissociation (ETD)
- UVPD

Why tandem MS?

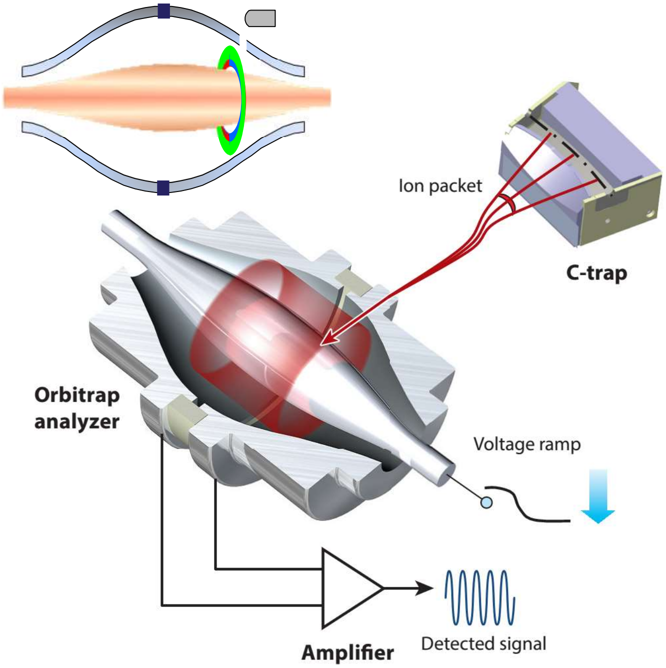
ex: small molecule & protein identification

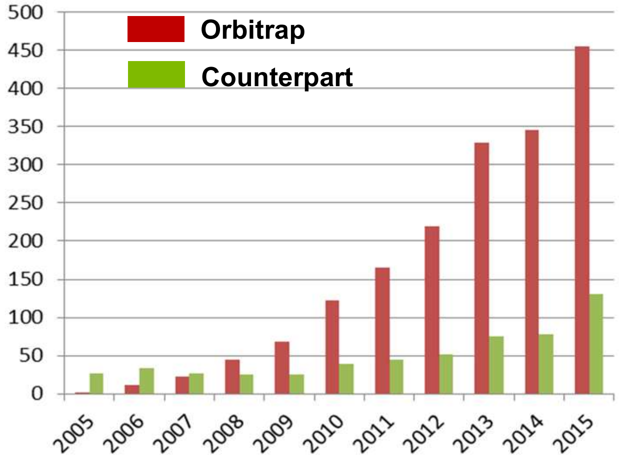
Measure of mass/charge ratio of ions

- Mass spectrum is a plot of Intensity as a function of the mass-to-charge ratio of ions
- With LC as a function of RT (retention time)



Orbitrap: leading technology in HRMS since 2005





Unmatched **H**igh **R**esolution, **A**ccurate **M**ass performance

Dr. Alexander Makarov
Inventor of Orbitrap

Provide Versatile, Scalable Mass Spec Platforms and Workflows

Native Ab Unknowns Omics SCP Metabolomics Profiling Multi-matrix Multi-Omics

Structural , Discovery and Translational Platforms / Workflows → *Targeted Verification*

Thermo Scientific™ Orbitrap™ Ascend Editions Tribrid™ Mass Spectrometers

Thermo Scientific™ Hybrid Orbitrap Mass Spectrometers

Thermo Scientific™ Orbitrap™ Astral™ Mass Spectrometer

Thermo Scientific™ Stellar™ Mass Spectrometer

↓

Routine Diagnostic Workflows

Thermo Scientific™ Triple Quadrupole Mass Spectrometers (GLE)

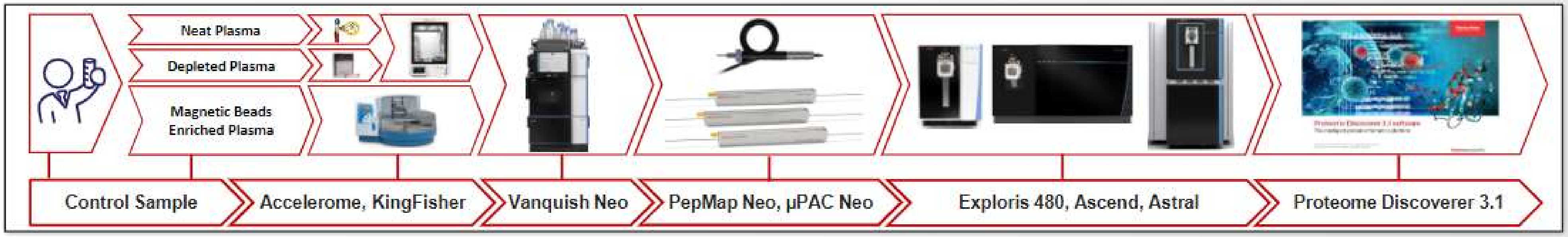
Thermo Scientific™ Altis MD Triple Quadrupole Mass Spectrometers (IVD)

Tackling unmet needs in Omics and Proteomics for Discovery to Clinical

Biomarker Discovery Proteomics Workflow Overview

Translational Research Proteomics- Plasma

Sample Prep
Separation
Detection
Software (Acquisition, Processing, Reporting)


Neat Plasma
Depleted Plasma
Magnetic Beads Enriched Plasma
Control Sample
Accelerome, KingFisher
Vanquish Neo
PepMap Neo, µPAC Neo
Exploris 480, Ascend, Astral
Proteome Discoverer 3.1

Core Proteomics applications


Peptide ID
LFQ
TMT SPSMS3
Phosphorylation
Glycoproteomics
Crosslinking
TMT MS2
SILAC
PRM
Top Down
Ubiquitination
IBAQ
Metabolomics
Lipidomics
iTRAQ MS2
Glycomics
Spectral Counting
Dimethyl Labeling
Acetylation
DIA
Intact Analysis
Middle Down
Methylation
HDX
ADP Ribosylation
DiLeu Labeling
Denovo Sequencing
Other PTMs
iTRAQ SPS MS3
WISIM DIA
SUMOylation
Glycation
Single Cell
Peptide Mapping
Oxidation
S-nitrosylation
SIM
Metabolic Labeling 15N
IodoTMT
TOMAHAQ
S-Palmitoylation
NeuCode
Hydroxylation
Glutathionylation
Disulfide Mapping
Citrullination
aminoxyTMT
Acylation
Absolute Protein Quan
γ-carboxylation
Thiol Modifications
TAILS
SWARM
Sulfur-containing Amino Acids
Sulfation
Succinylation
S-sulfination
S-sulfhydration
S-sulfenylation
SLIM
S-glutathionylation
S-[illegible]
Propionylation
Prolyl Hydroxylation
Prenylation
Phosphoribosylation of Ubiquitin
Peptide Epimer Analysis
Pegylation
N-TAILS
NSAF
Native MS
Metabolic Labeling HCl
Metabolic Labeling 13C glucose, 13C acetate
Malonylation
Limited Proteolysis
Lasso Peptides
IP-MS
Hydroxyproline
Gamma Carboxylation
Farnesylation
Disulfide Structures
Disulfide Bridges
DIPyrO
[illegible]
Deamidation
Cysteine Residue
Covalent Labeling
Combinatorial Isobaric Mass Tags
Carbamylation
Biotinylation
BioID
Arginylation
AP-MS
AIM

>80 proteomics applications

1. However, most researchers buy instruments for Peptide ID and Quantitation
   - LFQ DDA
   - LFQ DIA
   - TMT
2. They might also buy for PTM analysis
   - Phosphorylation
   - Glycosylation

Olink is Part of Thermo Fisher Scientific

The proprietary and innovative Olink proteomics discovery technology is ***highly complementary*** *to Thermo Fisher's leading life sciences and mass spectrometry platforms.*


Olink is now part of Thermo Fisher Scientific

Enhance our capabilities to create customer value in the high-growth proteomics market

https://olink.com/

Olink solutions are used by labs around the world

OVER

1000+

Leading biopharma & academic customers

ALL

Top 30

Largest biopharma companies (by rev)

MORE THAN

2000+

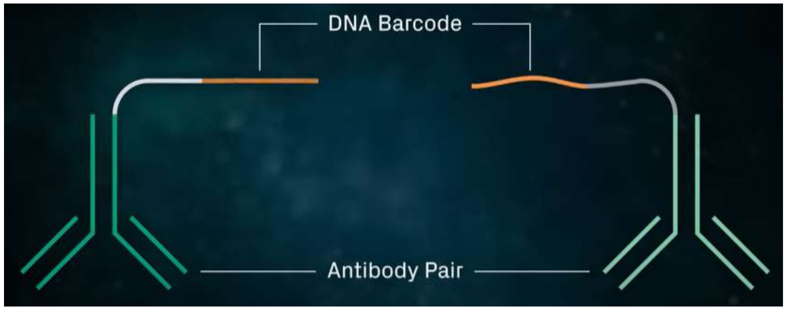
Peer reviewed publications

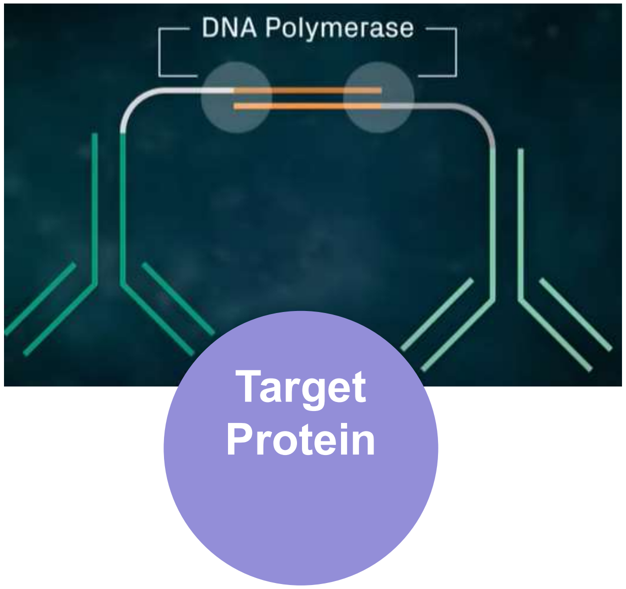
OVER

4M+

Samples analyzed on Olink platform

Olink Proximity Extension Assay (PEA）





qPCR or NGS

Olink: From Discovery to Translation, on One Platform

Olink's innovative, modular proteomics solutions support the complete drug development workflow*

Discovery

Olink Explore

Measure proteins across the proteome using minute sample

Proteins

5,400+

With proven specificity

Runs on

NGS

Automated workflow

Validation

Olink Target

Modular panels for specific diseases or processes

Proteins

1,100+

On 15 targeted panels

Runs on

Signature Q100

Benchtop instrument

Translation

Olink Flex & Focus

Custom panels to help transition from discovery to clinical utility

Proteins

Up to 21

Custom assays

Runs on

Signature Q100

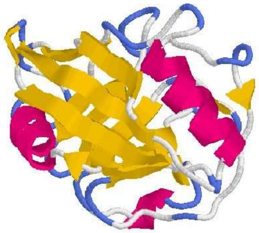
Benchtop instrument

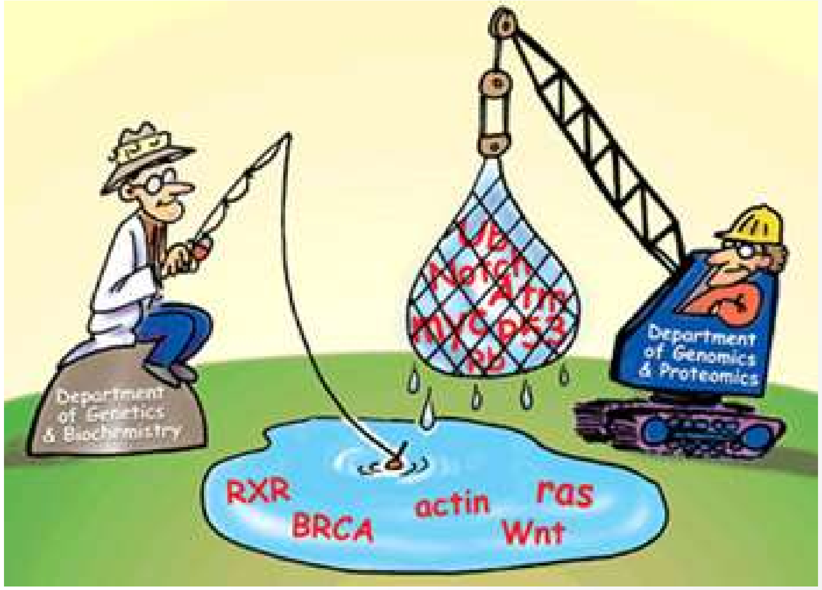
*Olink products are for research use only (RUO)

Proteomics on Mass Spectrometry

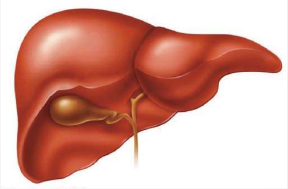
Traditional technologies vs. Mass spectrometry

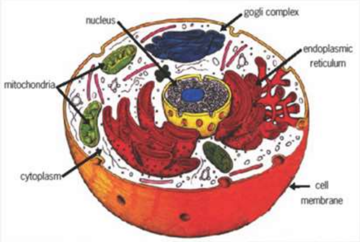
Traditional technologies





Mass spectrometry

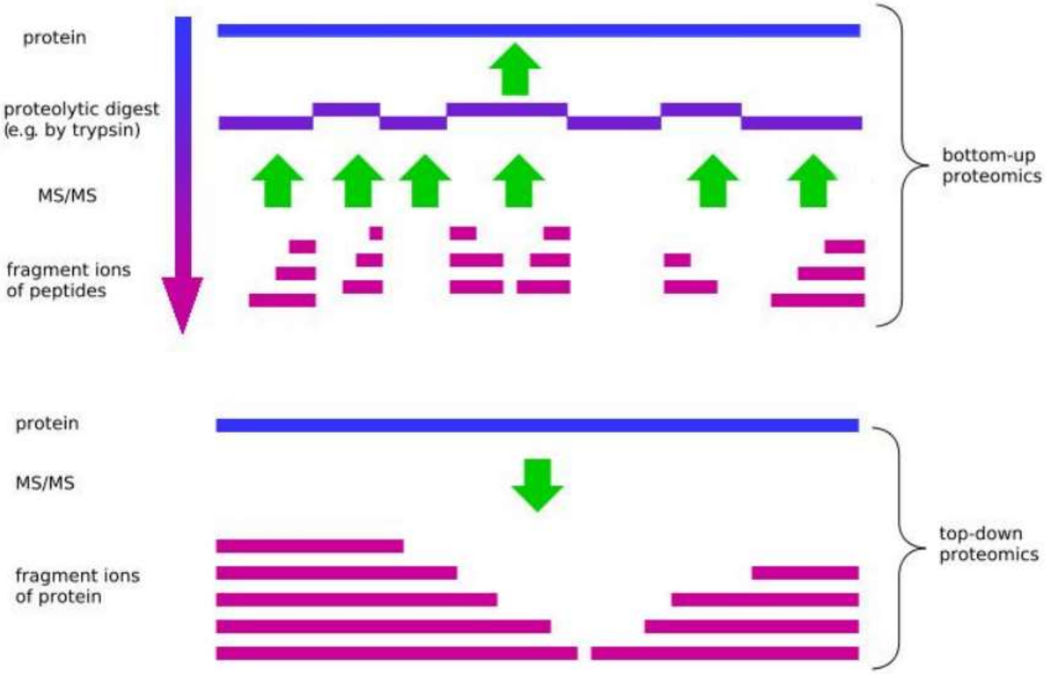




- Mass spectrometry can provide solutions in proteomics with **higher throughput, higher sensitivity, deeper coverage, more accurate and precise quantitation.**

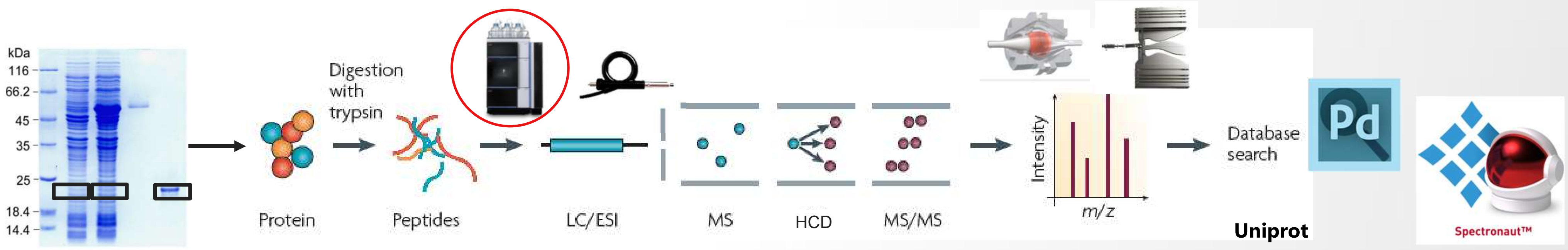
Different analysis strategies in proteomics

Top-down V.S. Buttom-up

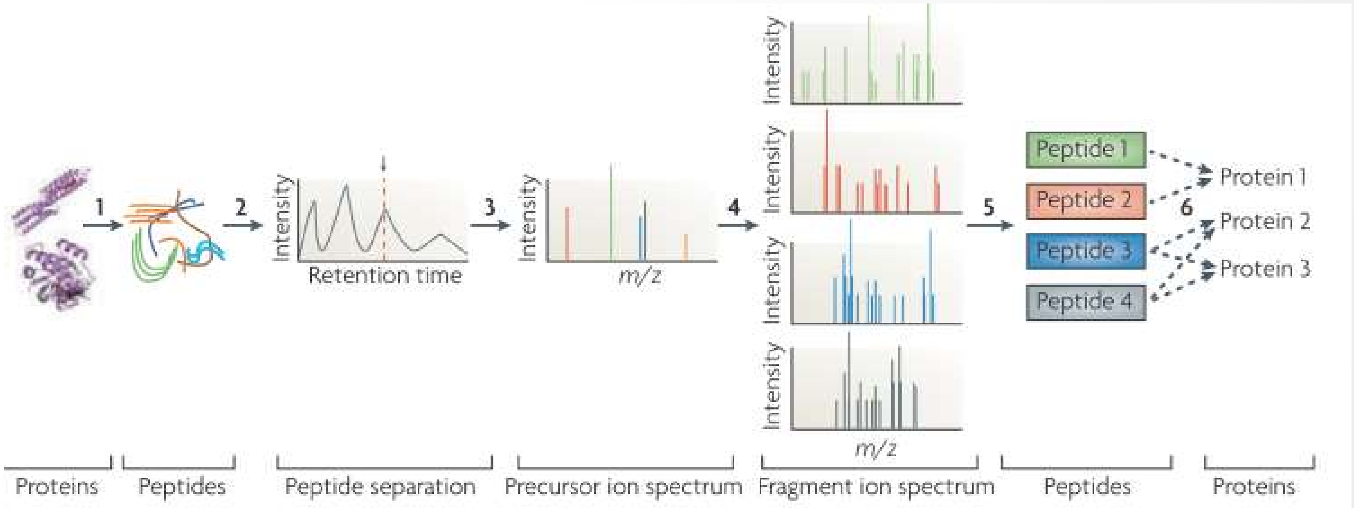


- Buttom-up: sensitivity and higher throughput have become the main ideas of proteomics
- Top-down: better to reflect the different modification and selective shearing state of protein

Bottom-up Proteomics



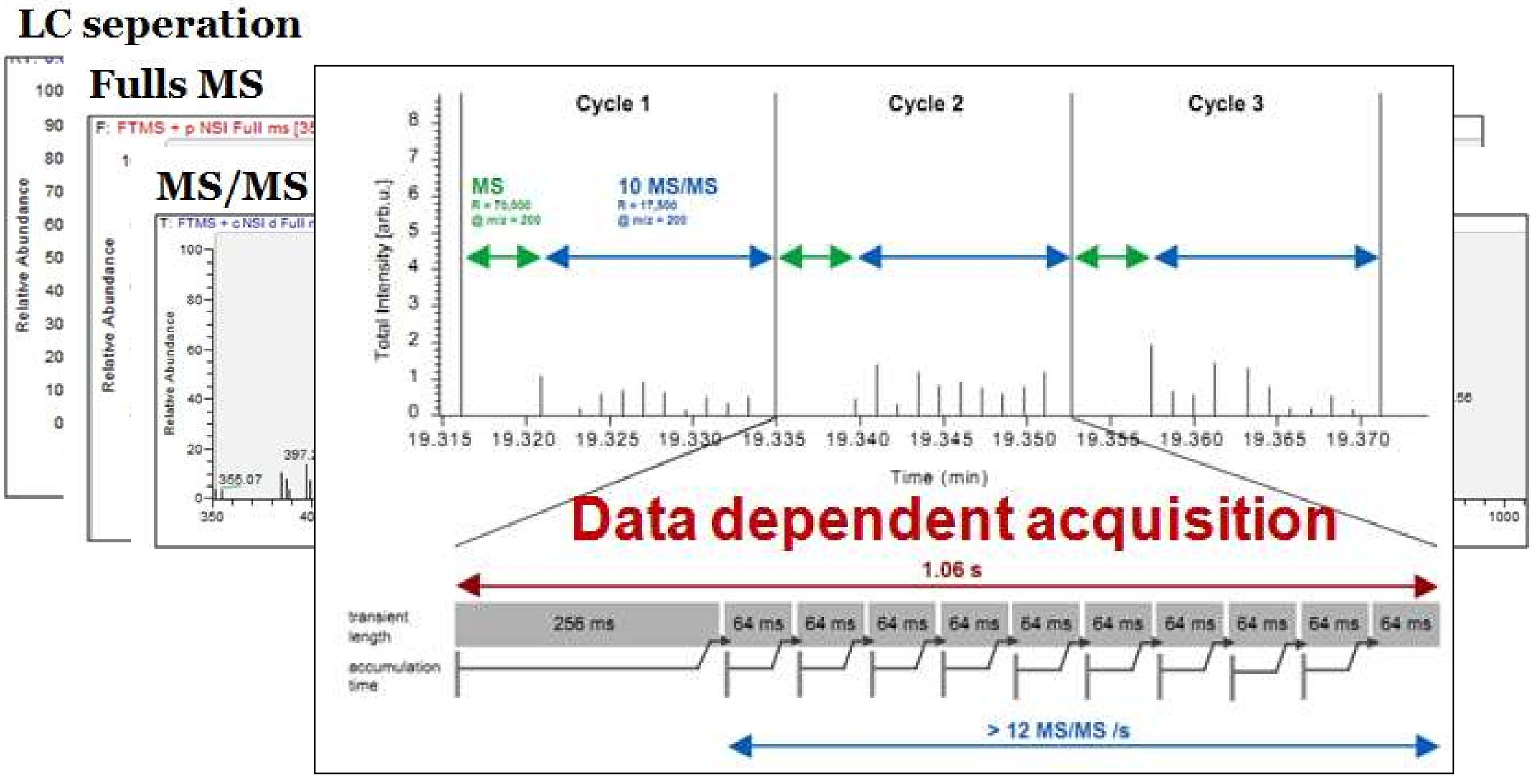
Cells, tissues…



- The precise mass of the parent ion and the fragment ion information were used to determine the peptide sequence
- Usually rely on protein sequence databases

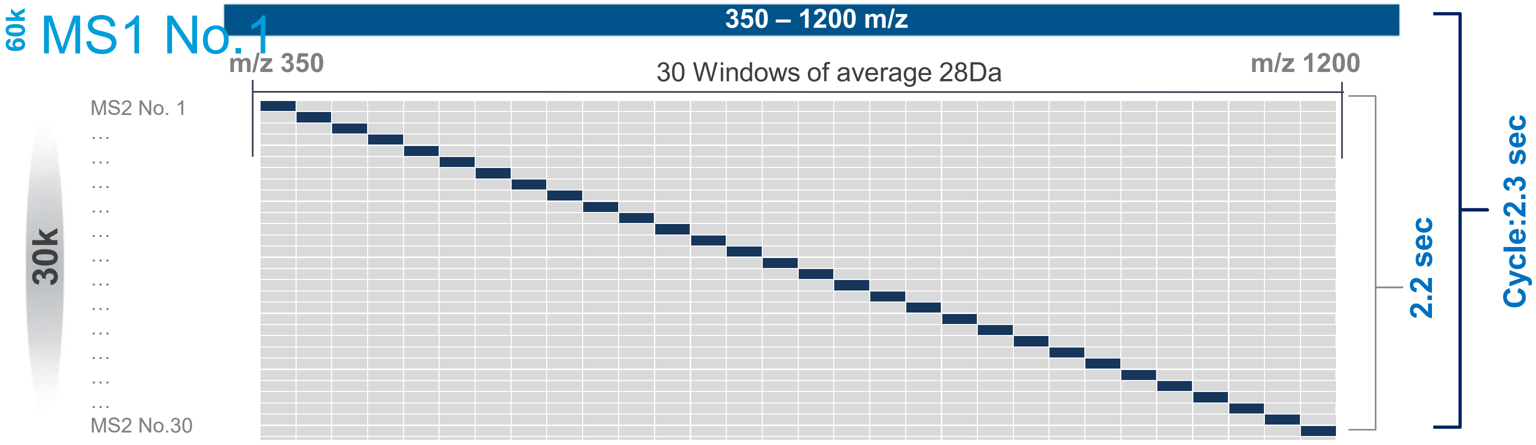
Typical data dependence acquisition (DDA) mass spectrometry

Lysis → Reduction/Alkylation → Digestion → Separation /enrichment → purification



Data Independent Acquisition

Cycle time：28Da windows covering the mass range from 350 to 1200



60k MS1 No.1

350 – 1200 m/z

m/z 350

30 Windows of average 28Da

m/z 1200

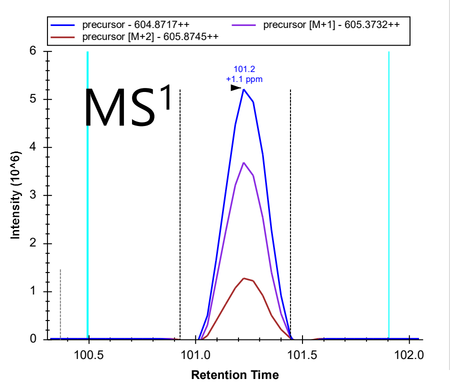
MS2 No. 1
…
…
…
…
…
…
…
…
…
…
…
…
MS2 No.30

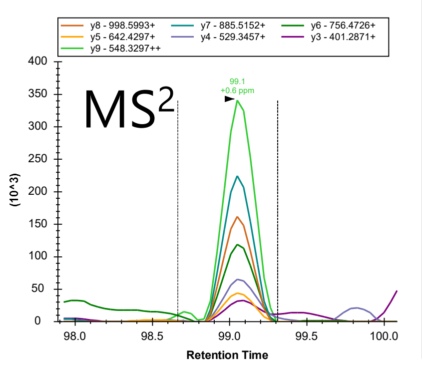
30k

2.2 sec

Cycle:2.3 sec

Both MS1 and MS2 can be used for quantification





Mol Cell Proteomics 11, no. 6 (2012): O111 016717.

Data-Independent Acquisition (DIA) – Minimizing Missing Values

Maximum Quantitative Precision and Accuracy with No Compromise in Coverage

DIA Workflow Assisted by Deep Neural Networks

Step 1

In Silico PROSIT Peptide Library Creation

Step 2

Spectral Library Building Experiment

Step 3

MS-1 Quantitative Experiment (DIA)

Fasta File

Predicted Peptide Library

m/z 380-460

m/z 680-760

m/z 755-835

m/z 455-535

m/z 530-610

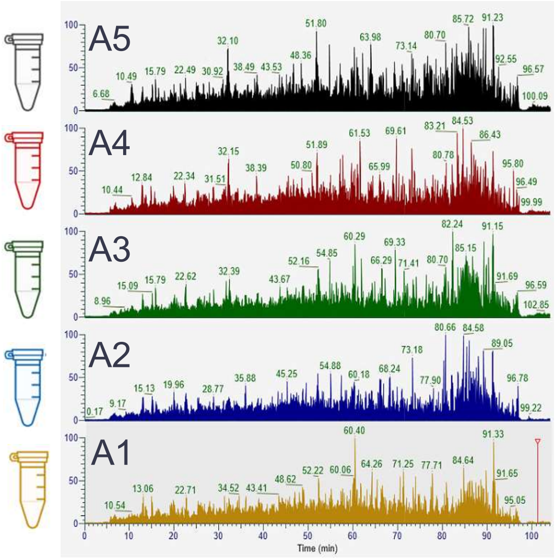
m/z 830-910

m/z 605-685

m/z 905-985

8-injection GPF-DIA of pool sample

3 Da Isolation Window with 1 Da Overlap

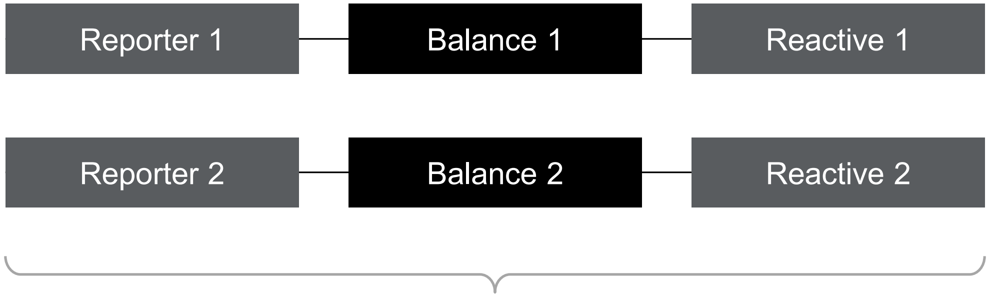


10 Da Isolation Window- 3 Replicate Injection per Sample (n=5)
m/z 380-980

Note：Result from middle-end Orbitrap mass spectrometer

How do Isobaric Tags Such as TMT Work?

Delivering on Quantitative Precision

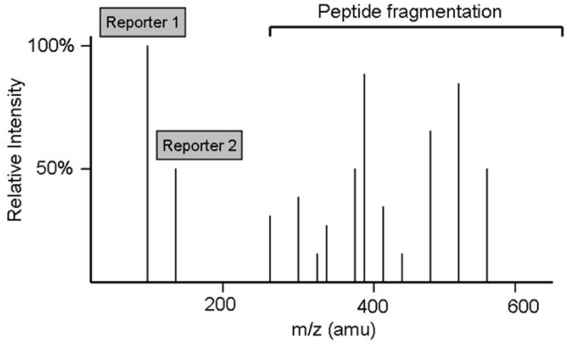


Peptide from Patient 1

Peptide from Patient 2

229.163 Da

The tagged peptides behave exactly the same, except during fragmentation.

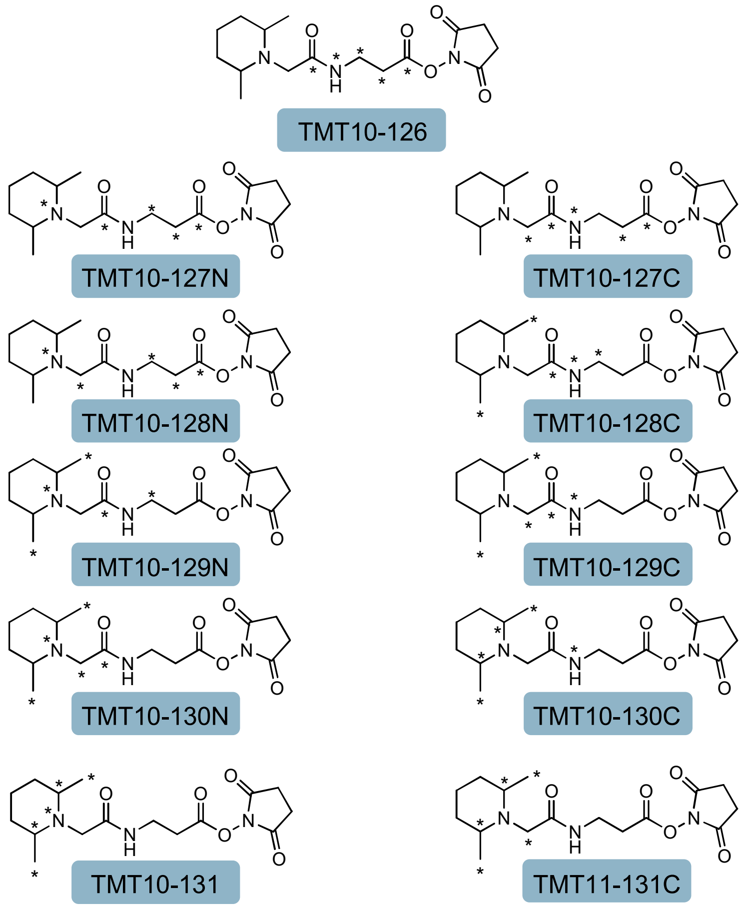


This spectra indicates that this protein is upregulated in patient 1 approximately 2 fold

Up to 11 samples can be analyzed in a single scan using TMT11plex

- TMT11-131C can be used in combination with Thermo Scientific™ TMT10plex™ Label Reagents to multiplex 11 different samples for MS analysis
- TMT11plex data analysis is supported by Thermo Scientific™ Proteome Discoverer™ software (versions 2.1 -2.4).

Thermo Scientific™ TMT11plex Reagents



	Reporter Ion Mass
TMT10-126	126.1277261
TMT10-127N	127.1247610
TMT10-127C	127.1310809
TMT10-128N	128.1281158
TMT10-128C	128.1344357
TMT10-129N	129.1314706
TMT10-129C	129.1377905
TMT10-130N	130.1348254
TMT10-130C	130.1411453
TMT10-131	131.1381802
TMT11-131C	131.144999

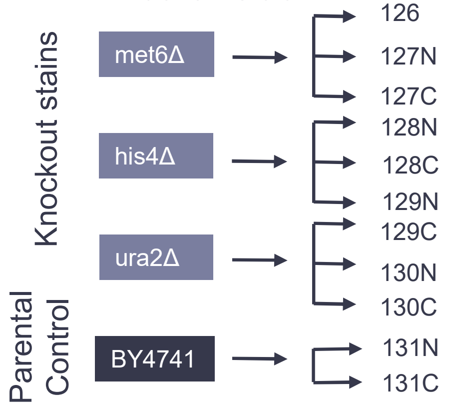
Tandem Mass Tag and TMT are trademarks of Proteome Sciences plc.

TMT Multiplexing

Maximum Reproducibility and Accuracy

Experimental Design

4 strains of *Saccharomyces cerevisiae*



Knockout stains

met6Δ → 126, 127N, 127C

his4Δ → 128N, 128C, 129N

ura2Δ → 129C, 130N, 130C

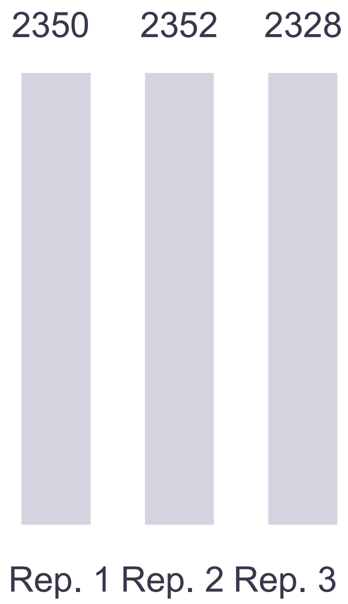
Parental Control

BY4741 → 131N, 131C

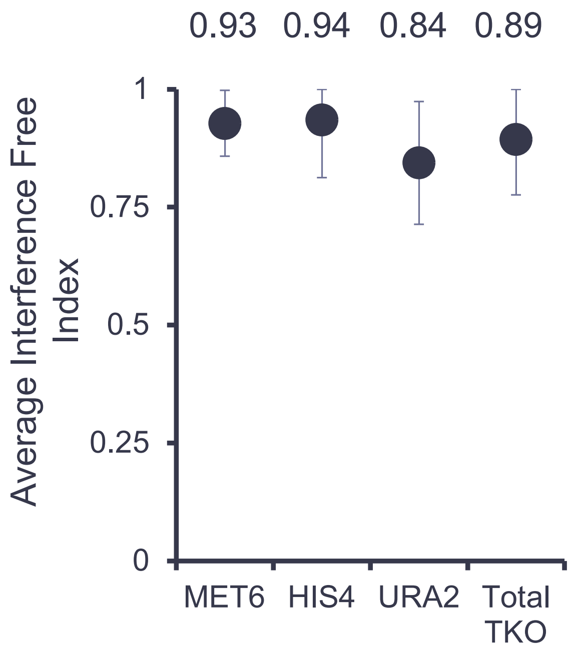
- TMT Yeast Digest Standard
- 500ng- 120 minutes LCMS analysis

Quantified Peptides

Quantified Proteins



Accuracy



Note：Result from middle-end Orbitrap mass spectrometer

Targeted Protein Quantification

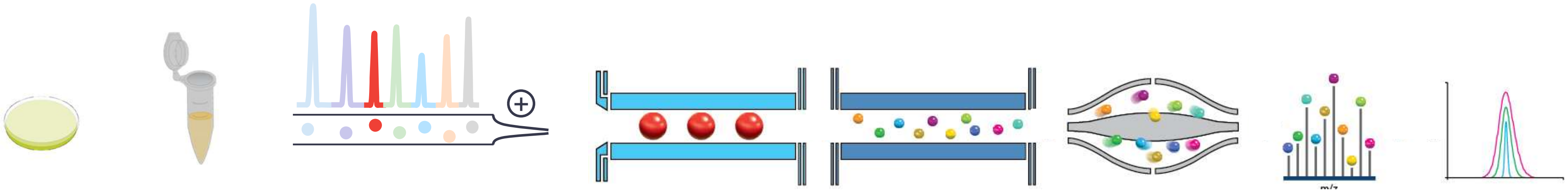
Parallel Reaction Monitoring (PRM)

A label-free discovery proteomics workflow that allows unmatched proteome coverage with reproducible and precise quantification of up to hundreds of proteins per sample.

Protein extraction, digestion and clean-up

LC separation and MS data acquisition

Peptide confirmation and HR/AM quantitation



Sample

Purified peptides

Peptide separation and ionization

Precursor ion isolation

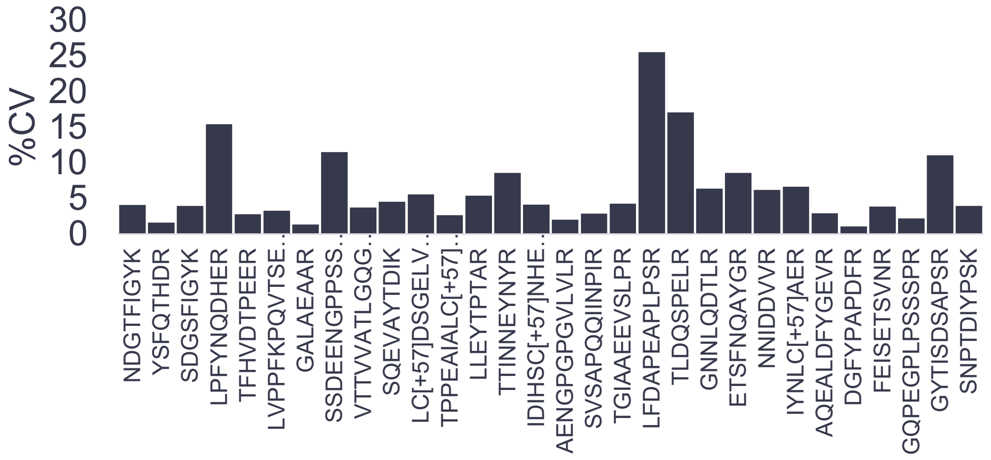
Precursor ion fragmentation

Simultaneous fragment ion detection by Orbitrap analyzer

Sequence ion MS/MS spectra

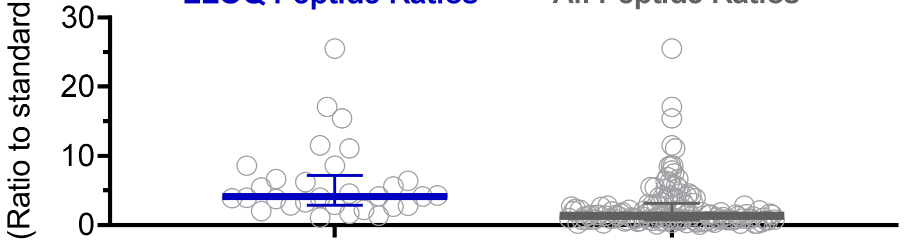
MS^2 quantification

Reliable Precision and Accuracy



Precision at LLOQ ➡ 83% of peptides CV<10%

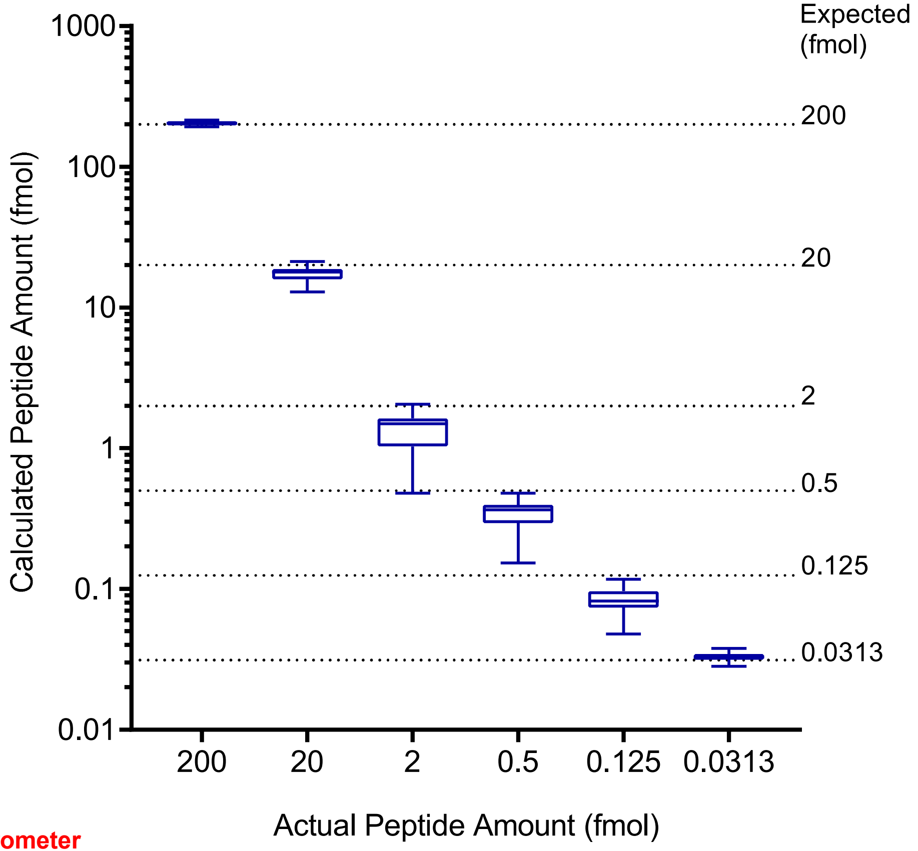
LLOQ Peptide Ratios **All Peptide Ratios**



Median %CV:	4.13	1.36

Note：Result from middle-end Orbitrap mass spectrometer

Accurate quantitation across 5 orders of dynamic range



Thermo Scientific Orbitrap's Success…

50+

Different proteomics workflows enabled by Orbitrap MS technology

> 100,000

Peer-reviewed Orbitrap publications since introduction in 2005

100

Orbitrap Astral peer reviewed publications since launch in 2023

> 6000

Orbitrap Hybrids Installations worldwide

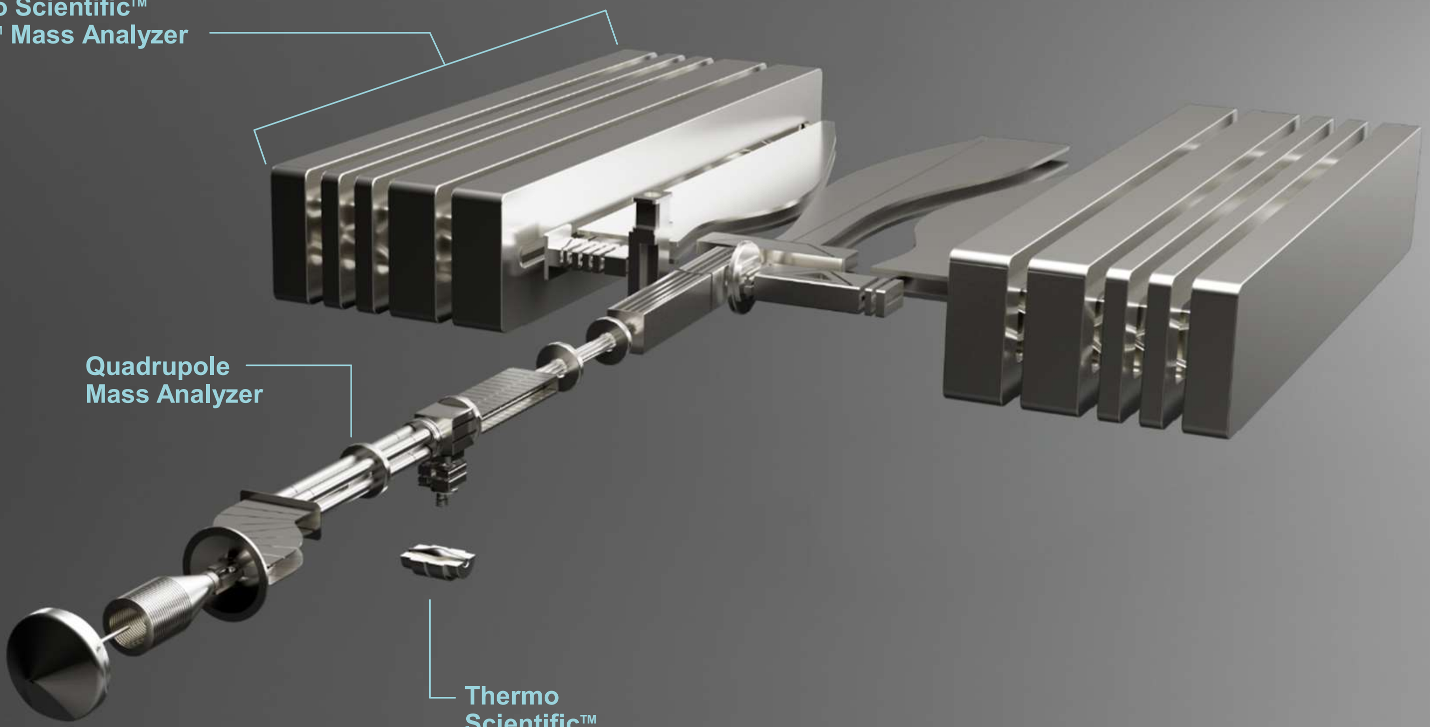
> 1000

Orbitrap Tribrid Installations worldwide

> 200

Orbitrap Astral Installations worldwide

The Orbitrap Astral MS



For Research Use Only

Core technology of ASymmetric TRAck Lossless analyzer

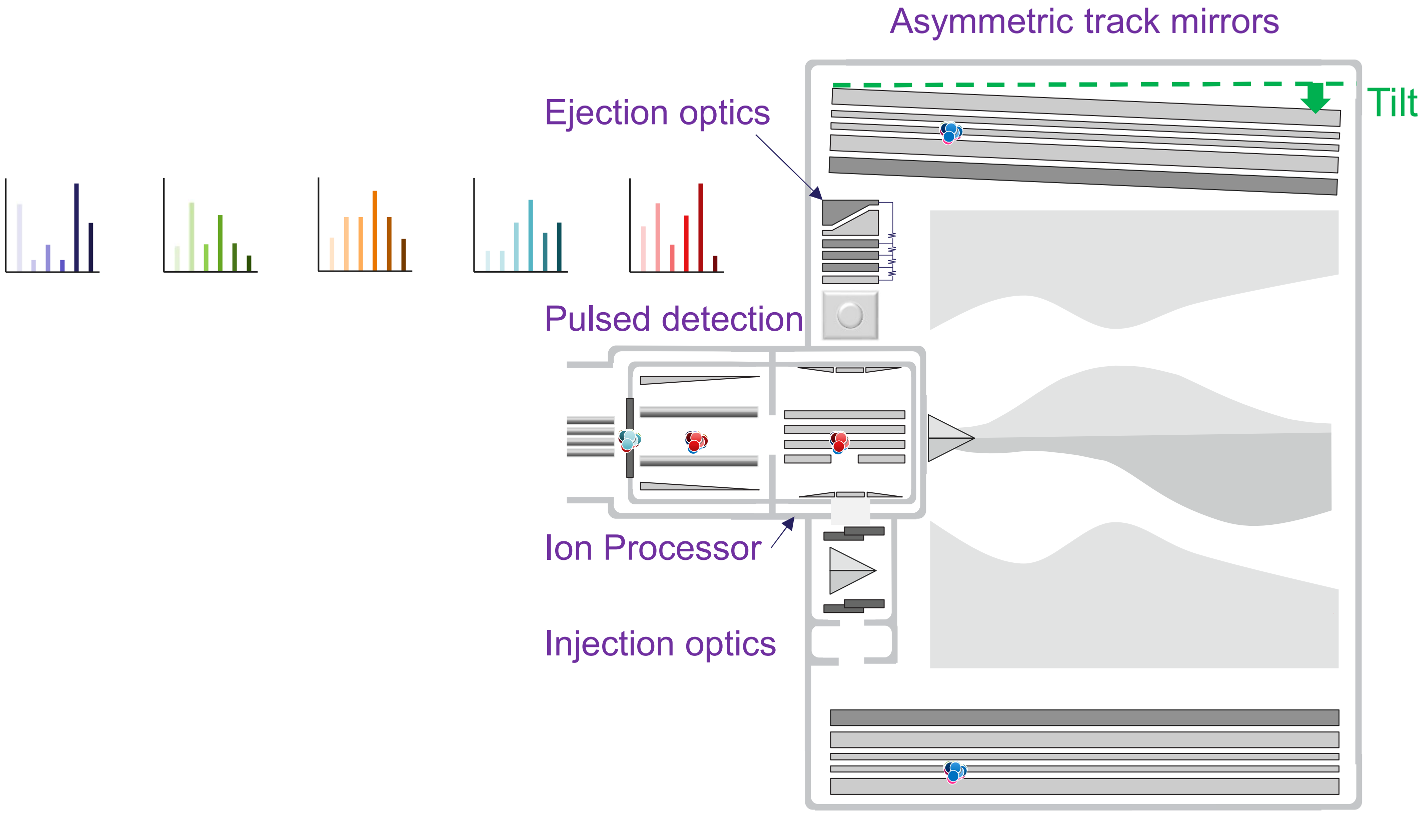
Astral analyzer =

= Ion Processor

+ Injection optics

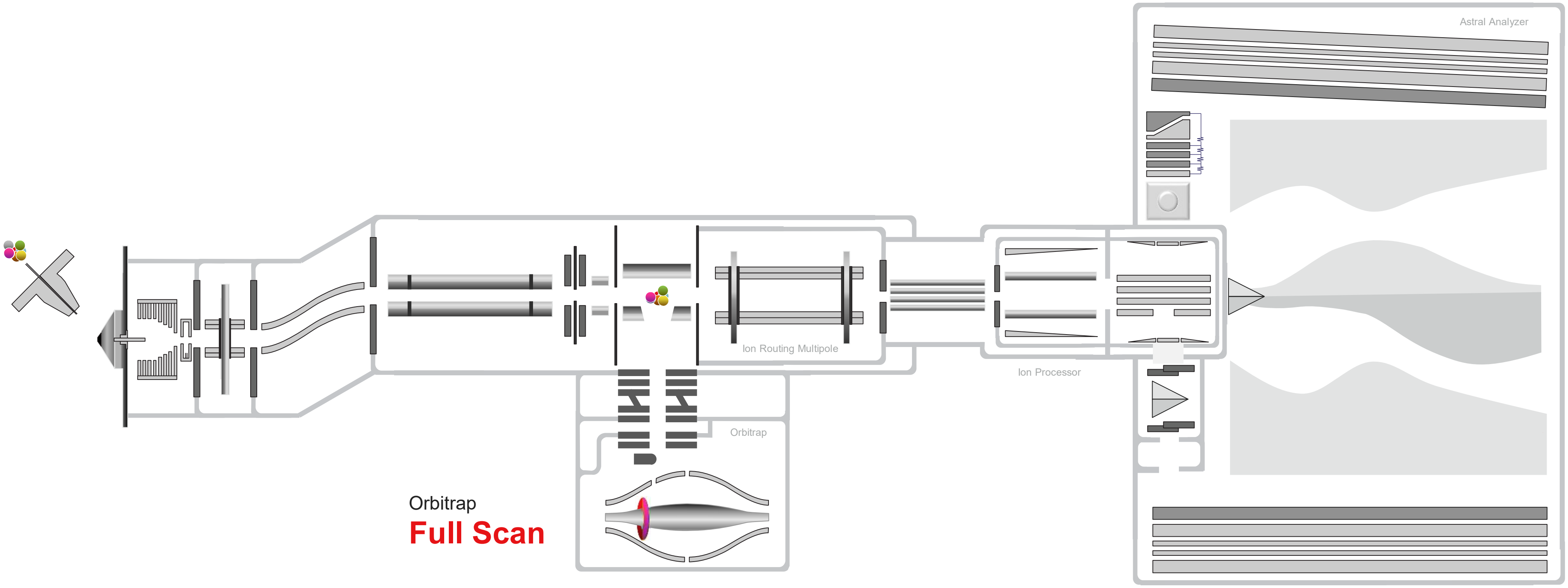
+ Multi-reflection
 asymmetric mirrors

+ High dynamic range
 pulsed detection



200 spectra/second

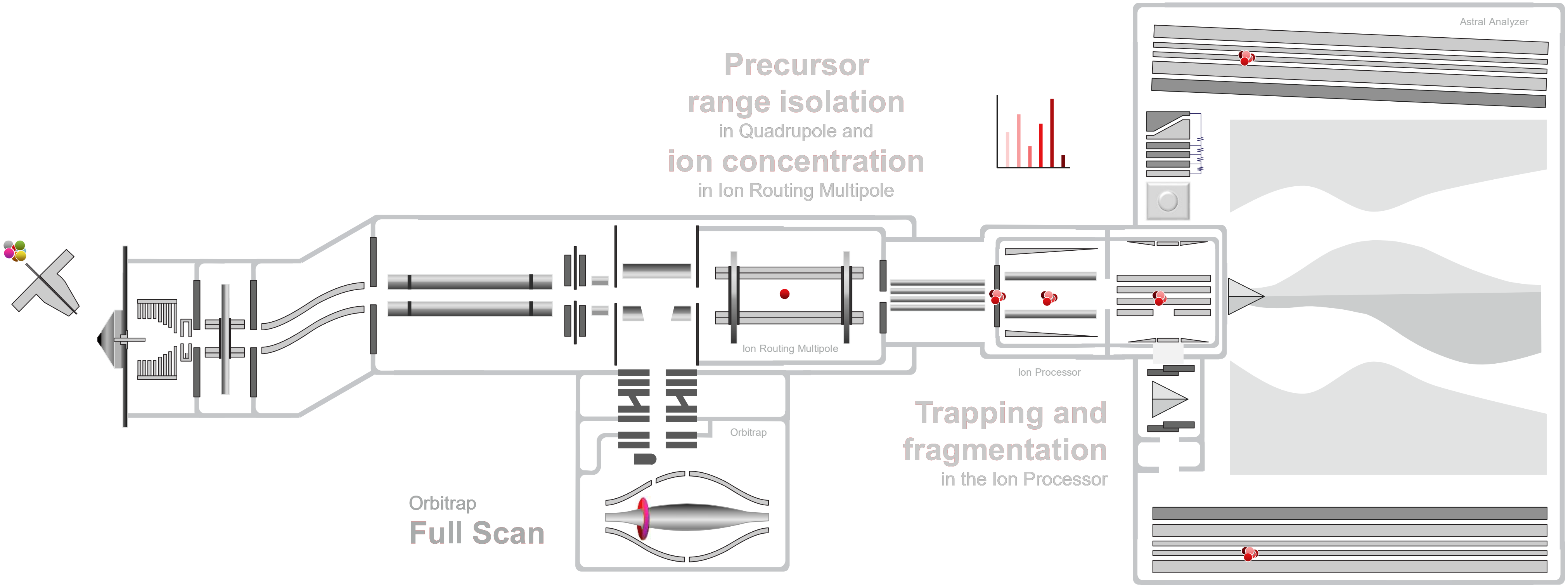
Orbitrap Astral mass spectrometer in operation



Orbitrap
Full Scan

Orbitrap Astral mass spectrometer in operation

Ejection and scanning
in the Astral analyzer



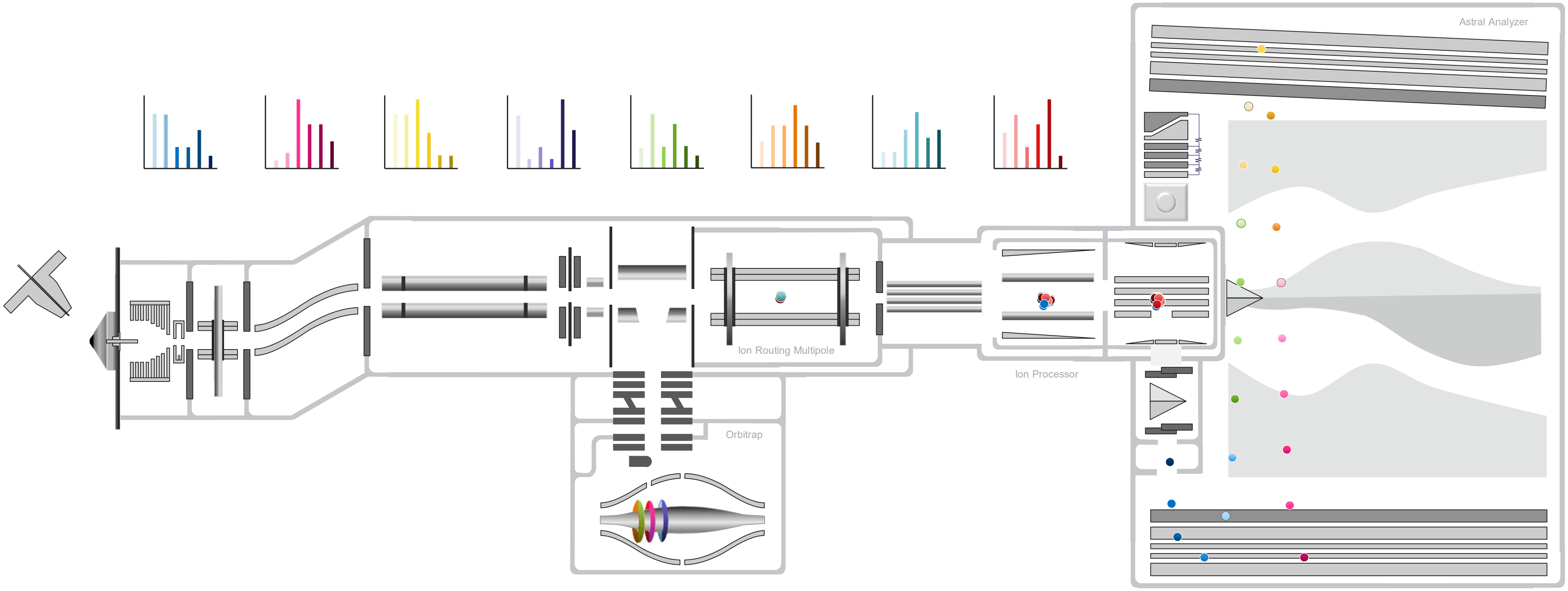
Precursor range isolation
in Quadrupole and
ion concentration
in Ion Routing Multipole

Trapping and fragmentation
in the Ion Processor

Orbitrap
Full Scan

Orbitrap Astral mass spectrometer in operation

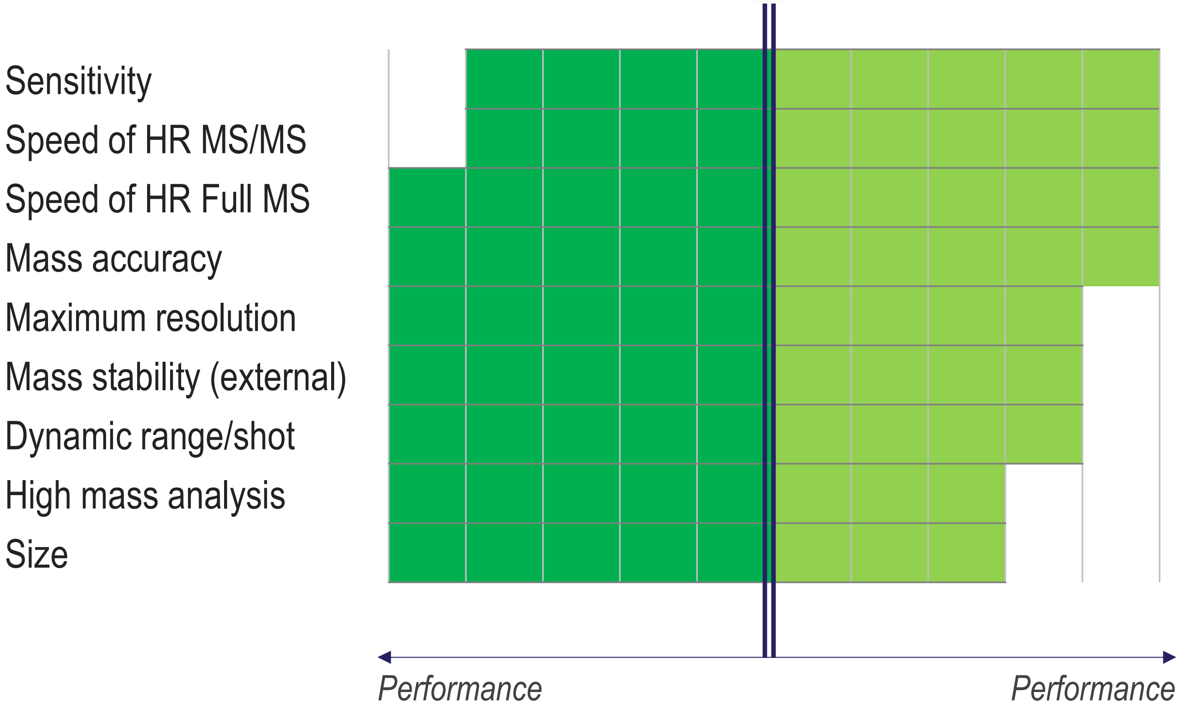
5 ion packets are simultaneously processed in parallel with dynamic ion control



Complementarity of analyzers

Orbitrap analyzer

Astral analyzer



Conclusion:

A combination of Orbitrap and Astral analyzers delivers a practically perfect performance envelope

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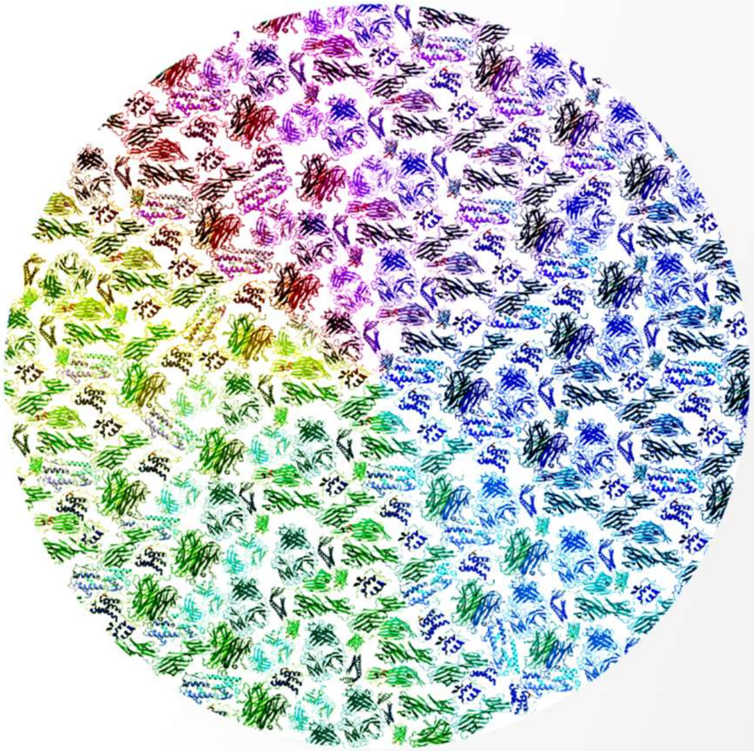
ThermoFisher
SCIENTIFIC

Analyze one sample in only 8 minutes

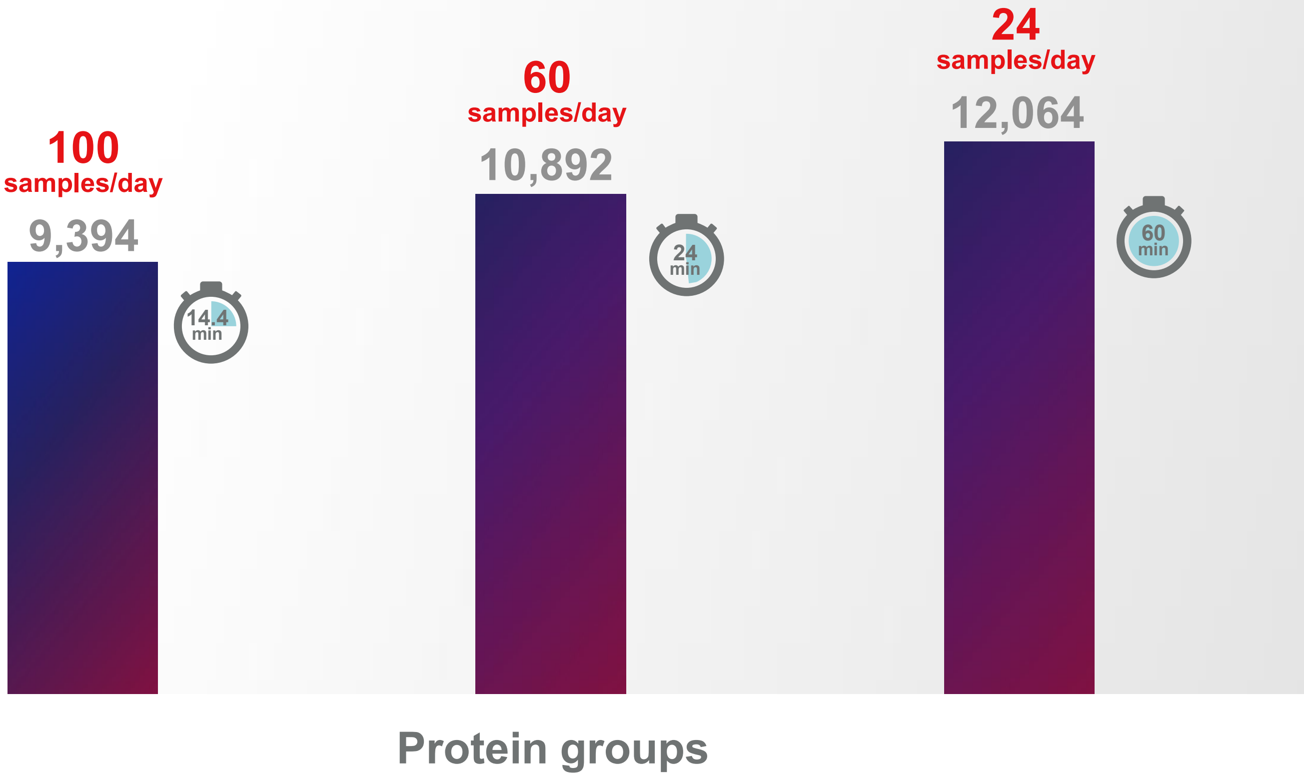


8,135

protein groups

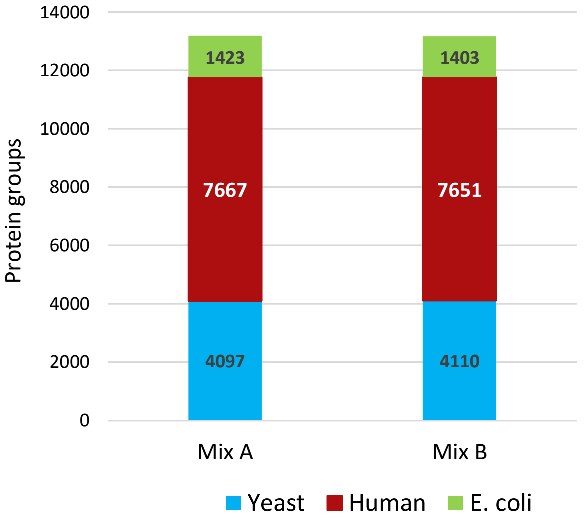
1 sample 8min

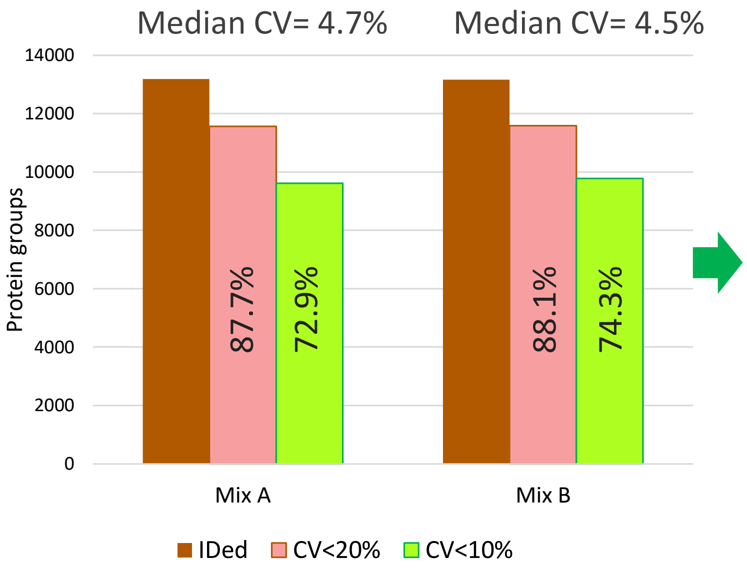
Incredible flexibility to deliver high coverage at high throughput or unprecedented depth in 1 hour

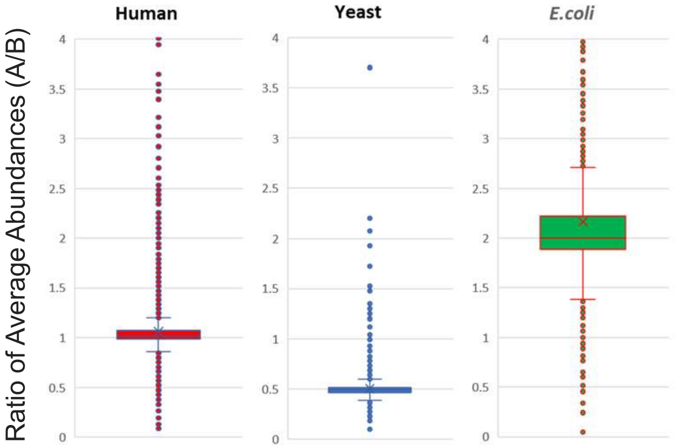


Orbitrap Astral MS in quantitative analysis

- Mixture A: 36% *E.coli*, 46% HeLa and 18% yeast
- Mixture B: 18% *E.coli*, 46% HeLa and 36% yeast







Obtained Ratio 1.017 **Obtained Ratio 0.491** **Obtained Ratio 1.998**

Expected Ratio 1 **Expected Ratio 0.5** **Expected Ratio 2**

500 ng HeLa | Vanquish Neo UHPLC | 50cm µPAC™ Neo column | 20 min gradient | 250 nL/min | Spectronaut 17/ DirectDIA

Pashkova A. et al. “A Benchmarking Workflow for High-Throughput DIA Label-Free Quantification using a Novel High-Resolution Accurate Mass Platform”. **ASMS’23, MP 731.**

JA1

Quantitation of target proteins in affected pathways

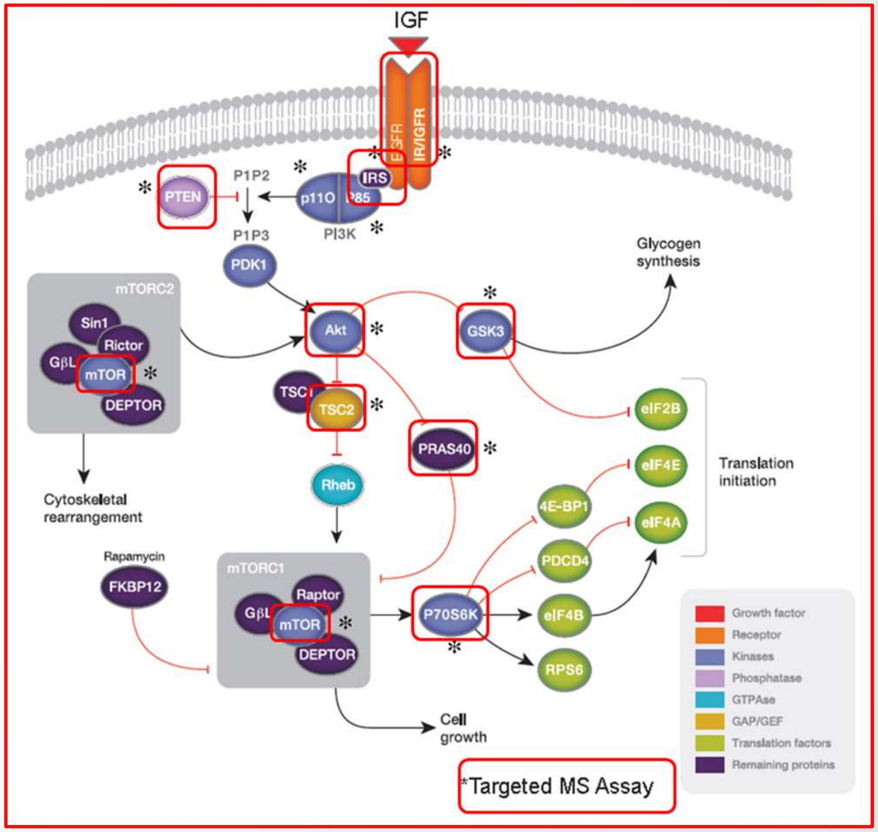
Enabling pathway biology targeting entire AKT/mTOR network

Many genetic alterations in cancer cells modify the protein expression from AKT, RAS and TP53 pathways.

Quantitative measurement of alterations in the expression of pathway proteins and post-translational modifications (PTM) is necessary for classifying disease states, monitoring cancer progression and determining treatment response.

Sensitivity and selectivity are required to quantify these target proteins in a high throughput manner enabling biomarker in large cohort biomarker verification studies.

AKT/mTOR pathway



*Targeted MS Assay

Slide 53

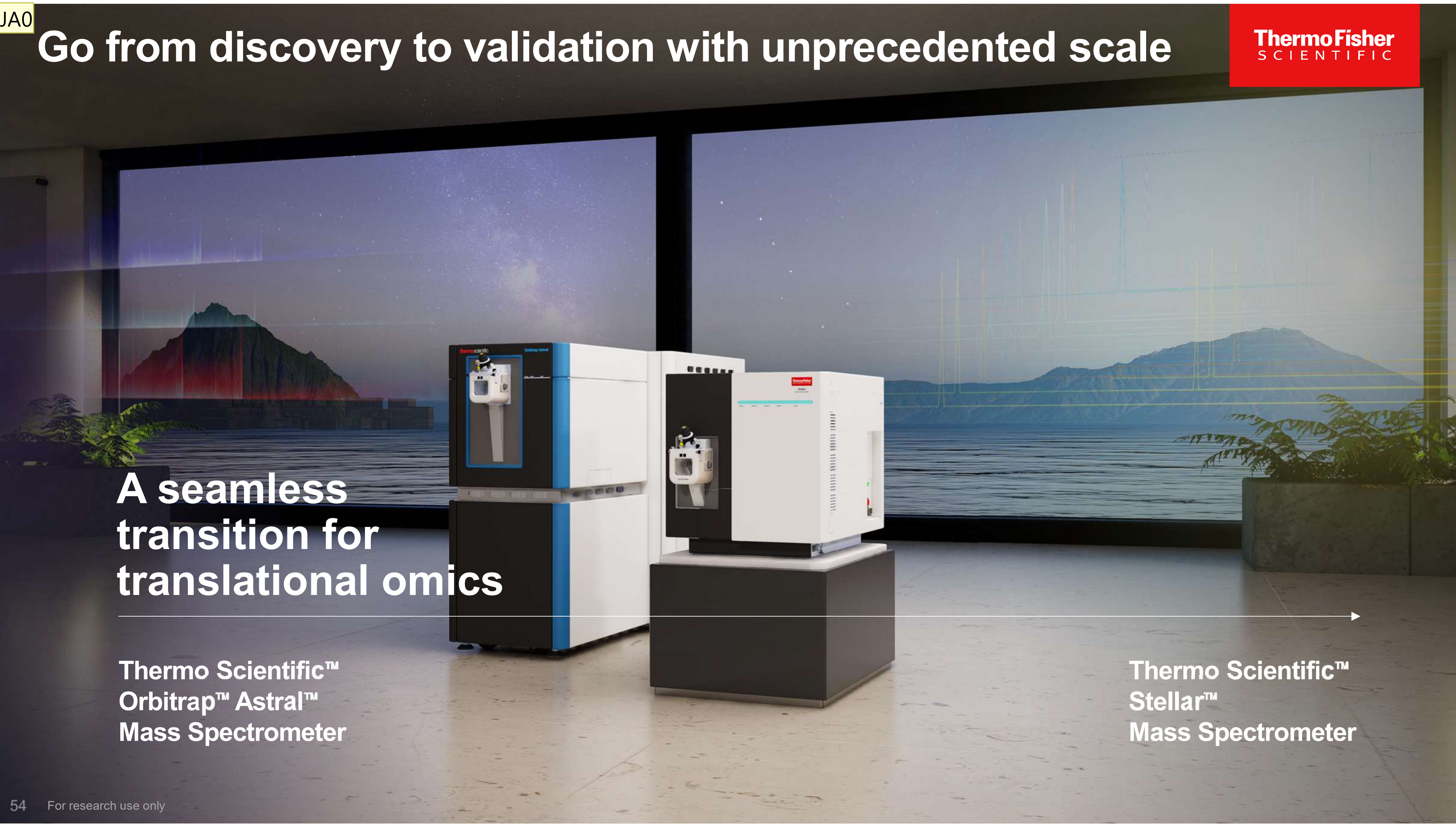
JA0 More comments from CMD Brand: Extra space in subhead, The "A" in Assay in bottom of image should be lower case. And in third paragraph, change "is" to "are" in first line.
Johnson, Ann; 2024-04-30T01:04:19.434

JA1 Doublechecking, should the headline say "targeted" vs. "target"?
Johnson, Ann; 2024-04-30T01:42:48.798

JA0

Go from discovery to validation with unprecedented scale

ThermoFisher
SCIENTIFIC



A seamless transition for translational omics

**Thermo Scientific™
Orbitrap™ Astral™
Mass Spectrometer**

**Thermo Scientific™
Stellar™
Mass Spectrometer**

Slide 54

JA0 The big dipper is backwards and the XICs, as well.

Johnson, Ann; 2024-04-29T17:43:18.046

From discovery to clinics

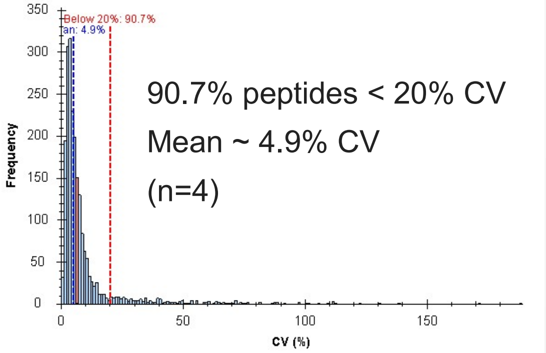
The case of more than 2000 SIL peptides

- Cohort samples acquired on Orbitrap Astral
- 2100 peptides of interest for biomarker verification
- Synthetized 2100 SIL peptides for quantitation
- Development of targeted assay to run cohort
- **QQQ technology** Several months of method development

Stellar MS

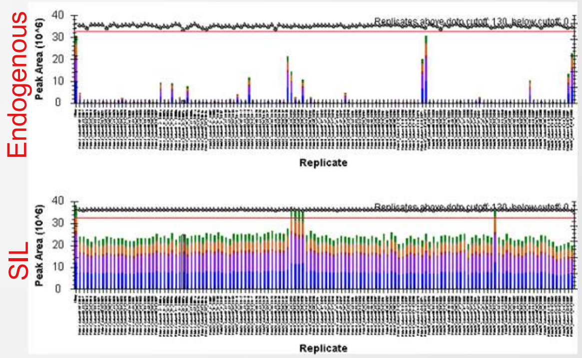
1 Week

2111 SIL peptides – generate Prosit library
Throughput – 24 SPD
Acquire 4Th DIA
Defined RT
Evaluate SILs quality of transitions and reproducibility



90.7% peptides < 20% CV
Mean ~ 4.9% CV
(n=4)

Small Cohort: 4222 precursors



Patient samples

Collaborator

- Bruce Wilcox – PrognomiQ

Stellar MS accelerates the verification/ validation of biomarkers

PT0

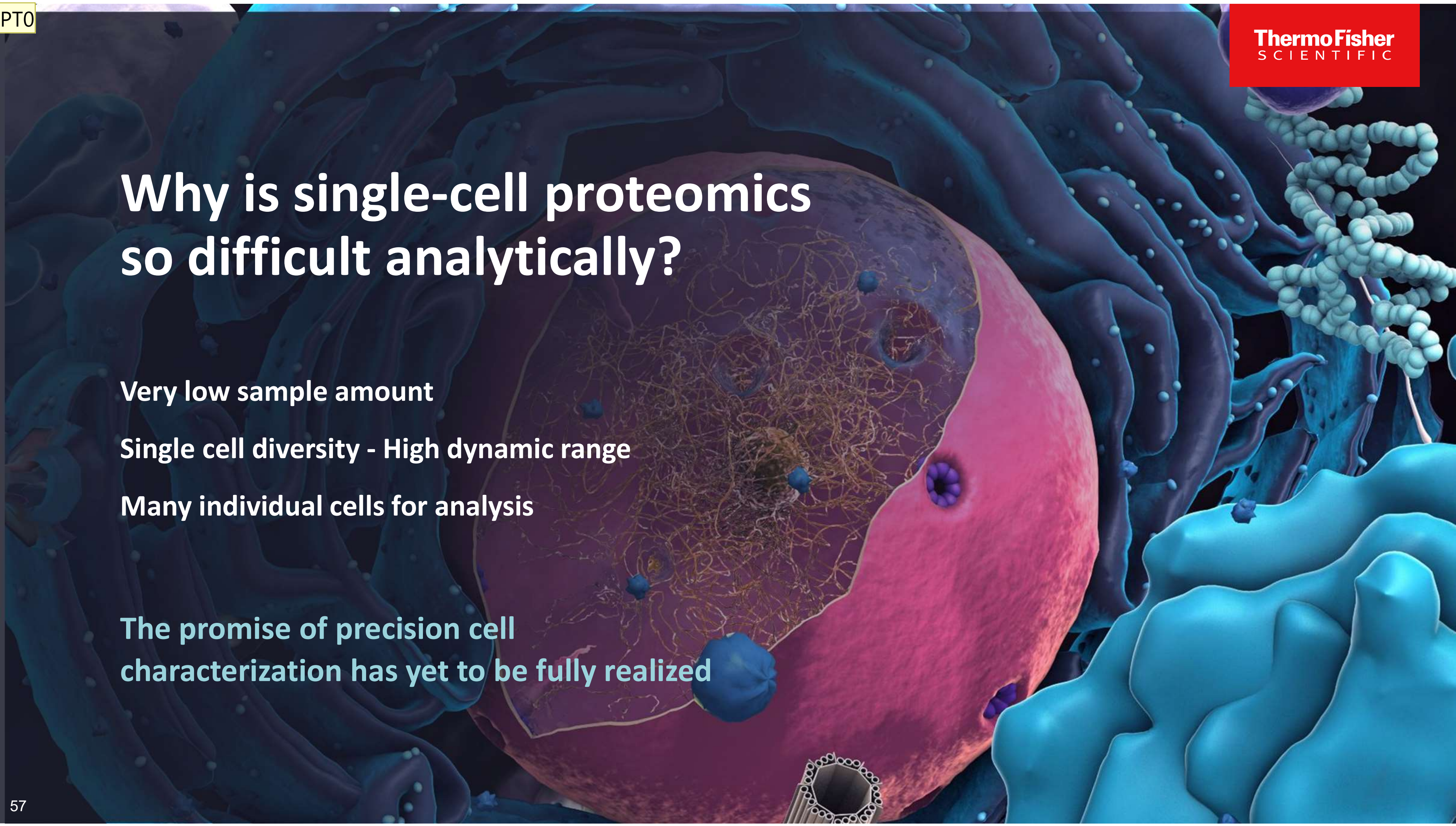
Single-cell proteomic analysis

Slide 56

PT0 [@Saba, Julian] Background photo?

Pekar Hart, Tonya; 2024-01-18T19:05:59.820

PTO



Why is single-cell proteomics so difficult analytically?

Very low sample amount

Single cell diversity - High dynamic range

Many individual cells for analysis

The promise of precision cell characterization has yet to be fully realized

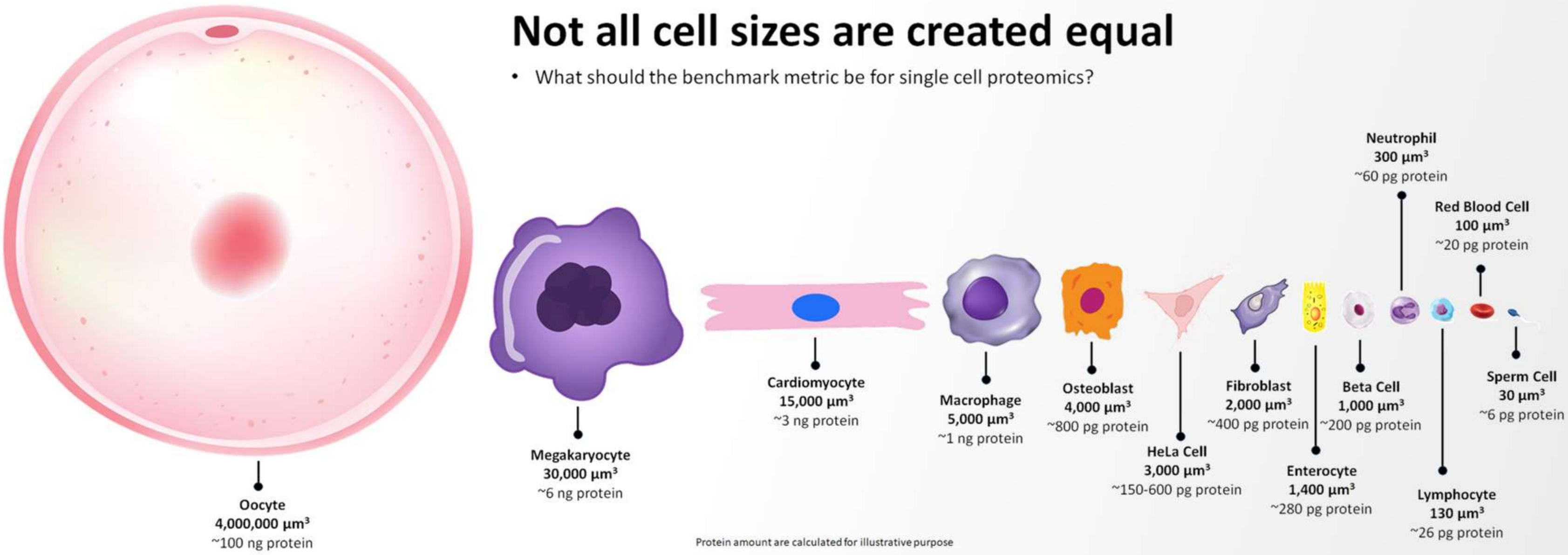
Slide 57

PT0 Why are we putting all of these introductory slides at the back now? I think we need some introduction at the front of the presentation
Pekar Hart, Tonya; 2024-01-17T19:01:56.800

PT0 0 I would move slides 26 - 36 to front of presentation. Then put two 'break' slides in the deck--one before the dilution series data, one before the real single cell data.
Pekar Hart, Tonya; 2024-01-17T19:04:33.040

DB0 1 that is what we decided...
I'll chage it
Delanghe, Bernard; 2024-01-18T14:32:41.856

Why single-cell analysis?



Not all cell sizes are created equal

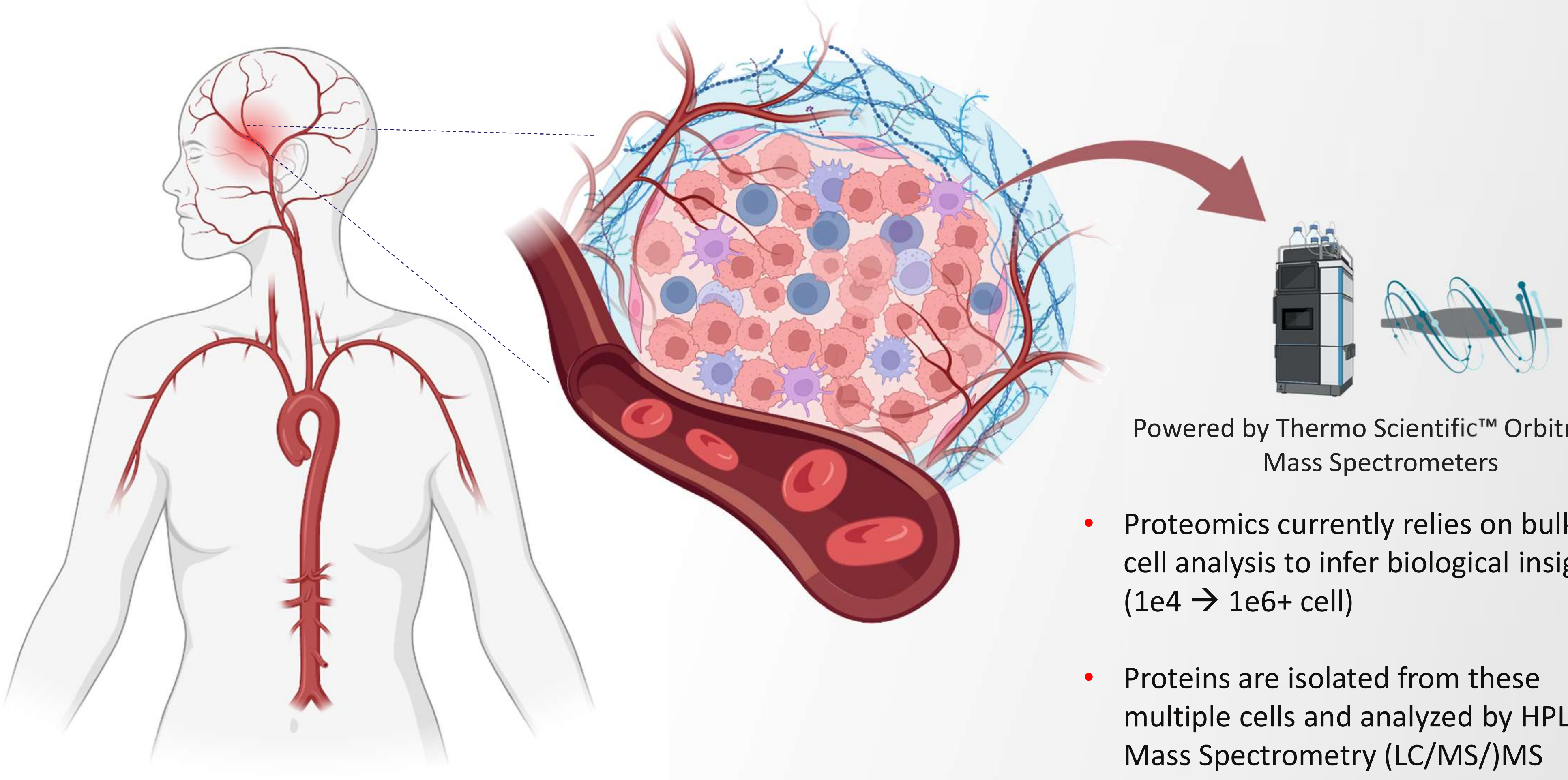
- What should the benchmark metric be for single cell proteomics?

Protein amount are calculated for illustrative purpose

Study:

- **Rare Cells:**
  Stem cells
  Circulating tumor cells (CTC)
  Fetal cells
  Infected cells
- **Cell Differentiation:**
  Stem cells
  Cancer Cells
- **Heterogenous Cell Populations:**
  Stem cells
  Cancer Cells

Population vs single-cell tumor proteome resolution



Powered by Thermo Scientific™ Orbitrap™ Mass Spectrometers

- Proteomics currently relies on bulk cell analysis to infer biological insights (1e4 → 1e6+ cell)
- Proteins are isolated from these multiple cells and analyzed by HPLC Mass Spectrometry (LC/MS/)MS

Average population vs single-cell tumor proteome resolution

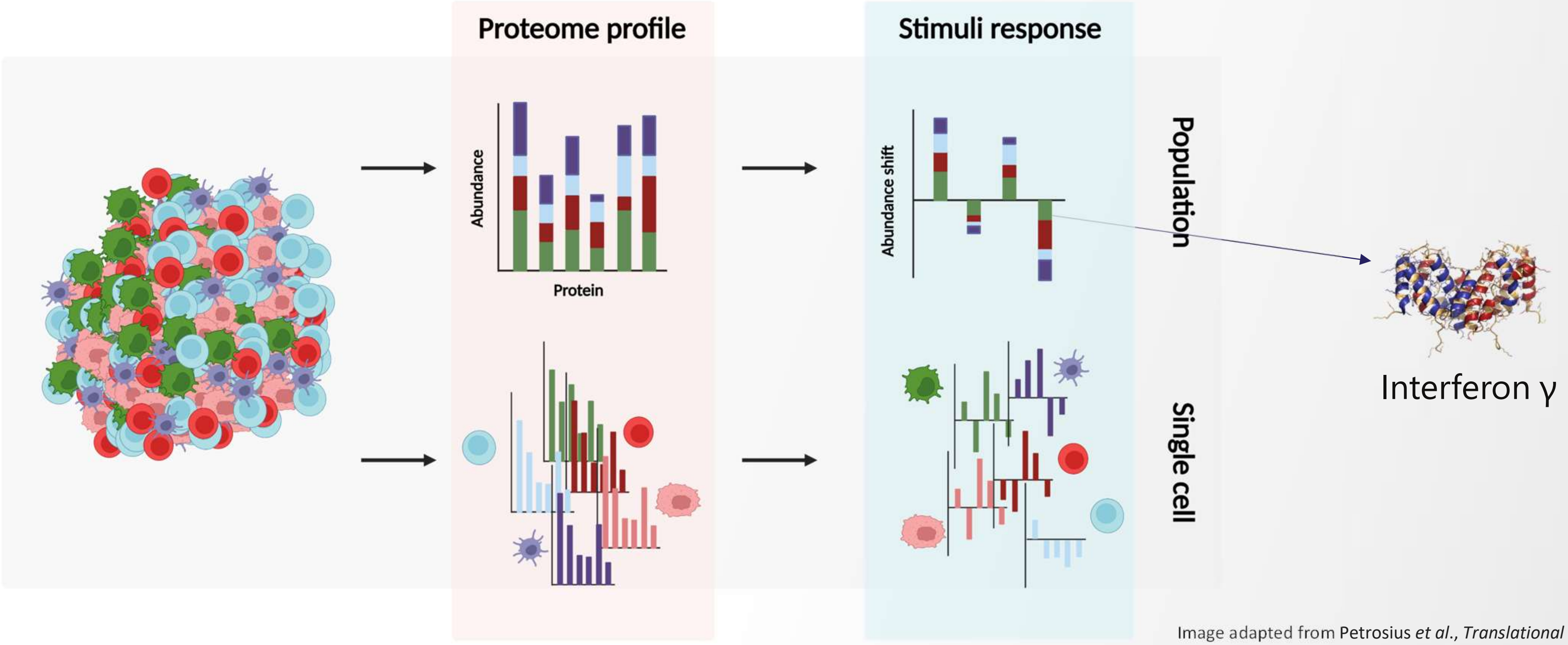


Image adapted from Petrosius *et al.*, *Translational Oncology*, 27, 2023, 101556

- Tumors are comprised of multiple different cell types that have unique proteome profiles and responses to different stimuli.
- Population (bulk) based techniques only capture an average view and often preclude the identification of distinct cell-state driven events and their phenotypes.

Workflow for label-free DIA for low load samples

- This setup is our recommendation for low load applications since it has been successfully reproduced in different sites and different customer labs

50 SPD method

Columns

Ultimate TS 25cm
IonOpticks
&
IonOpticks heater

Thermo
Scientific ™
Vanquish ™ Neo
UHPLC System

Thermo
Scientific ™
EasySpray ™
ion source

Thermo
Scientific™
FAIMS Pro Duo
interface

Thermo
Scientific ™
Orbitrap ™ Astral ™
MS

Data
Analysis

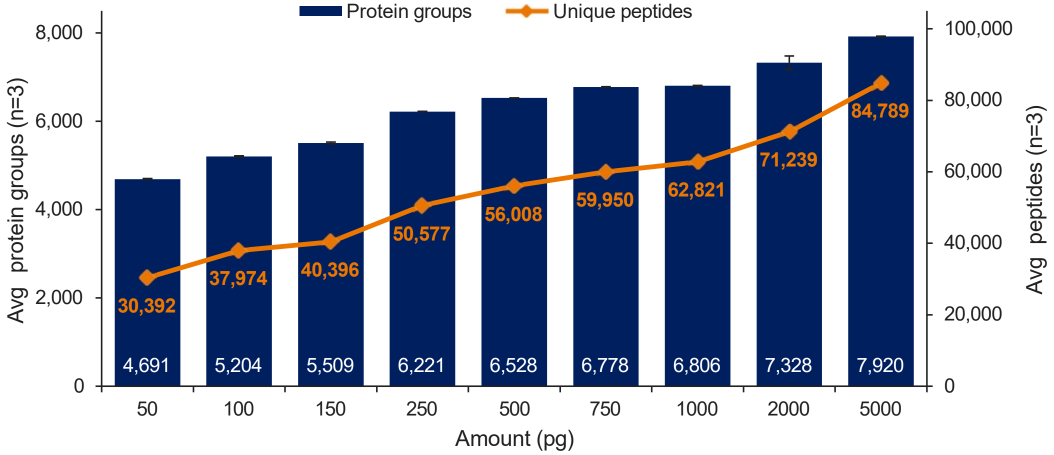
Spectronaut™
powered by Pulsar

CHIMERYS
2.0

HeLa peptide injections – 50 SPD method

LC-MS DIA	
Column	IonOpticks 25 cm column
Active gradient	19.5 min
Total run time	25min
Samples per day (SPD)	50
FAIMS Pro Duo interface	CV-48
Database	*Homo sapiens* (Uniprot ~ 20k entries)

directDIA Spectronaut 18 Software (3 replicates processed together)

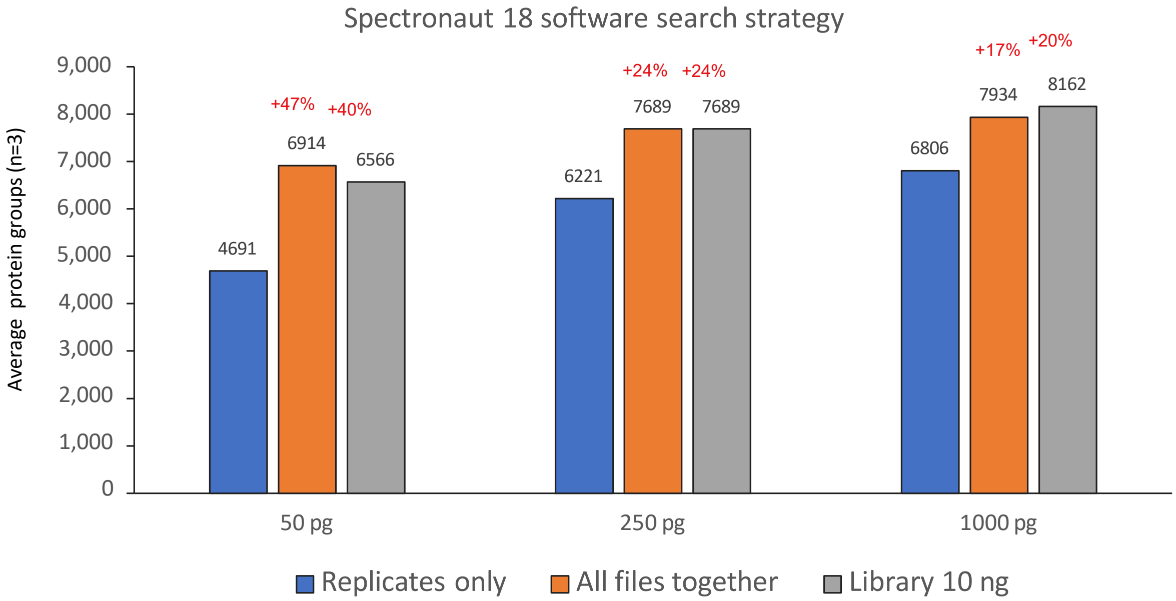


Fernanda.salvato@thermofisher.com| May 30th

HeLa peptide injections – 50 SPD method

Effect of using different processing strategy

Processing all files together or using a library will increase the number of quantified protein groups for lower amounts

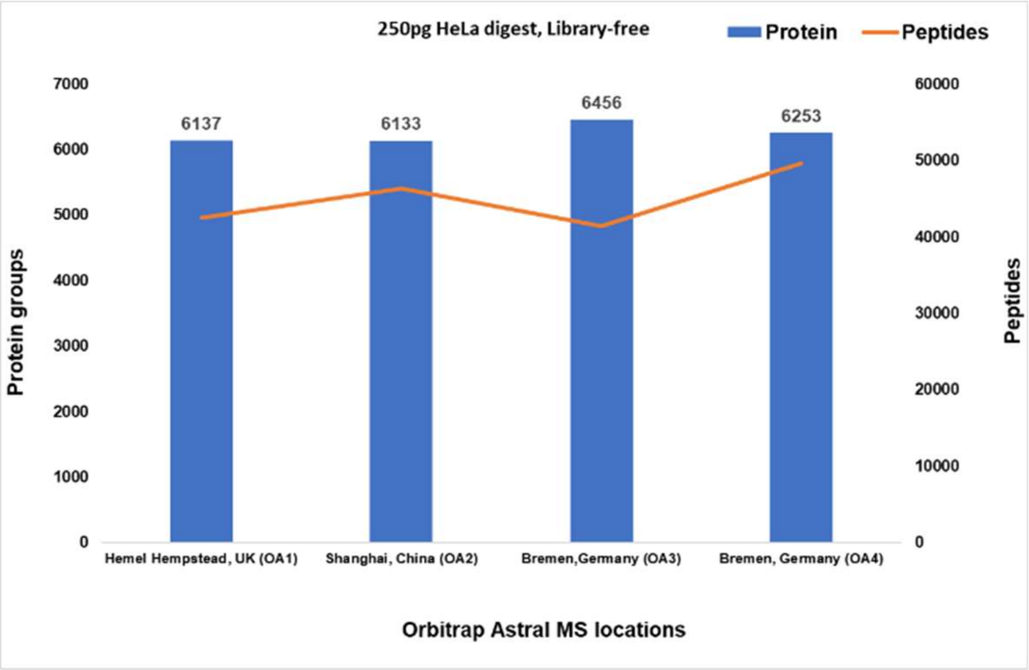


Fernanda.salvato@thermofisher.com| May 30th

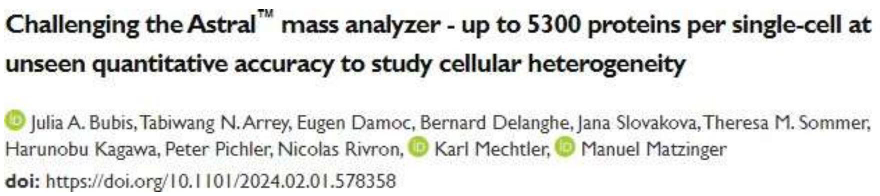
Reproducibility inter-labs

50 SPD method is reproducible between different labs

- ~ 6,000 protein groups detected by library-free



Example of different throughputs using Aurora column

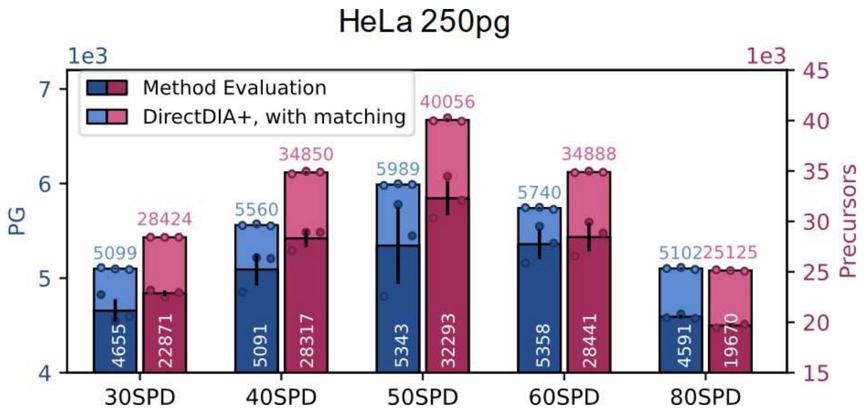


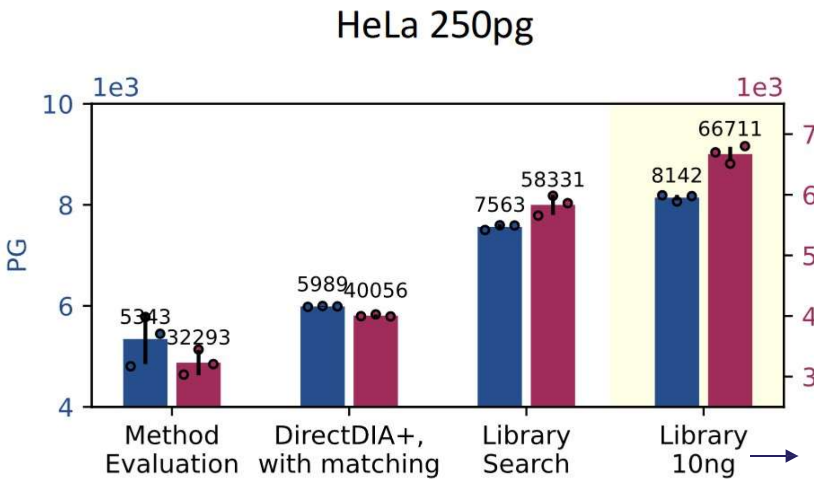
Challenging the Astral™ mass analyzer - up to 5300 proteins per single-cell at unseen quantitative accuracy to study cellular heterogeneity

Julia A. Bubis, Tabiwang N. Arrey, Eugen Damoc, Bernard Delanghe, Jana Slovakova, Theresa M. Sommer, Harunobu Kagawa, Peter Pichler, Nicolas Rivron, Karl Mechtler, Manuel Matzinger

doi: https://doi.org/10.1101/2024.02.01.578358

bioRχiv
THE PREPRINT SERVER FOR BIOLOGY





10 ng load used for library

- *Demonstration of better numbers obtained with the 50 SPD method*

- *> 5,900 protein groups were detected by library-free search*
- *>7,500 protein groups were detected using spectral library (using 10ng library)*

Quantitation accuracy – 50 SPD method

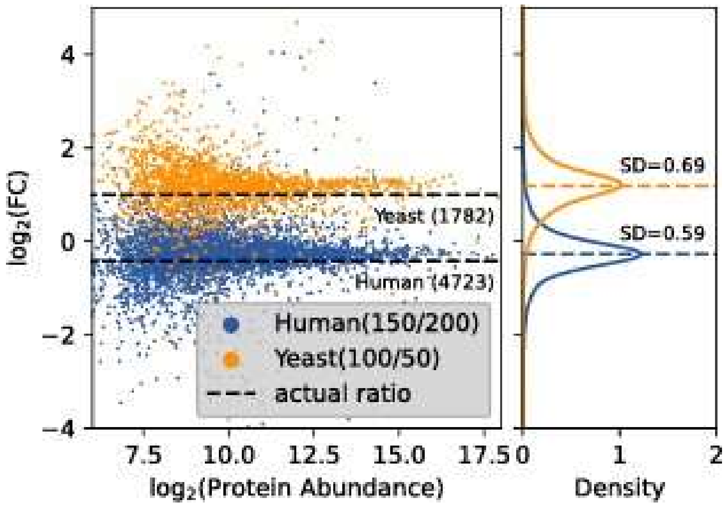
Challenging the Astral™ mass analyzer - up to 5300 proteins per single-cell at unseen quantitative accuracy to study cellular heterogeneity

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

Julia A. Bubis, Tabiwang N. Arrey, Eugen Damoc, Bernard Delanghe, Jana Slovakova, Theresa M. Sommer, Harunobu Kagawa, Peter Pichler, Nicolas Rivron, Karl Mechtler, Manuel Matzinger

doi: https://doi.org/10.1101/2024.02.01.578358

250pg injection of Human: Yeast mixtures

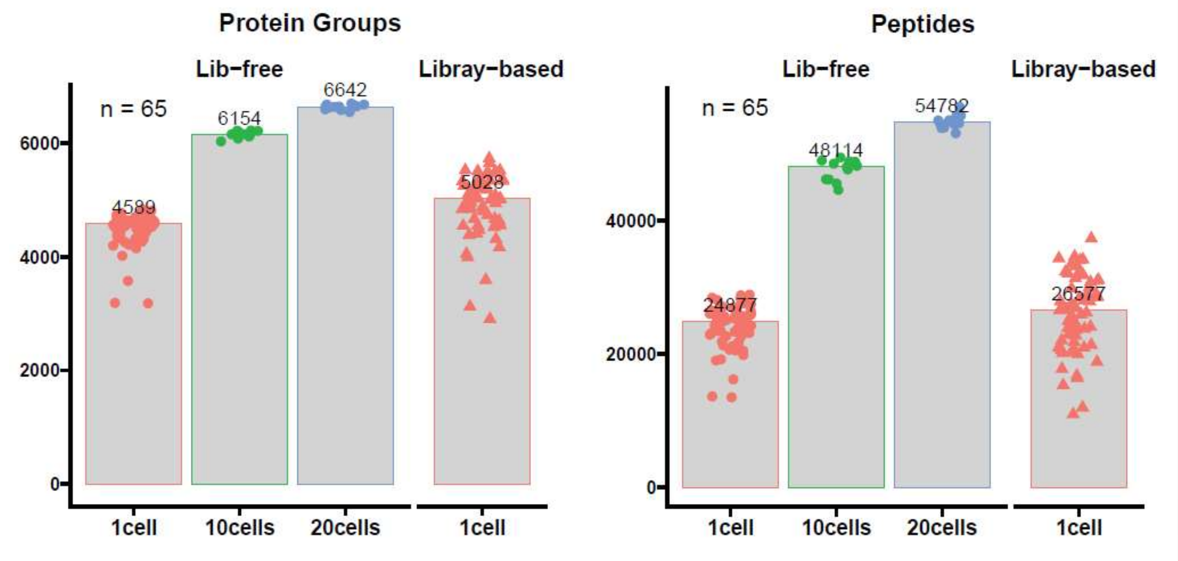


- Very accurate quantitation demonstrated by 2-proteome mix samples
- Orbitrap Astral MS does an excellent job delivering a fold change in protein abundance very close to the expected one
- Density plots (right) depict distribution of log2 fold changes (left chart, dots). Low standard deviation (SD) to the expected fold change for the two proteomes (human or yeast)

Reference Orbitrap Astral MS with proteoCHIP EVO 96

- 12×20 cells, 12×10 cells, 65×single cell, 5×blank, cell φ15~22um

Spectronaut 18



2,000 more proteins for true single cells

65× Single cell：Library-free

- lowest：3183/ 13501
- highest：4836/ 28064
- median：4589/ 24877

- 65× Single cell： Library-based
- highest: 5734/ 37297 （+19%）
- median: 5028/ 26577

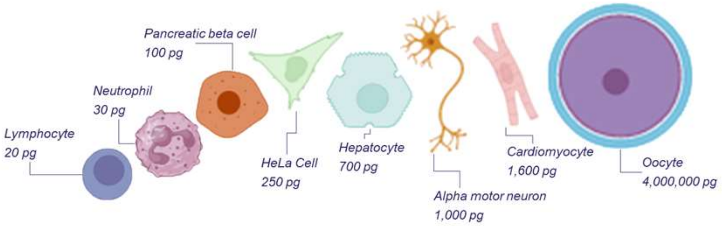
Targeted measurements of single cells on the Stellar MS

Discovery DIA experiments on high resolution instrument

Filter for quality and biological relevance with PRM Conductor in Skyline

Robust targeted quantitation of proteins of interest on Stellar MS

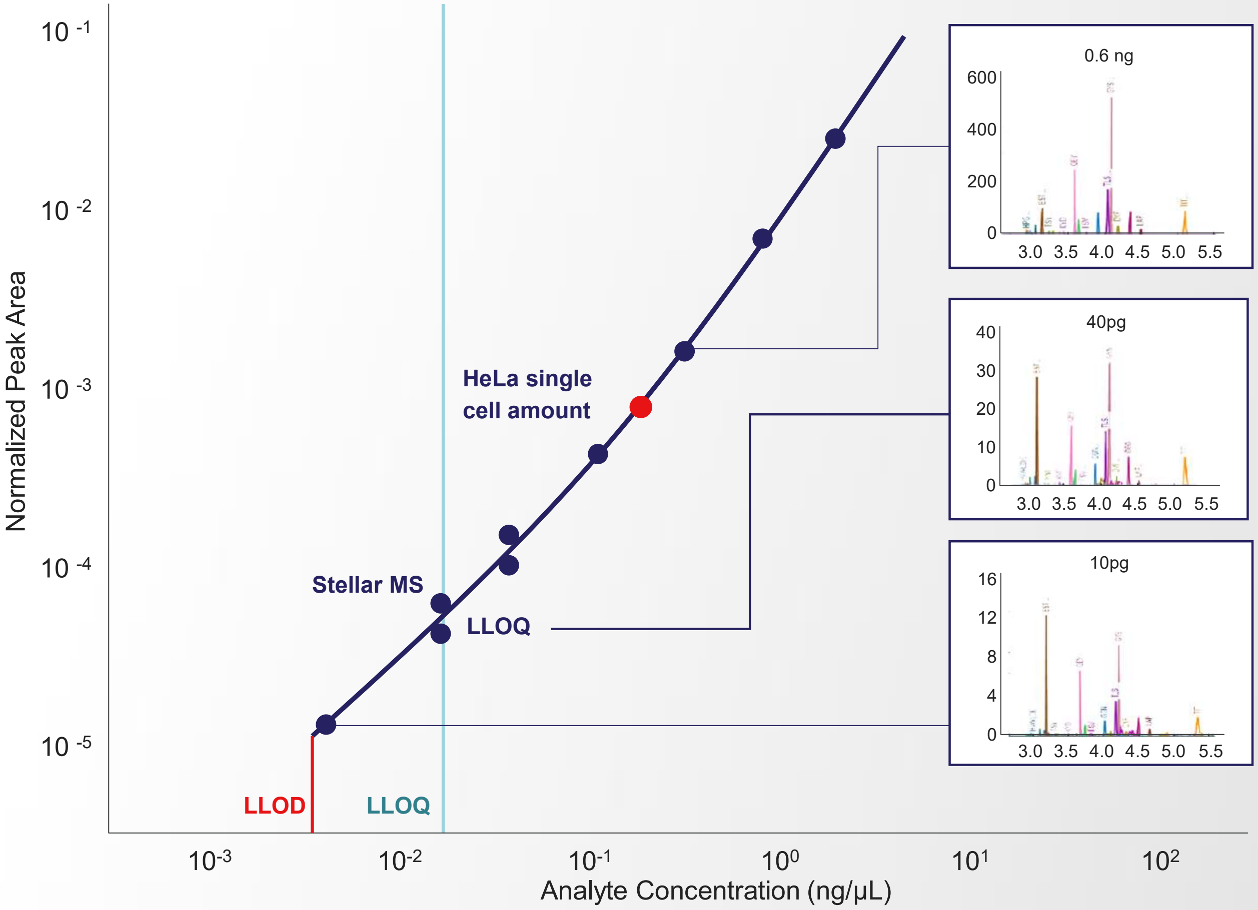
Targeted quantitation at single cell level and lower



Not all cells are the same size

Stellar MS

Next-Gen targeted MS platform



Stellar MS achieves high sensitivity for targeted single cell proteomics

Seer – Access to Deep, Unbiased Proteomics at Scale

Jointly promote Seer’s Proteograph™ Product Suite alongside Thermo Scientific Orbitrap Astral™ mass spectrometers

Seer Proteograph Key Attributes

- ❑ Unbiased coverage
- ❑ Deep access
- ❑ Rapid workflow
- ❑ Scalable technology

Case study | Orbitrap Astral Mass Spectrometer

Plasma proteomics: harnessing cutting-edge technologies for unprecedented depth and throughput

Proteomics

Unlocking secrets of the proteome

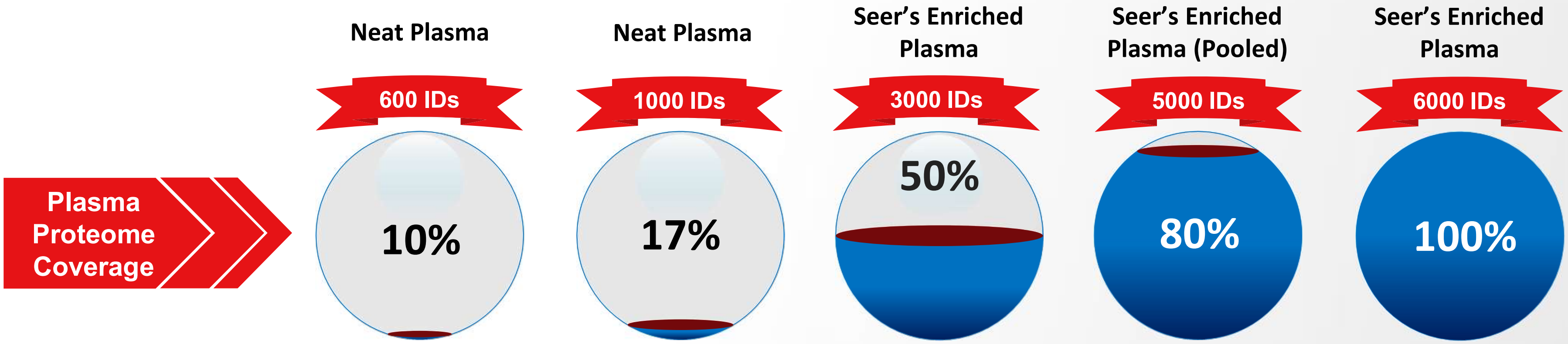
Mass spectrometry is considered a gold standard technique in proteomics and the most comprehensive approach to truly

Improve workflows for seamless sample-to-data experience combining Proteograph XT and Orbitrap Astral technologies

https://investor.seer.bio/news-releases/news-release-details/seer-enters-co-marketing-and-sales-agreement-thermo-fisher
https://seer.bio/technology/

Up to 6,000 protein groups in plasma

Depending on the experiment aim one can choose one of the following workflows for analysis:

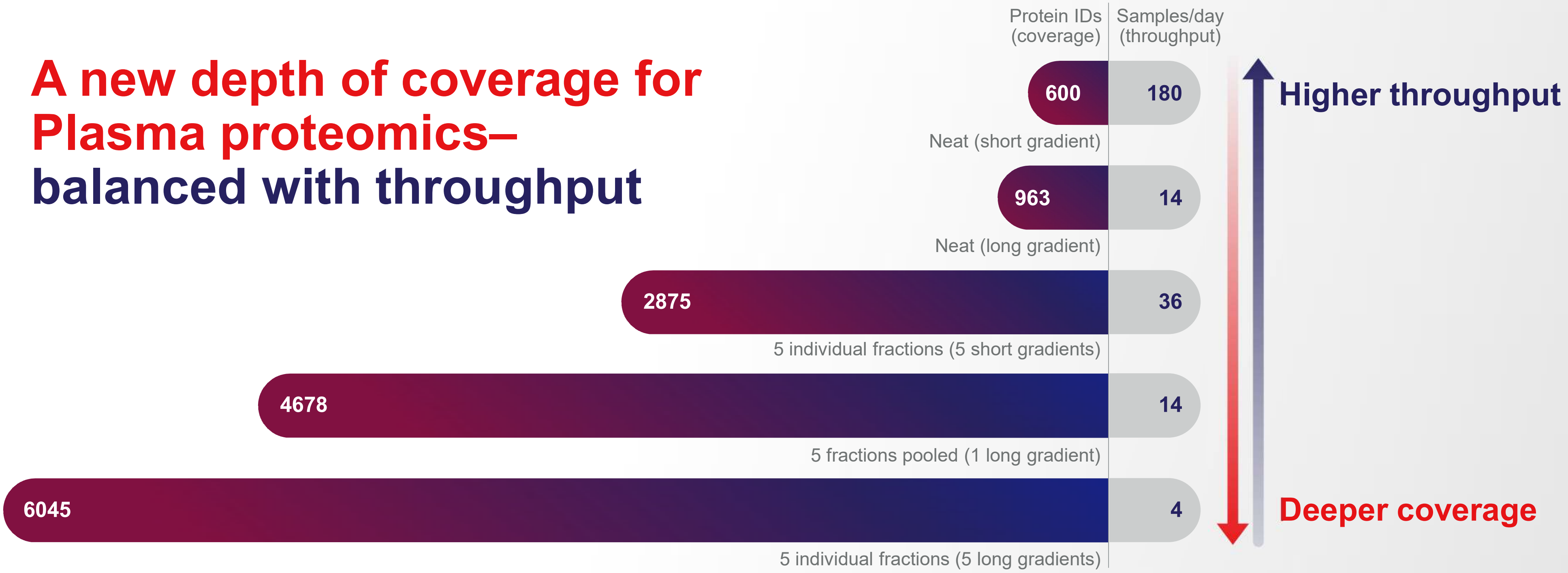


	Neat Plasma	Neat Plasma	Seer's Enriched Plasma	Seer's Enriched Plasma (Pooled)	Seer's Enriched Plasma
	600 IDs	1000 IDs	3000 IDs	5000 IDs	6000 IDs
Plasma Proteome Coverage	10%	17%	50%	80%	100%

	PepMap 15cm x 150um	PepMap Neo 75cm	PepMap 15cm x 150um	PepMap Neo 75cm	uPAC 110cm
Gradient	5.5 min	60 min	5.5 min	60 min	68 min
Total Run Time	8 min	107 min	5 x 8 min	107 min	5 x 80min
Samples/Day	180	13.5	36	13.5	3.6
Sample Load	0.5µg	1µg	0.5µg	2µg	1µg
Chromatography	+++	+++++	+++	+++++	++++
Workflow	Trap/Elute	Direct	Trap/Elute	Direct	Direct

Proprietary & Confidential

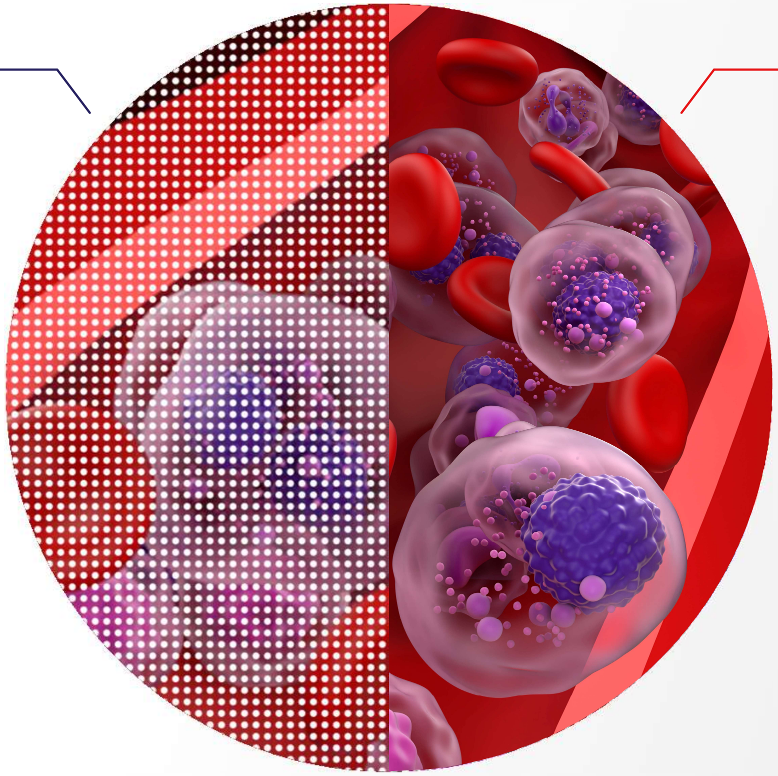
A new depth of coverage for Plasma proteomics– balanced with throughput



Comprehensive Plasma Proteome Analysis

Quantitative performance with massive throughput

Absolute quantitation methods across 582 plasma proteins



Limited visibility

Existing tech

QQQ MS

20

samples per day

HRAM PRM

24

samples per day

Full clarity

Stellar MS

100

samples per day

JA0

Massive throughput at scale

Absolute quantitation methods across 582 plasma proteins

Existing Tech

QQQ MS

20

samples per day

HRAM PRM

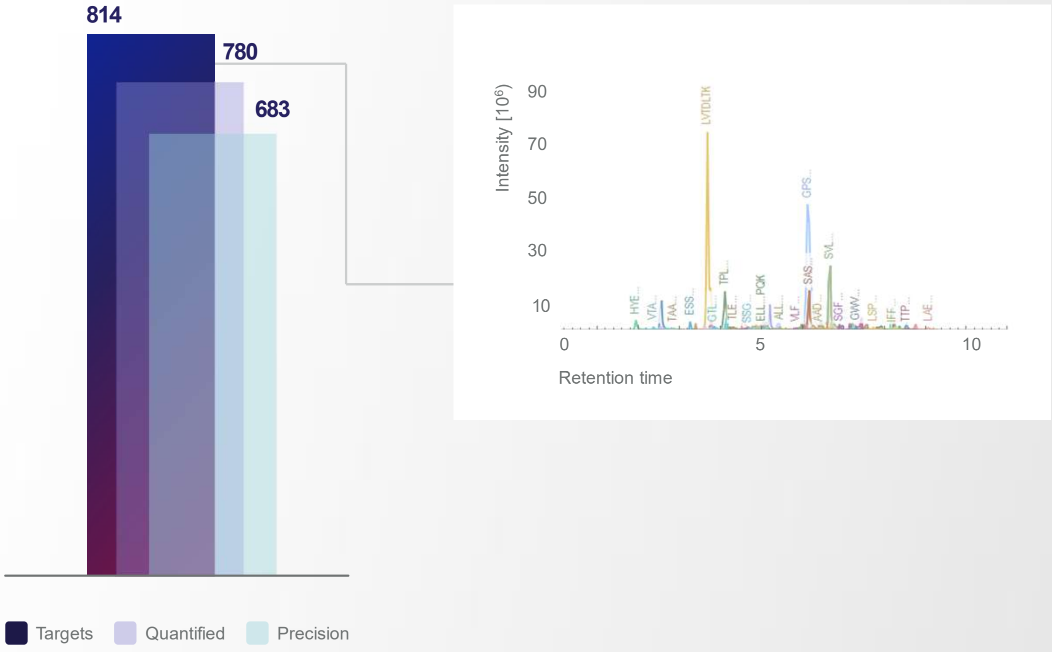
24

samples per day

Stellar MS

100

samples per day for 804 SIS peptides and 804 endogenous counterparts



Slide 74

JA0 Subheads should not be all caps. Should be sentence case.

Johnson, Ann; 2024-04-29T02:58:47.742

The World's Leader in Mass Spec Omics: Proteomics Workflow

Sample Prep — **Separation** — **Detection** — **Data Analysis**

Discovery

Accelerome Automated Sample Preparation Platform

µPAC Neo HPLC Column and Vanquish Neo UHPLC System

High throughput, deepest proteome coverage — **Orbitrap Astral MS**

PTMs and Structural Biology — **Orbitrap Ascend MultiOmics MS**

Affordable Discovery — **Orbitrap Exploris 480 MS**

High resolution mass spec HRMS

Proteome Discoverer Software with Ardia Platform

Targeted

KingFisher Flex Automated Purification System

EASY-Spray Column, and Vanquish Neo UHPLC System

Higher throughput Built in verification — **Stellar MS**

Highest Performance — **TSQ Altis Plus Triple Quadrupole MS**

Class I, IVD medical device — **TSQ Altis MD MS**

Nominal mass instruments

TraceFinder Software and Skyline

Olink Technologies and Mass Spectrometry

Olink's PEA technology presents complementary solutions to today's mass spectrometry solutions

- Need just a few µl of blood (equivalent to pinprick) in a standardized end-end methodology
- Ability to analyze important immune and inflammatory markers such as cytokines (very low level) and interleukins
- Ease of technology access due to large NGS install base (>15K)
- Easy to understand and standardized data output that enables cross-lab comparisons

Olink's PEA technology targets new and different customer segment from core mass spectrometry

- Non-mass spec experts –increasingly adopting proteomics as part of multi-omics studies. Genomics customers are looking to complement their GWAS study with proteomics.
- Biology labs are familiar with and comfortable using antibody-based technologies which are less complex than mass spectrometry
- Genomics core labs are expanding their proteomics capabilities

> *"… Mass spectrometry is* ***sometimes limited*** *in analysing biofluids* ***due to the wide range of protein abundance****…* ***these samples are where*** *techniques such as* ***SomaLogic and Olink really have a place*** *in the proteomics landscape …"*
>
> *Professor, The Scripps Research Institute*

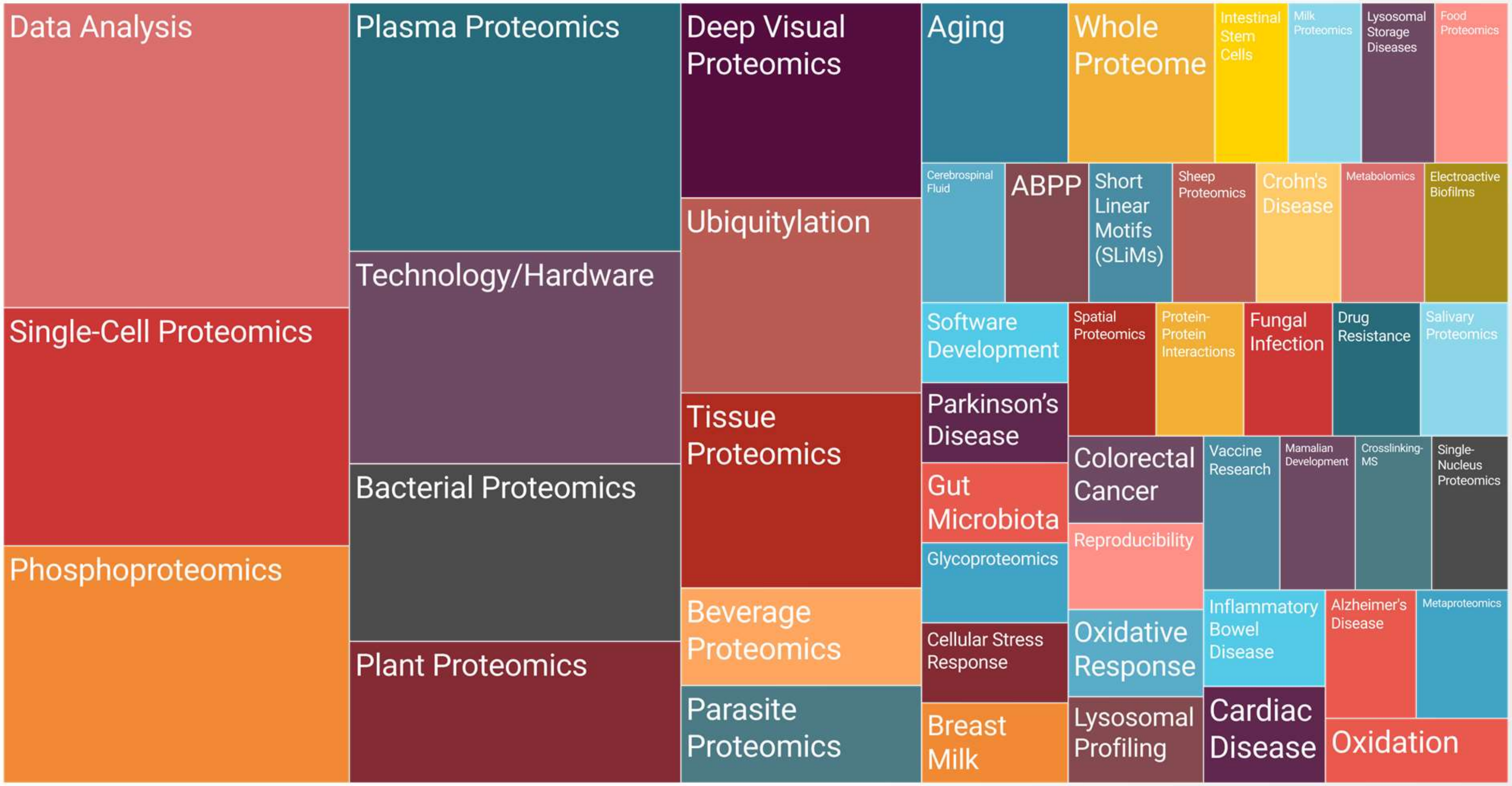
> *"… Some proteomics technologies like* ***Olink have created catalogues*** *where you can select panels for certain diseases, which has made it* ***more accessible****. If the same could be done for other technologies like mass spectrometry to have* ***standardized methods****, more people would use them …"*
>
> *Core Director, University of Massachusetts Medical School*

> *"Proteins are no longer a dirty word at AGBT…Large studies combining both DNA- & protein-based techniques are increasingly showing* ***how proteomics can empower genomics****, providing the link from genes to phenotypes*
>
> *- Genomeweb 2023*

How Can We Help with Your Proteomics Needs?

- What kind of samples are you analyzing?
  - **Olink** Human specimens including plasma, serum, blood, cell lysates, EVs, saliva, CSF, tears, urine, DBS. Complete workflows on qPCR and NGS technology
  - **Mass Spectrometry** Multiple sample types e.g., cells, tissues, plasma, biological fluids, cell lines from human, animals, plants, etc.
- What are your sensitivity requirements?
  - **Olink** Dynamic range of 10 orders, high sensitivity (fg-mg/ml)
  - **Mass Spectrometry** Dynamic range of up to 6 orders (higher w/ fractionation), zeptomolar levels
- Is there interest in measuring post translational modifications PTMs?
  - **Mass Spectrometry** Complementary capabilities to characterize and distinguish biological modifications of interest
- Is there consideration to bring the assay to the clinics, i.e., do you require an IVD solution?
  - **Mass Spectrometry** Class I registered IVD LC-MS/MS solutions for routine diagnostic applications

Orbitrap Astral Publication Landscape



- 97 articles published using Orbitrap Astral MS
- Diverse range of application

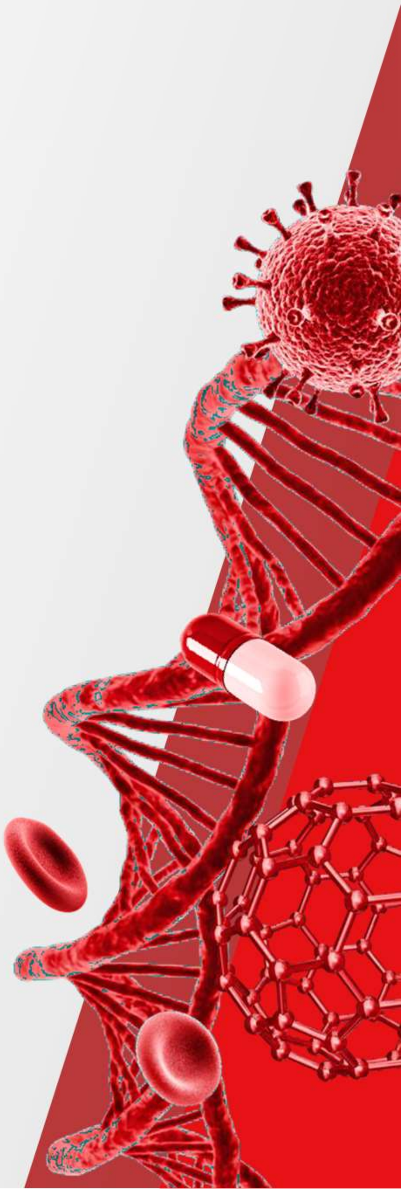
*as of Oct 2024

Comprehensive Metabolomics & Lipidomics Workflow

- Sample Prep
- Separation
- Detection
- Software (Acquisition, Processing, Reporting)

Metabolomics SQUAD Goals: Orbitrap workflows to empower your research

The world leader in serving science



What will we discuss??

1 Who is the Thermo Metabolomics Team and What do we do?

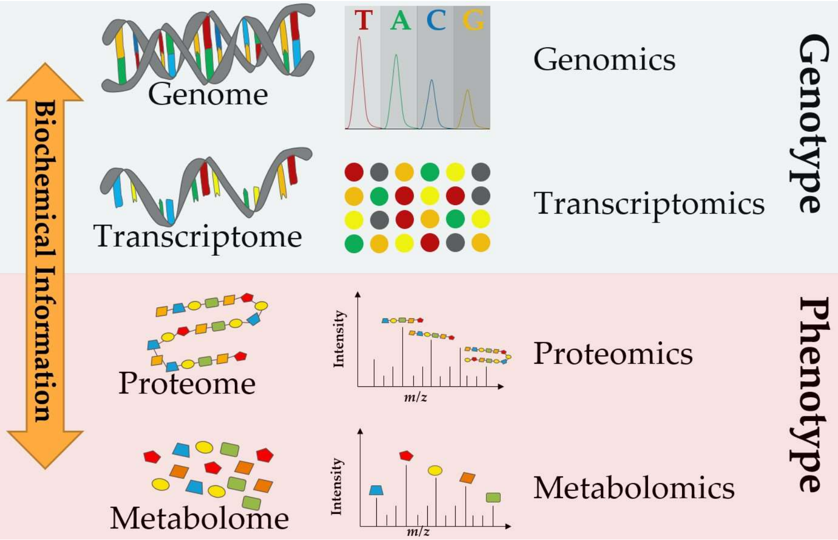
2 Introduction to SQUAD Metabolomics

- i SQUAD Metabolomics in Milk on OE 240
  - ii SQUAD on IQ-X & Astral teaser

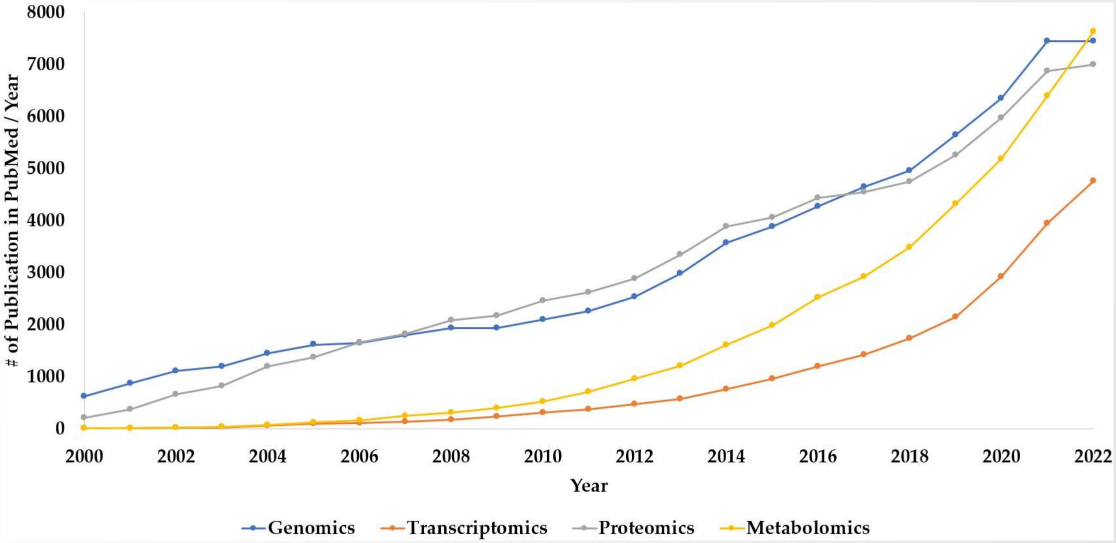
3 Brief Recap

The rise of metabolomics

Metabolomics: member of the “omics” family



A multi-omics approach allows the measurement of the flow of molecular information from genes to metabolites to explain or predict phenotype from genotype



A significant growing trend in the application of metabolomics-based research starting in 2010 made it to lead the trend among other “omics” family members for the last ten years

Addressing All Metabolomics and Lipidomics Workflows

Untargeted Discovery

- Ultimate Coverage
  - Breadth of analyte coverage
  - Number of pathways covered

Targeted Quantitation

- Ultimate Sensitivity
  - Depth of pathway coverage
  - Level 1 Identification
  - Analyte Concentration

Simultaneous Quantitation and Discovery (SQUAD)

Simultaneous Quantitation and Discovery (SQUAD)

- **Untargeted Discovery Workflow Pain point**
  - Lacks quantitative accuracy
  - Complicated data processing and unknown compound annotation

- **Targeted Hypothesis Driven Quantitation Workflow Pain point**
  - Biased biological targets
  - Omits potential metabolites of importance
  - Cannot retro mine for new insights

What do we mean by Quantitation??

What does your study require??

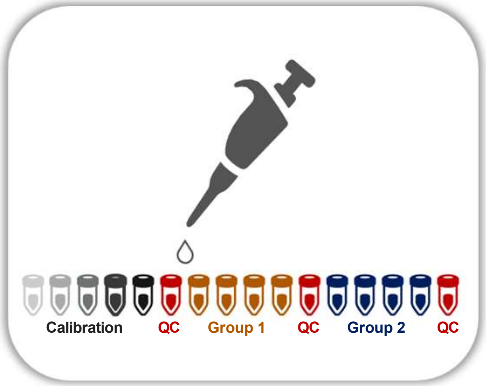
Do authentic standards exist for your targets of interest??

Do stable isotope-labeled internal standards exist for your targets??

1. Absolute and accurate quantitation using matrix matched calibration curves:
   - STD and IS
2. Quantitation using calibration curves
   - STD only
3. Quantitation using one-point calibration (relative quantitation)
4. Relative peak area comparison

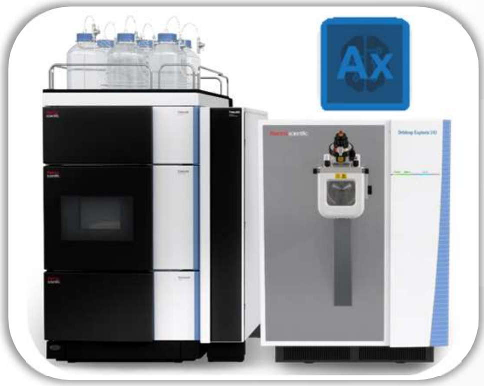
SQUAD Metabolomics & Lipidomics on OE 240

Single Sample injection!!



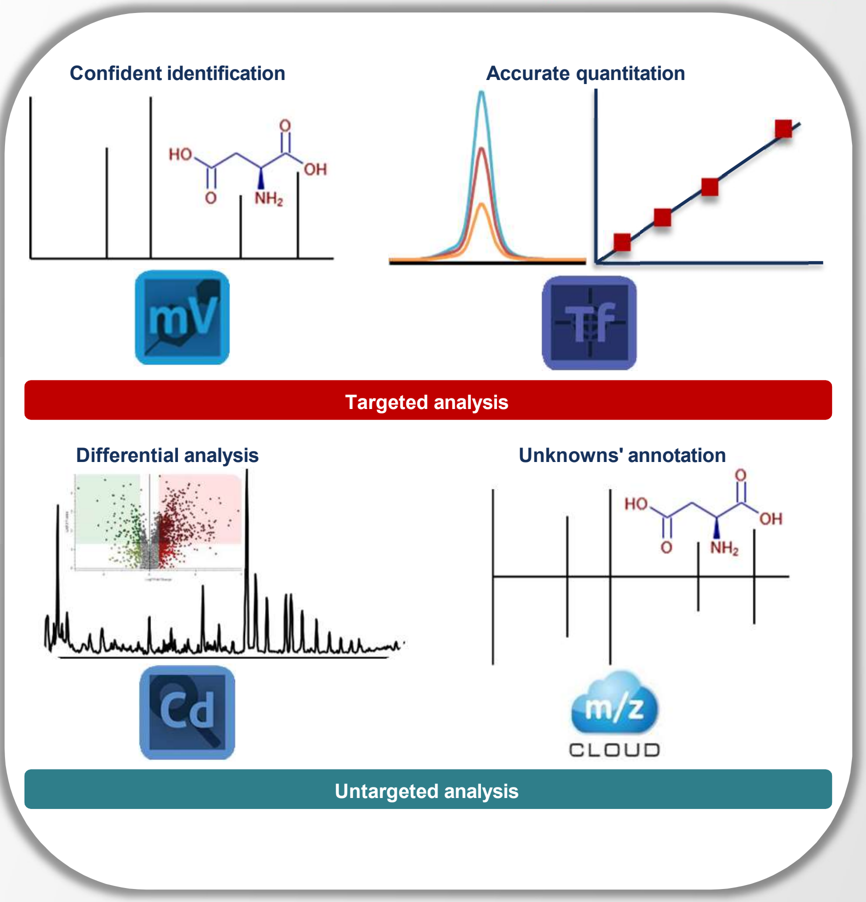
Sample preparation

- Utilizing isotopically labeled internal standards
    - confident identification
    - absolute quantitation
    - Instrument & method validation
- Incorporation of QC samples to ensure high-quality data



Data acquisition

- Robust LC analysis
- Ultra High-resolution accurate mass spectrometry
- Intelligent data acquisition for deeper metabolome coverage



Data analysis

- Sophisticated and comprehensive software solutions that enable fast data processing, accurate quantification of metabolites, advanced differential analysis, confident metabolite annotation utilizing spectral libraries and databases, and biological interpretation

HRAM importance for SQUAD

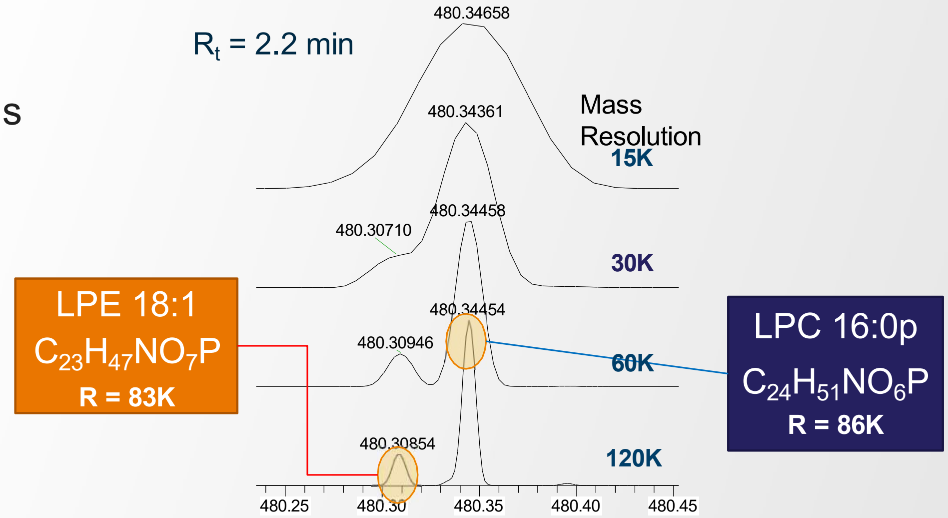
Annotation Specificity:

- Relies on excellent mass accuracy
  - Reduces the number of potential elemental compositions
  - Orbitrap Exploris Series are < 3ppm or < 1ppm with IC

- Relies on ultra high resolution
  - Separates isobars
  - Resolves isotopologues

Quantitative Accuracy:

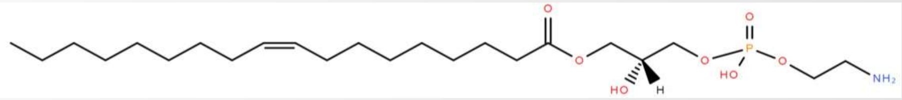
- Only achievable with fully resolved peaks
  - Provides selectivity in complex matrices



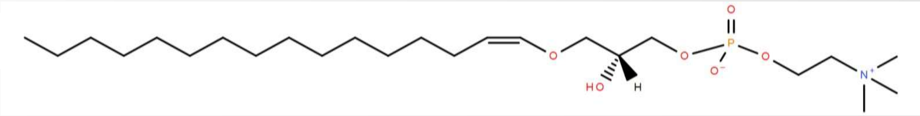
LPE 18:1
$C_{23}H_{47}NO_7P$
R = 83K

LPC 16:0p
$C_{24}H_{51}NO_6P$
R = 86K

LysoPE(18:1)

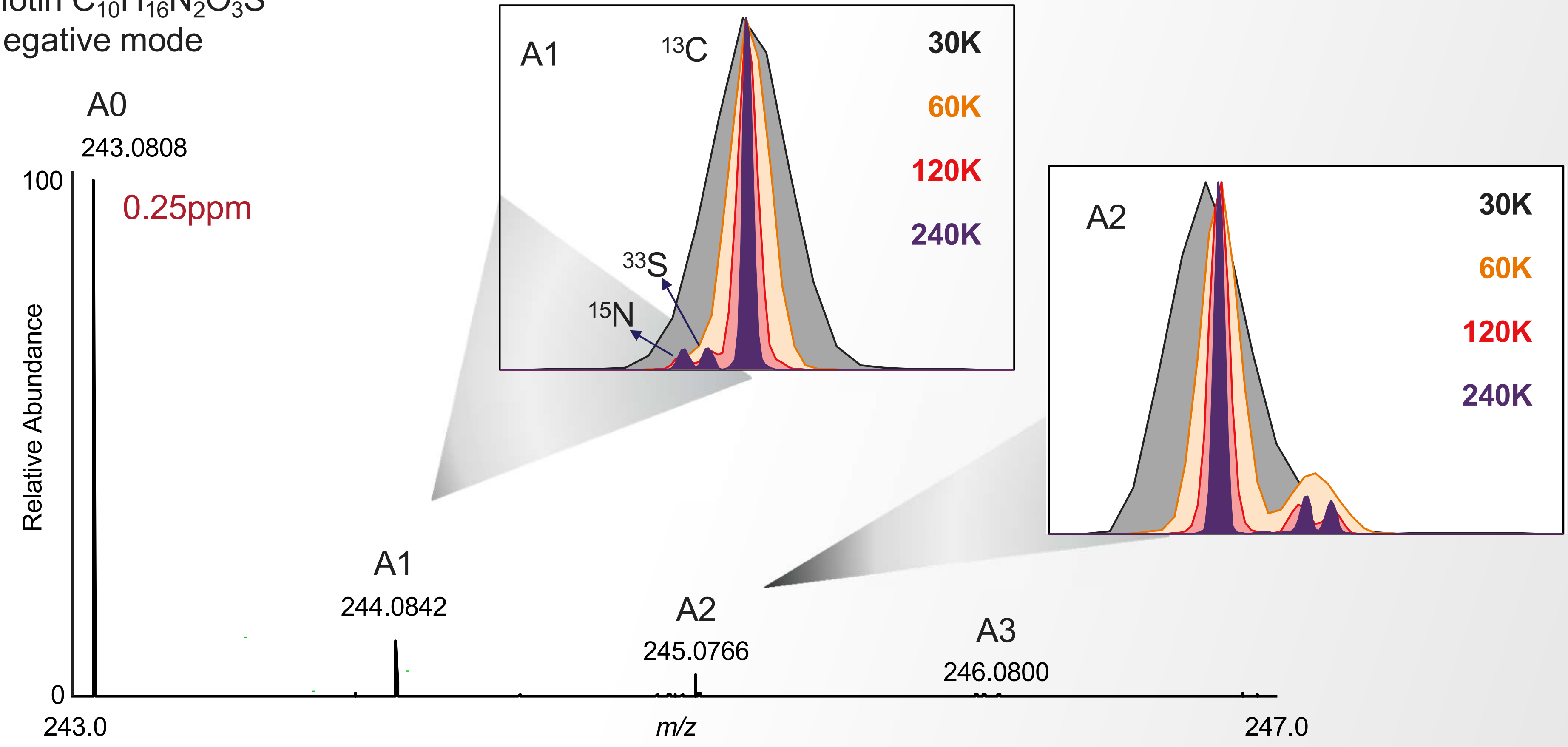


LysoPC(16:0p)



High Resolution for Fine Isotope Pattern Determination

Biotin $C_{10}H_{16}N_2O_3S$
Negative mode



HRAM for Annotation specificity and data reduction

Prediction by Mass Alone

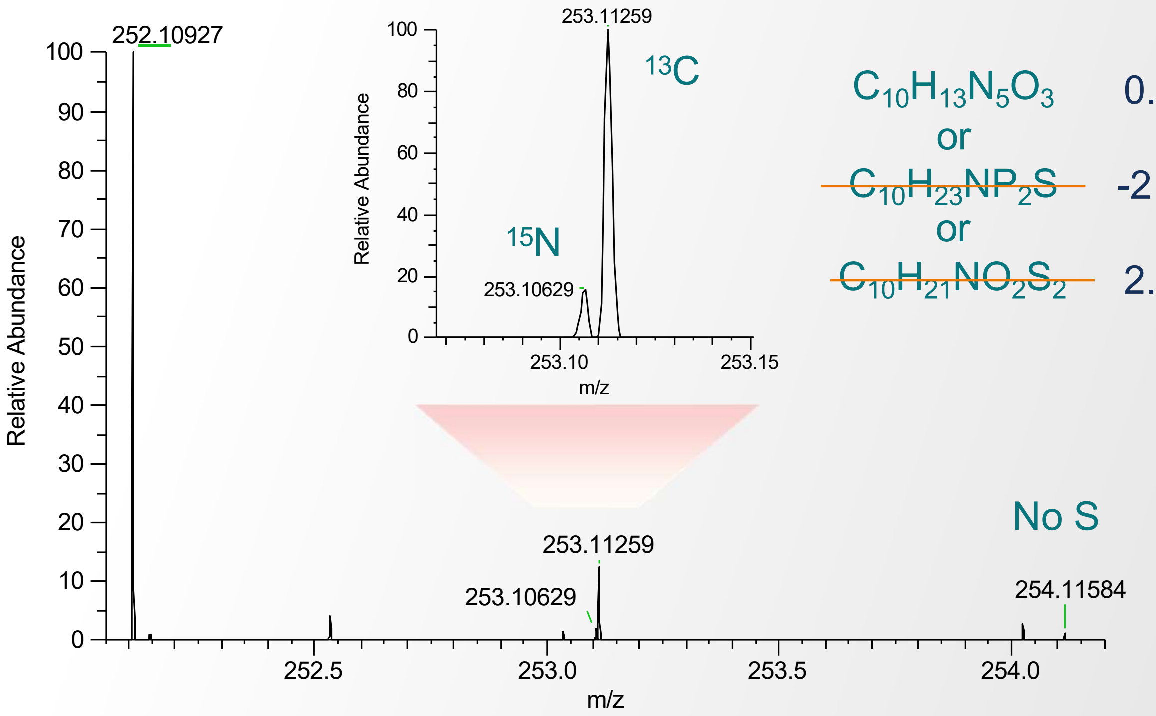
m/z 252.10930

Mass Tolerance (ppm)	# of Candidate Formulas
30	29
20	18
10	8
5	5
3	3
1	1

Elements C, H, N, O, S, Cl, P

Credentialed E. coli
120k, C18, 15min gradient

Prediction with Fine Isotope Structure



$C_{10}H_{13}N_5O_3$ 0.61 ppm

or

~~$C_{10}H_{23}NP_2S$~~ -2.59 ppm

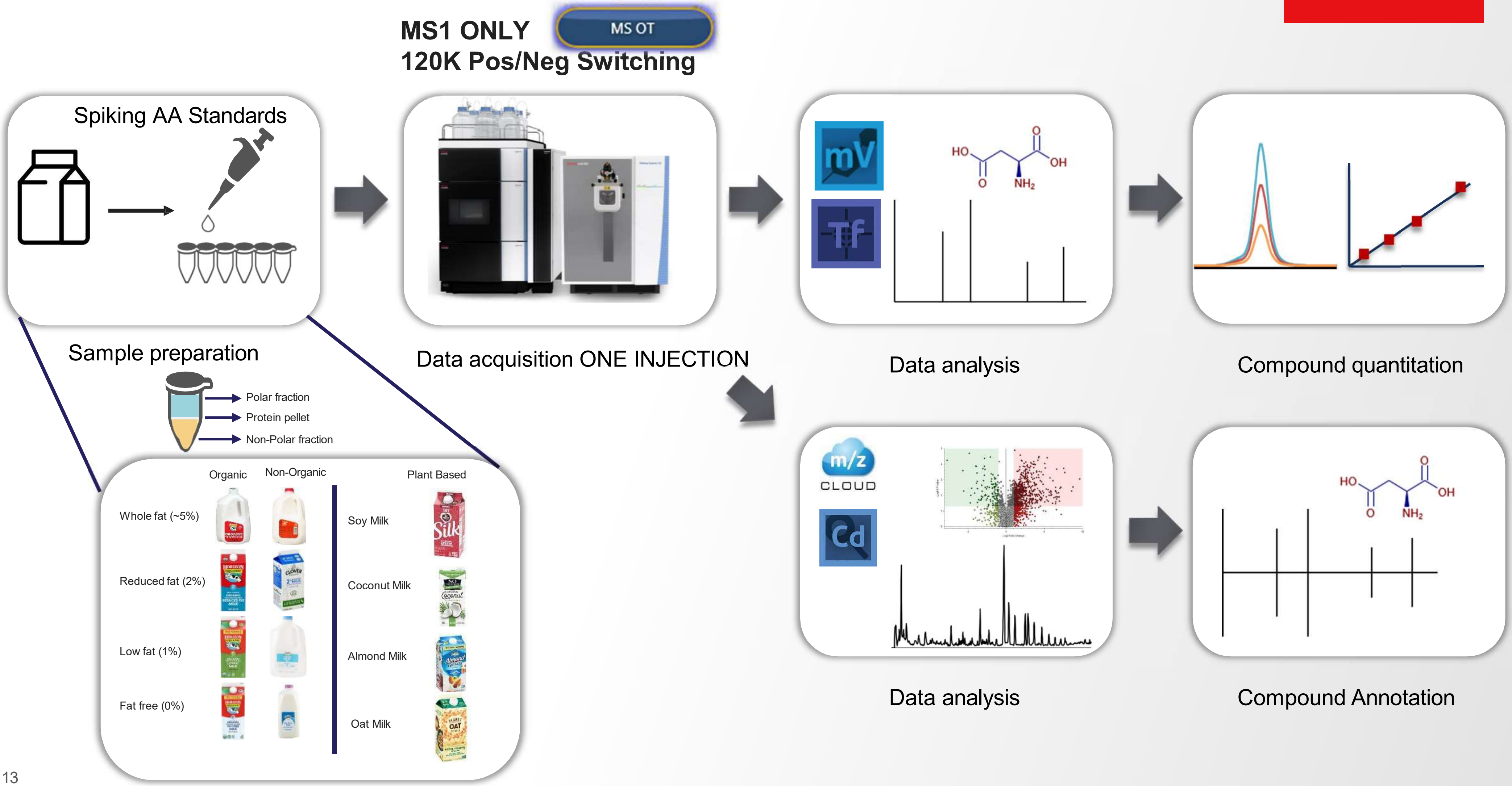
or

~~$C_{10}H_{21}NO_2S_2$~~ 2.48 ppm

No S

2'-Deoxyadenosine

SQUAD metabolomics workflow in milk



MS1 ONLY

MS OT

120K Pos/Neg Switching

Spiking AA Standards

Sample preparation

Polar fraction

Protein pellet

Non-Polar fraction

Organic

Non-Organic

Plant Based

Whole fat (~5%)

Reduced fat (2%)

Low fat (1%)

Fat free (0%)

Soy Milk

Coconut Milk

Almond Milk

Oat Milk

Data acquisition ONE INJECTION

Data analysis

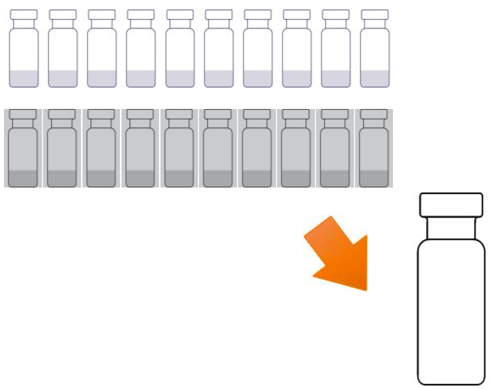
Compound quantitation

Data analysis

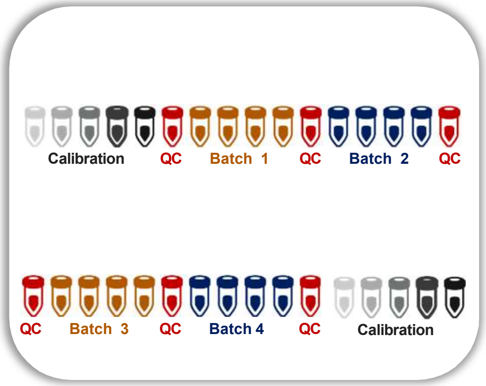
Compound Annotation

SQUAD | Experimental Setup

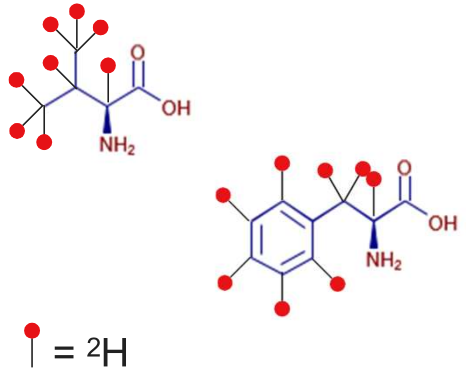
Building QA/QC into the Experiment



Pooled QC samples



Randomized order



Internal standards

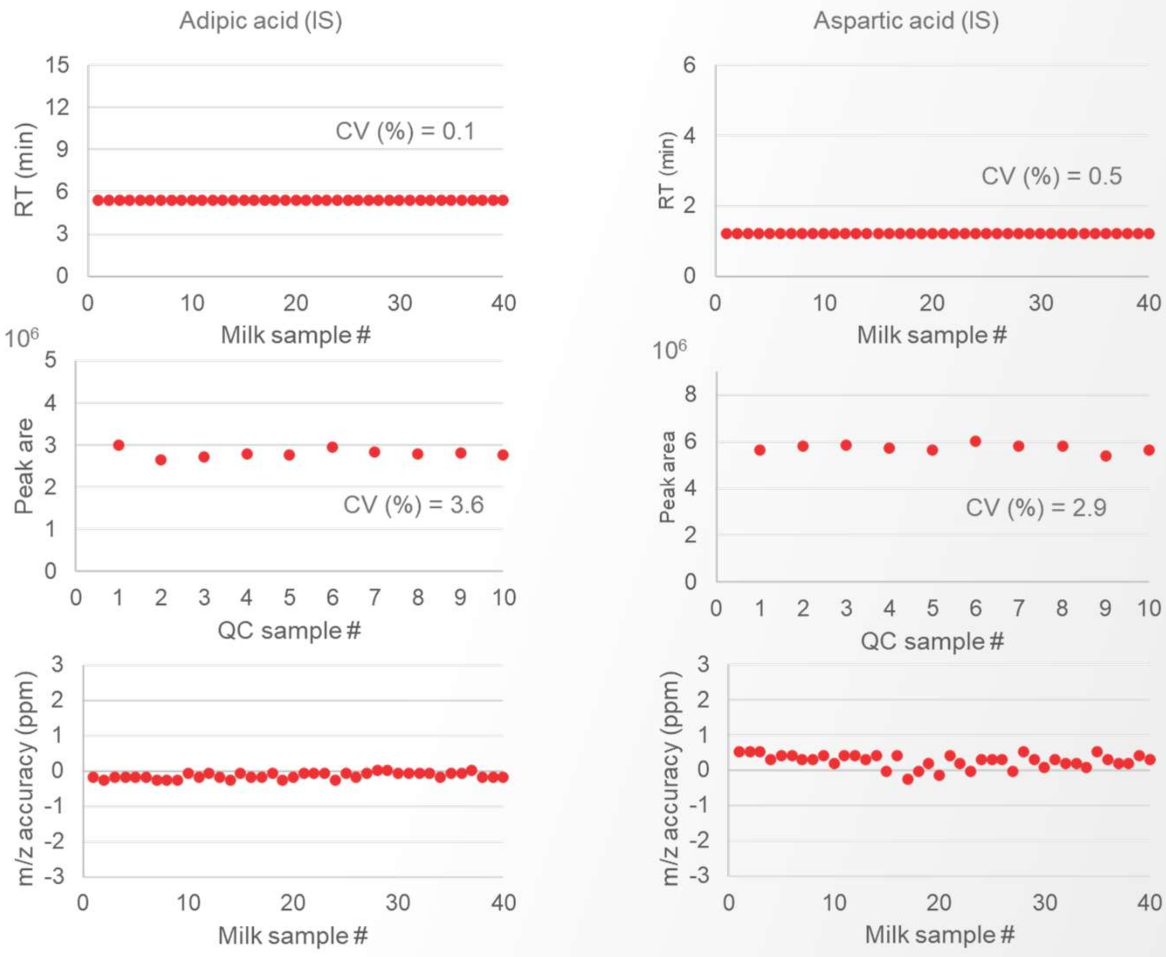
Scan Me for QA QC Tech Note

Quality assurance and quality control in metabolomics: achieving high-quality data for high-quality results

Metabolomics is a powerful analytical tool for the comprehensive detection of small molecules describing the biochemical phenotype in biological systems. By profiling polar metabolites and lipid species in biofluids and tissue samples, researchers gain knowledge of the physiology and pathophysiology of phenotypical endogenous metabolites and exogenous substances such as drugs or toxicants.

Achieving High-Quality Data

Instrument Stability Across 40 Injections



SQUAD Study in Milk

ThermoFisher SCIENTIFIC

Injection	Sample Type
1	System suitability Blank
2	System suitability Mix1
3 – 6	QC1 – 4 (system conditioning)
7 – 14	Calibration Curve
15	Extraction Blank
16 – 19	QC5 – 8 (system conditioning)
20 – 29	Biological samples 1 – 10
30	Pooled QC11
31 – 40	Biological samples 11 – 20
41	Pooled QC12
42 – 51	Biological samples 21 – 30
52	Pooled QC13
53	Extraction Blank
54-61	Calibration Curve
62-66	+ Pooled QC AcquireX MS^n 1 – 5
66-70	- Pooled QC AcquireX MS^n 1 – 5
71	System suitability Mix2

QC Frequency

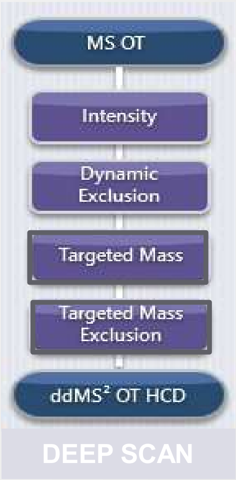
Varies depending on the QC requirements and analytical method

- ■ Calibration Curve
- 🟨 System suitability
- 🟧 System conditioning – 4X
- 🟪 Extraction Blank – 3X
- 🟧 Pooled QC – every 10 samples
- ■ Calibration Curve
- □ Pooled QC MSn – 5X

MS1 ONLY MS OT

120K Pos/Neg Switching

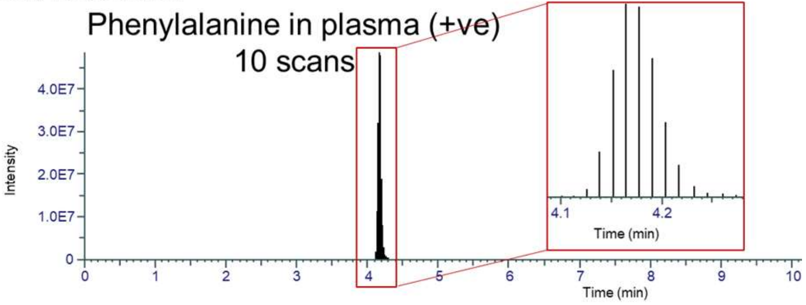
AcquireX Deep Scan
on Pooled Sample



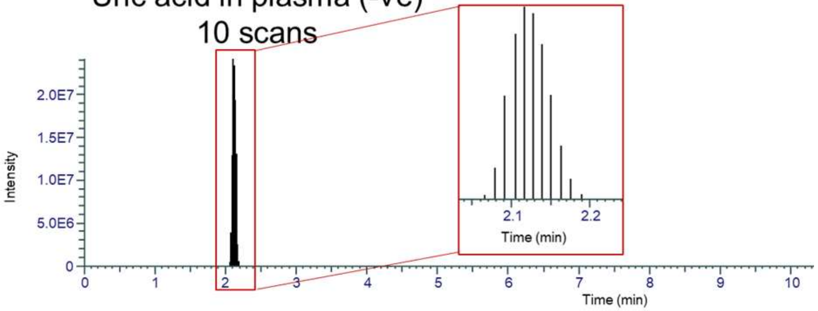
OE240 Polarity switching for full scan profiling of samples

60k resolution

Phenylalanine in plasma (+ve)
10 scans

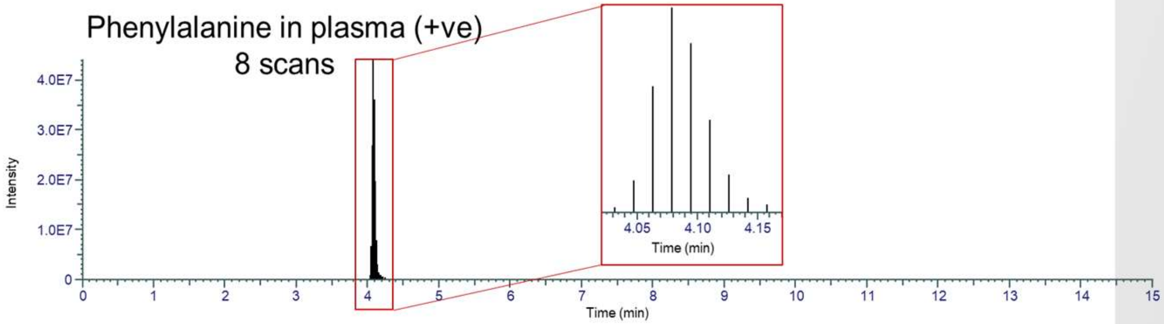


Uric acid in plasma (-ve)
10 scans

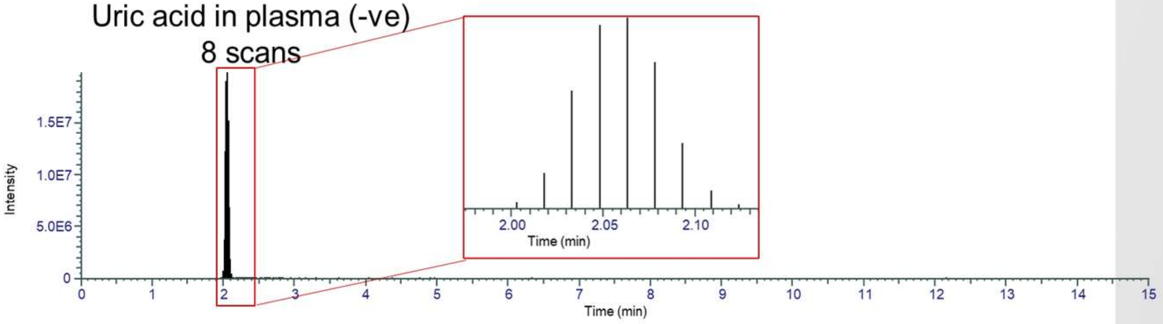


120k resolution

Phenylalanine in plasma (+ve)
8 scans



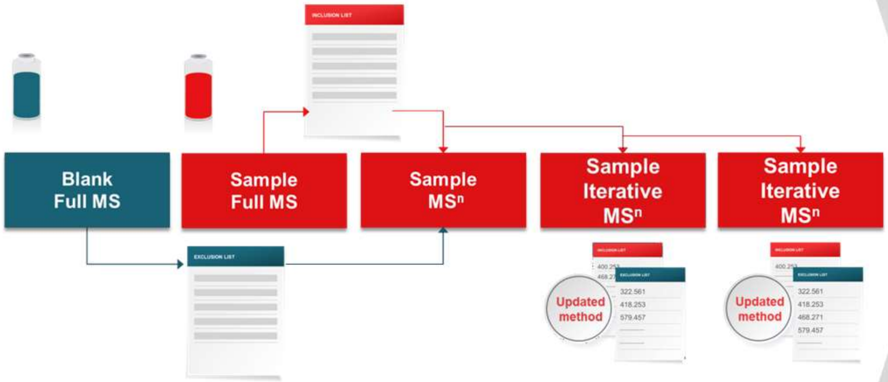
Uric acid in plasma (-ve)
8 scans



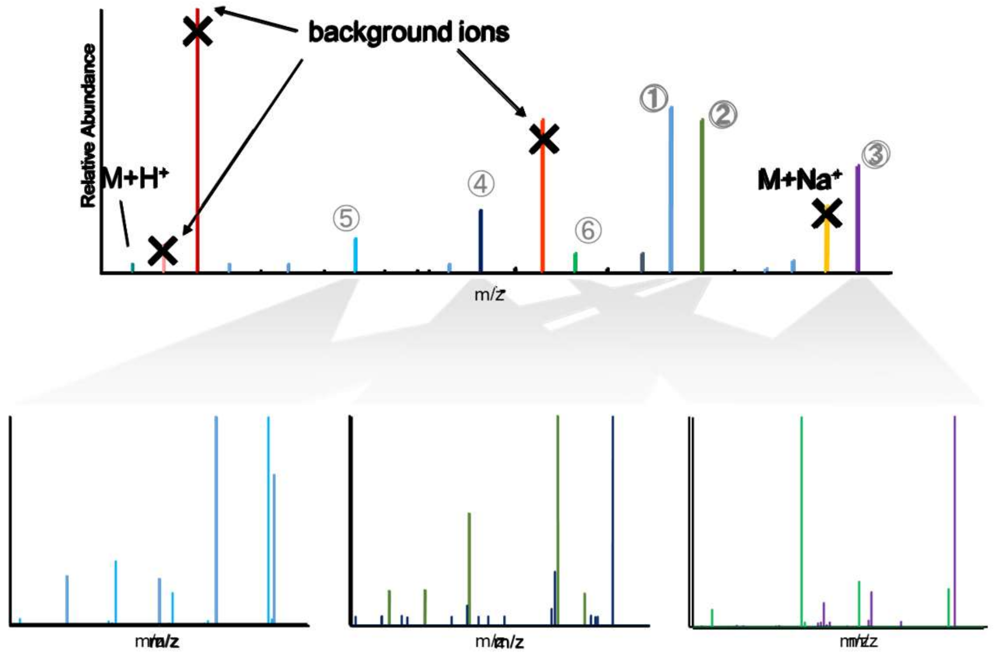
AcquireX Deep Scan – Intelligent Data Acquisition

Collect More Meaningful Data, Not Just More Data

Maximize productivity with automation for deep coverage of unknown compounds



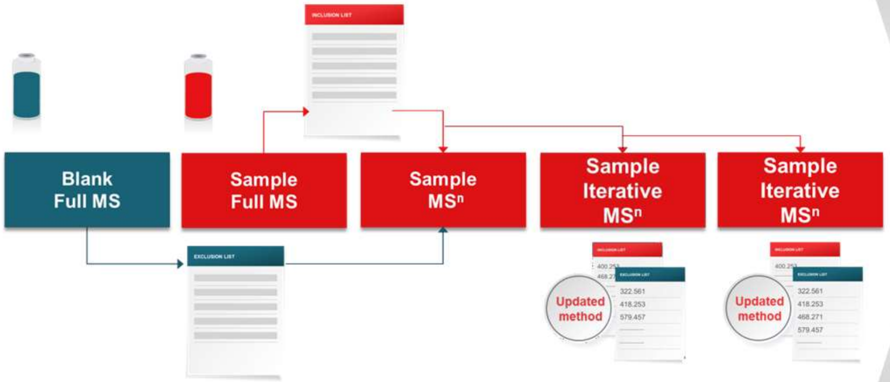
Automatically updated run-to-run inclusion/exclusion



AcquireX Deep Scan – Intelligent Data Acquisition

Collect More Meaningful Data, Not Just More Data

Maximize productivity with automation for deep coverage of unknown compounds



Blank Full MS

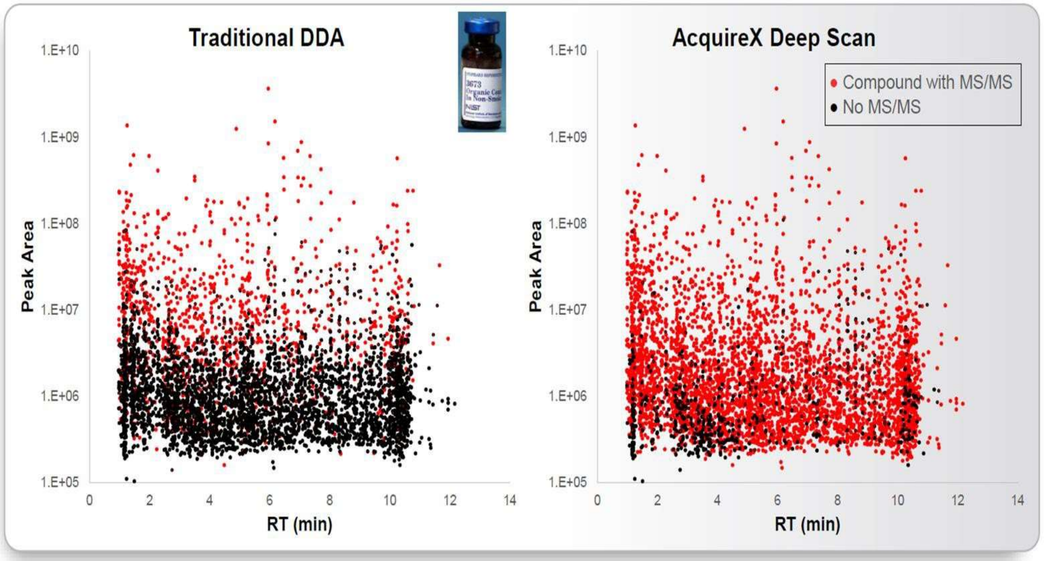
Sample Full MS

Sample MSⁿ

Sample Iterative MSⁿ

Sample Iterative MSⁿ

Automatically updated run-to-run inclusion/exclusion



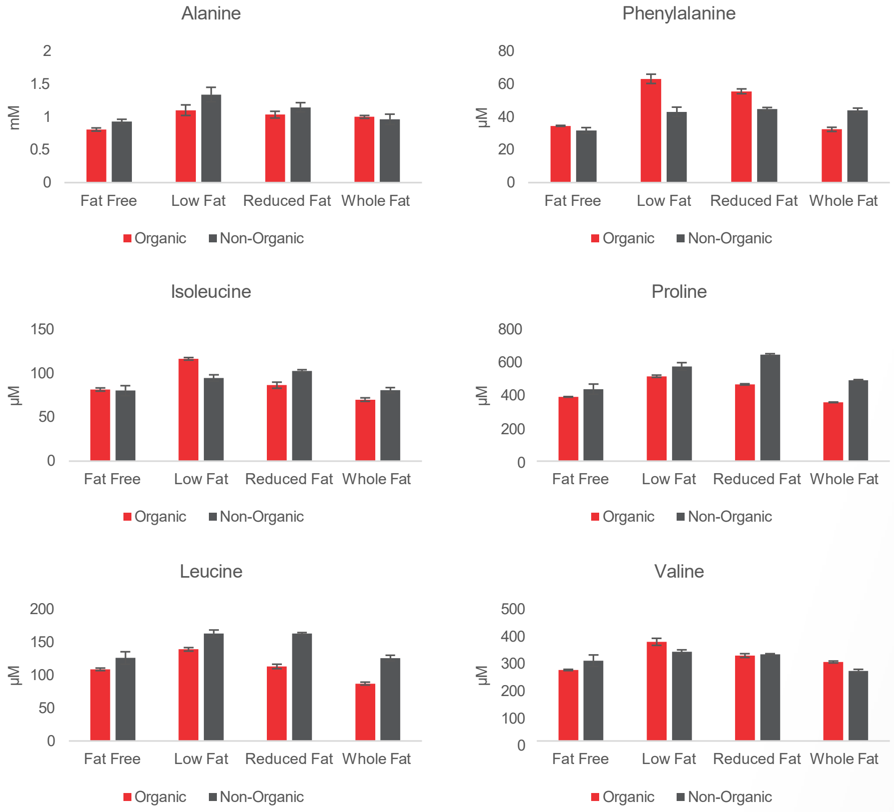
Traditional DDA

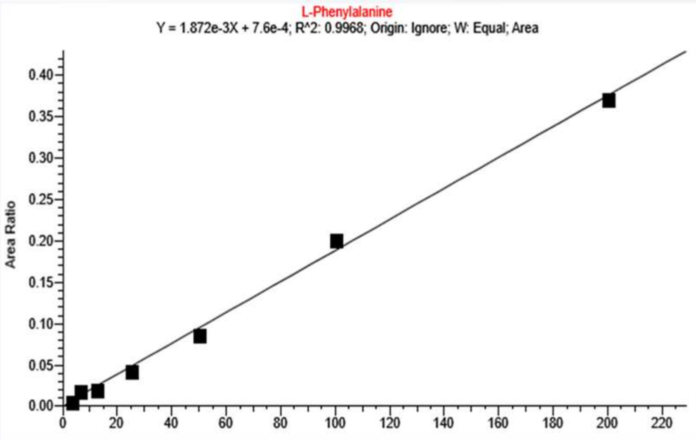
AcquireX Deep Scan

Comparison of traditional DDA and AcquireX Deep Scan for **SRM3673 Non-smoker's urine** (4951 detected compounds) shows increased depth of MS/MS fragmentation coverage with the AcquireX acquisitions, as illustrated after four injections.

SQUAD metabolomics workflow in cow’s milk

Targeted analysis

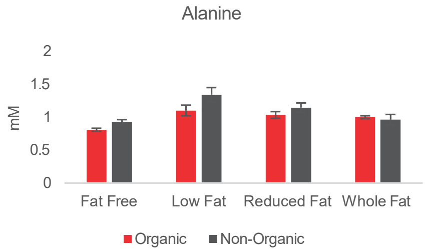


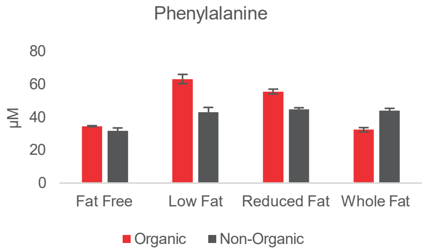


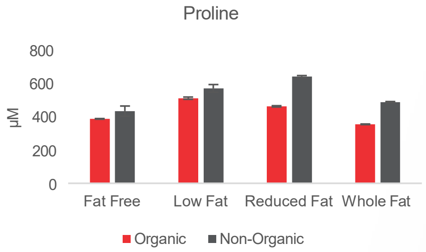
	LOQ (µM)	LOD (µM)
Alanine	0.39	0.39
Isoleucine	1.56	1.56
Leucine	6.25	1.56
Phenylalanine	3.13	1.56
Proline	6.25	0.39
Valine	0.39	0.39

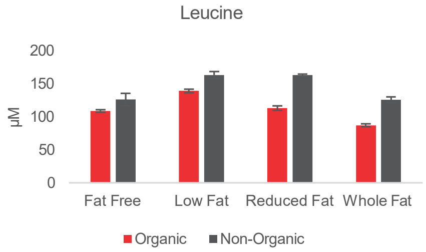
SQUAD metabolomics workflow in cow’s milk

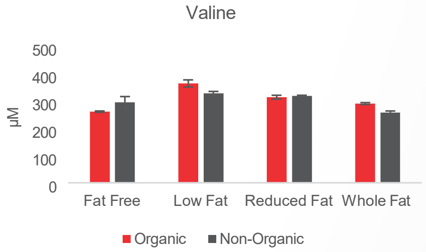
Targeted analysis



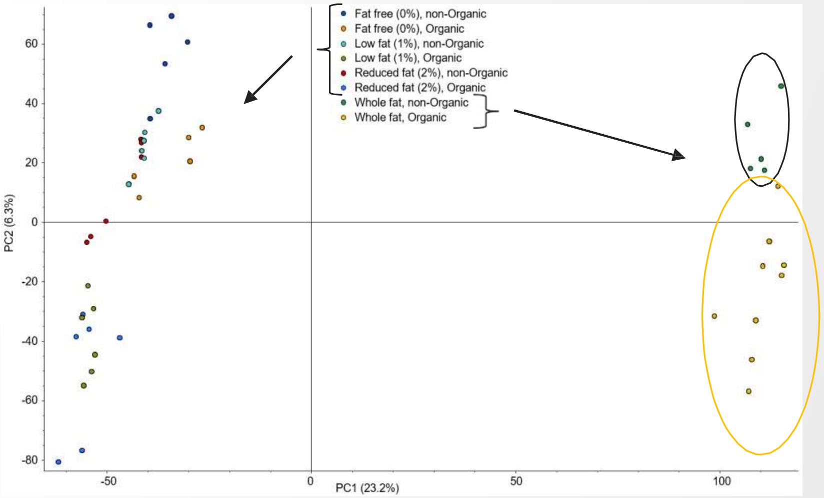


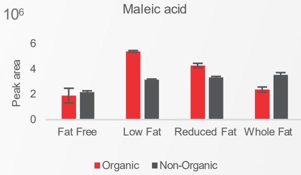


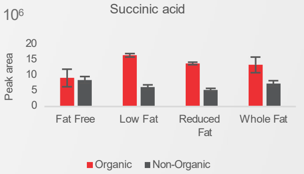


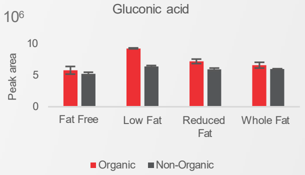


Untargeted analysis



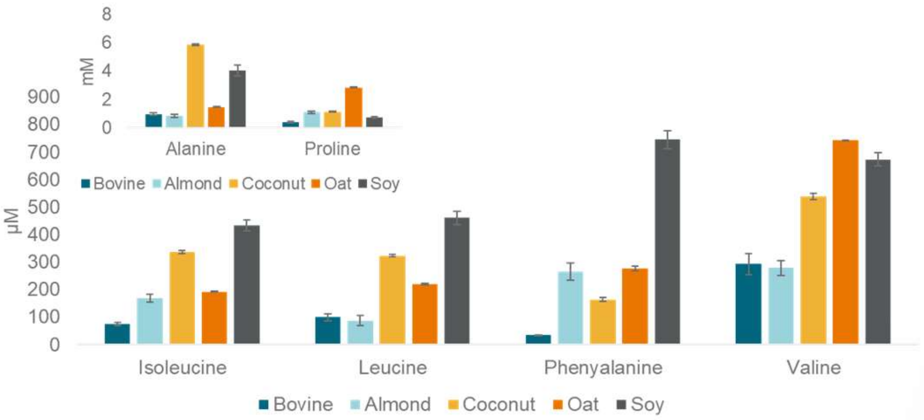




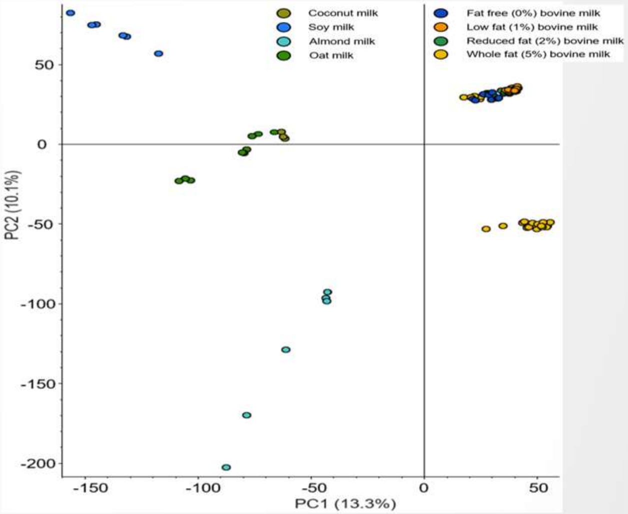


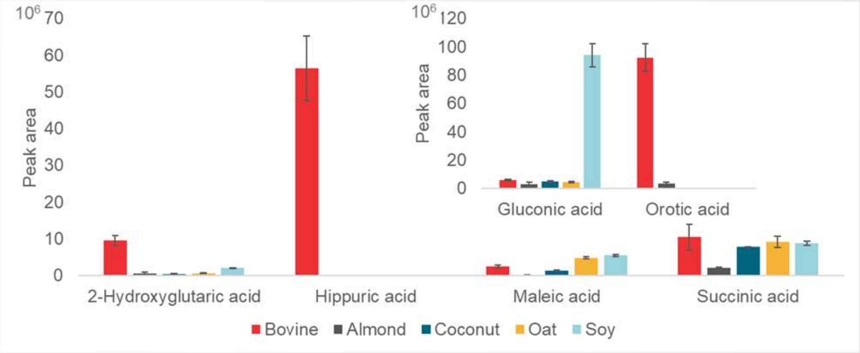
SQUAD metabolomics workflow in cow’s milk vs. Plant Milk

Targeted analysis



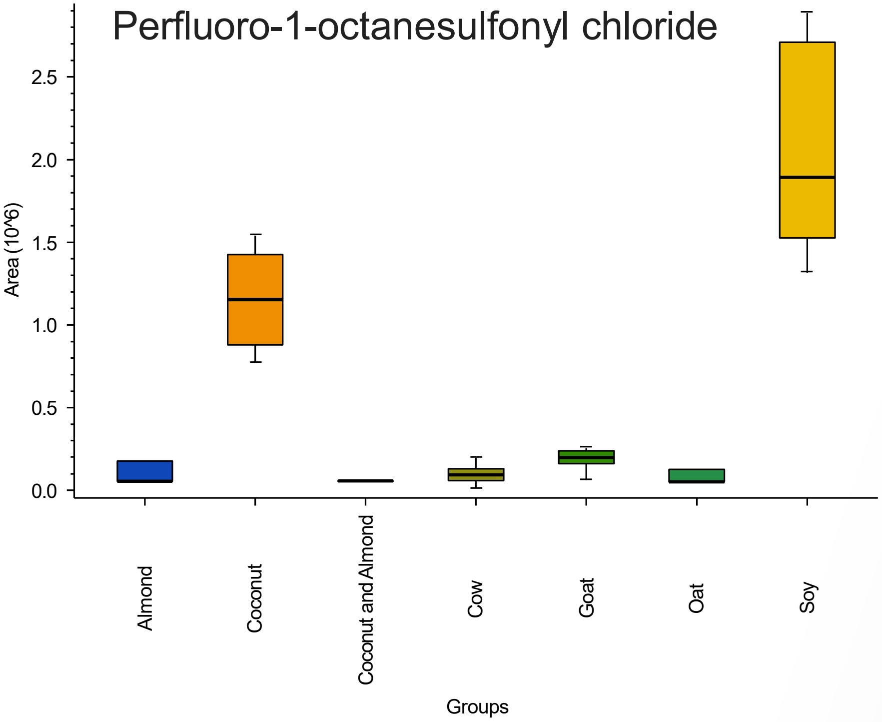
Untargeted analysis

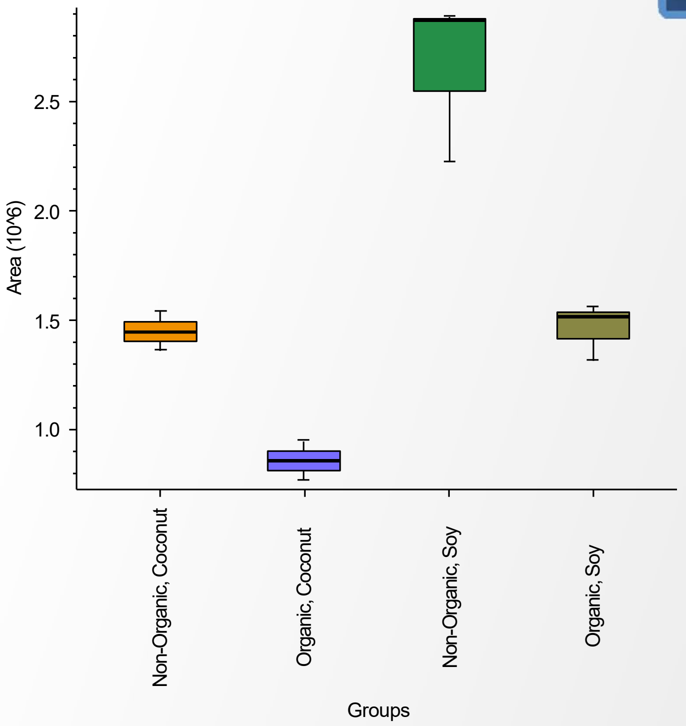




SQUAD importance for discovery data

Retro-mine your data and discover even more!!





Visit the oral presentation by Brandon Bills on Wed Jun 7 2:50 – 3:10 pm| General Assembly C

Visit poster WP 177 by Juan Sanchez on Wed Jun 7

10:30 am – 2:30 pm

SQUAD Workflow on Exploris 240 Recap

- **Get more from a single injection!! …**
  - Positive/Negative full scan analysis
- **Determine your specific research question and methodology without compromise**
  - Maximize sensitivity of targets
  - Maximize untargeted discovery

- **Labeled Internal Standards provide:**
  - QA/QC information on instrument performance and method
  - Absolute quantitation
- **AcquireX allows for deep sample annotation that maps back to study samples**

Simultaneous Quantitation and Discovery (SQUAD) Analysis: Combining the Best of Targeted and Untargeted Mass Spectrometry-Based Metabolomics

by Bashar Amer *, Rahul R. Deshpande and Susan S. Bird

Thermo Fisher Scientific, San Jose, 95134 CA, USA
* Author to whom correspondence should be addressed.

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(This article belongs to the Section Advances in Metabolomics)

Solutions tailored for metabolomics and lipidomics

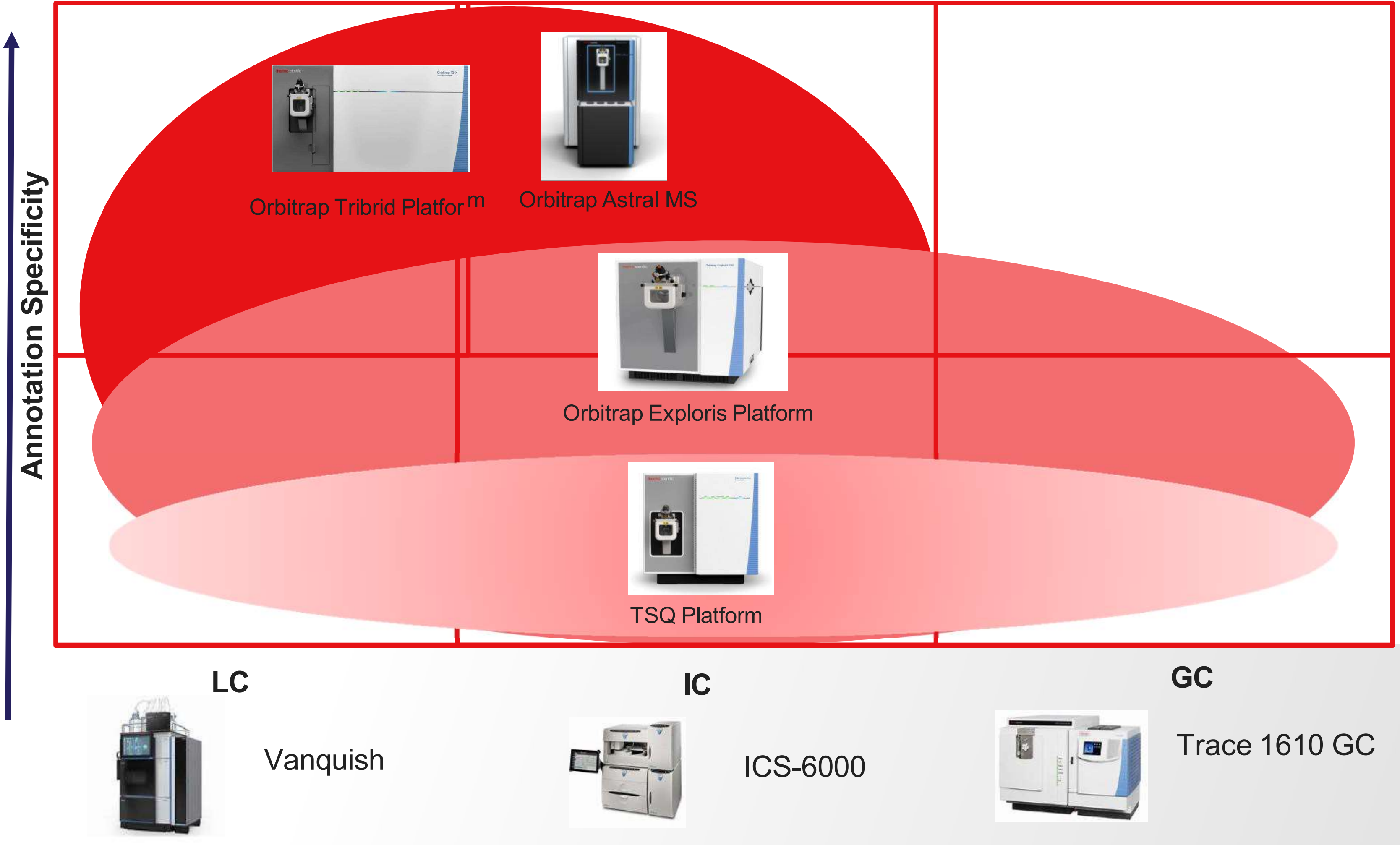
ThermoFisher SCIENTIFIC

Discovery
(Unknowns & Uncharacterized)

Mf Cd Ls
m/z CLOUD mV Ax

Targeted
(Quantitation of Knowns)

Tf



Separation Compatibility

SQUAD considerations on a Tribrid

UCDAVIS Fiehn Lab

ThermoFisher SCIENTIFIC

WOC 3:30

Oliver Fiehn & Elys Rodriguez
West Coast Metabolomics Center,
UC Davis

Orbitrap IQ-X Tribrid mass spectrometer

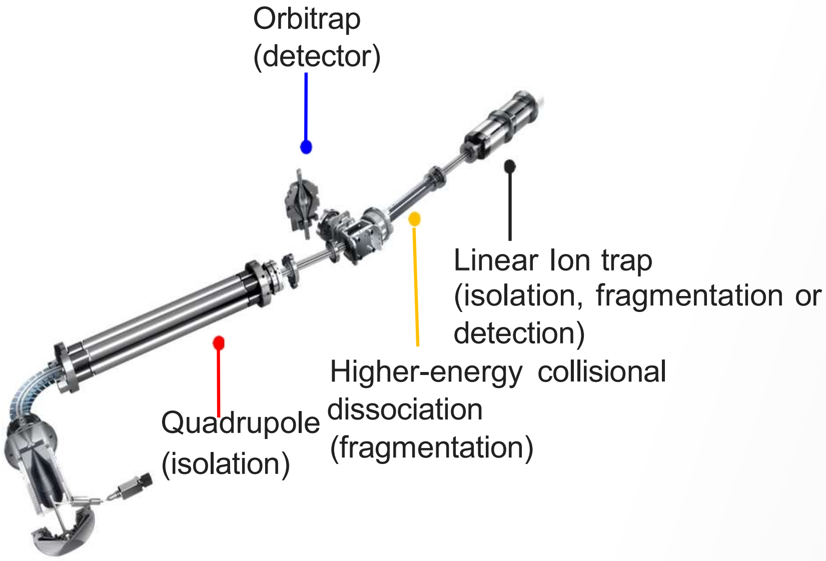


Figure 1. Orbitrap IQ-X Tribrid mass spectrometer schematic

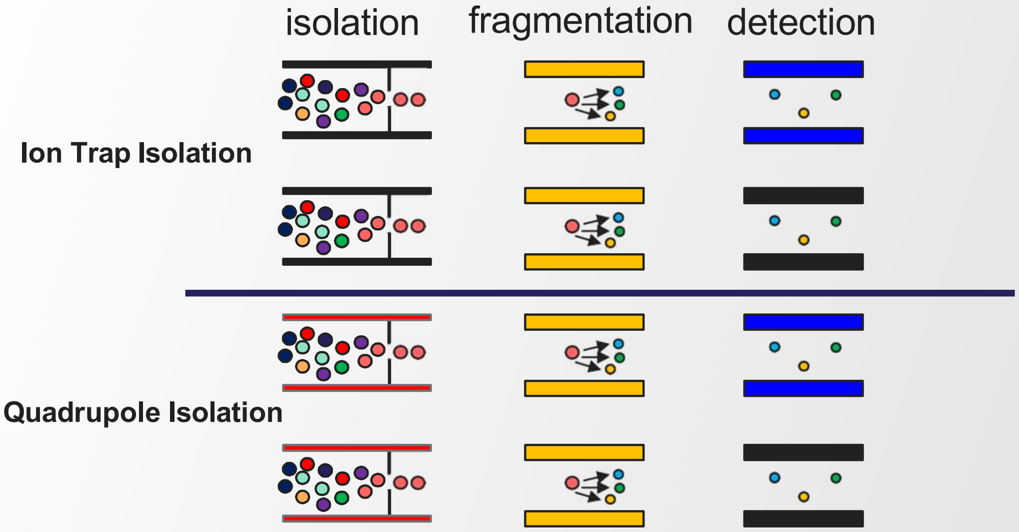
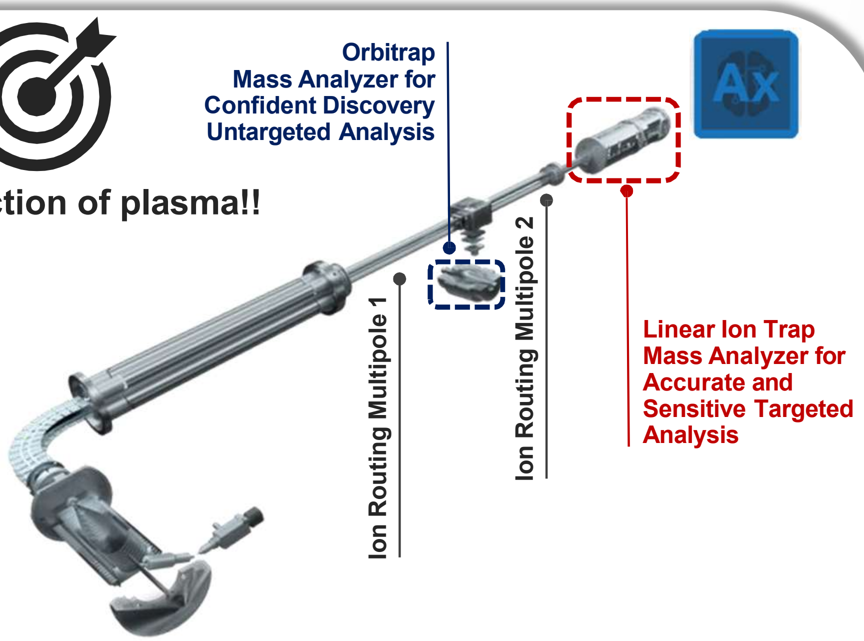


Figure 2. Possible ion isolation and detection ion routes

SQUAD Analysis on Ascend Tribrid MS

Single Injection of plasma!!



Orbitrap Mass Analyzer for Confident Discovery Untargeted Analysis

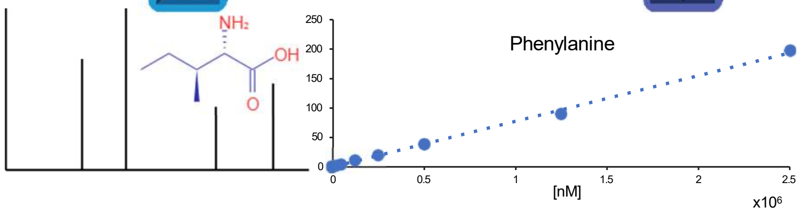
Ion Routing Multipole 1

Ion Routing Multipole 2

Linear Ion Trap Mass Analyzer for Accurate and Sensitive Targeted Analysis

Single Injection-Based Mass Spectrometry Metabolomics

Data acquisition

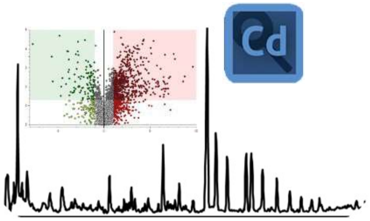


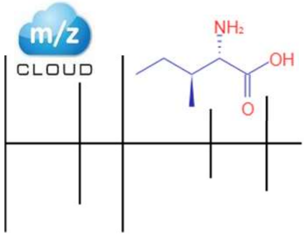
LOQ of 5 Femto mole with 6 orders of magnitude linear dynamic range

Targeted Analysis

+

Untargeted Analysis





55% more MS¹ ions and 25% more MS² ions are measured with Ascend compared to IQ-X

Data analysis

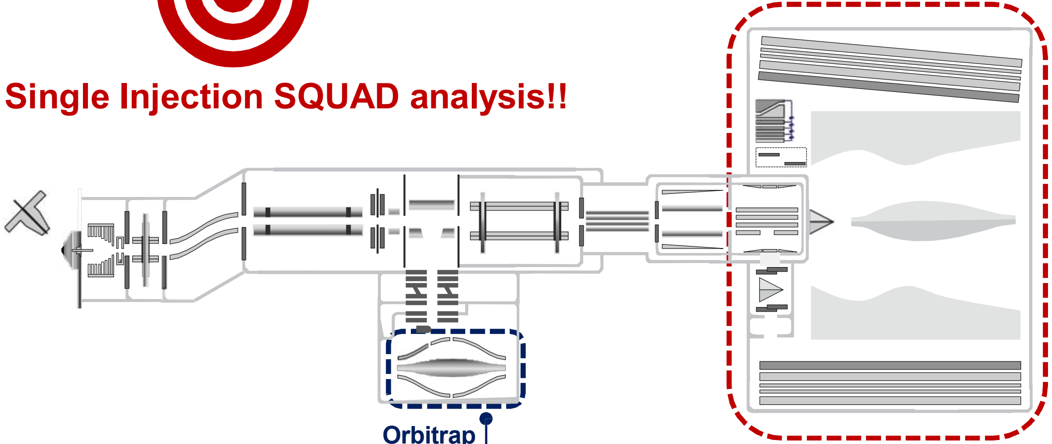
SQUAD on Orbitrap Astral novel mass analyzer

Parallel, fast, and accurate analysis

Visit Monday's breakfast workshop "A new platform for comprehensive metabolomics and lipidomics"

7:00 – 8:00 am| Convention Center - Room 361CF

Single Injection SQUAD analysis!!

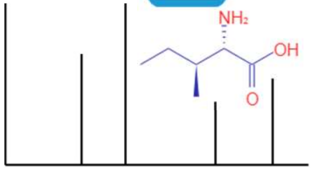


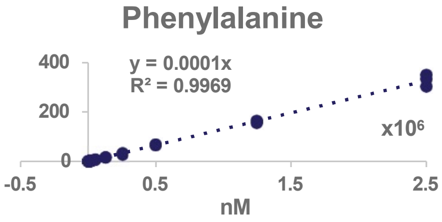
Orbitrap Mass Analyzer for Confident MS¹ Discovery and sensitive MS¹ Quantitation

Astral Mass Analyzer for Fast and Deep MS² Detection

Single Injection-Based Mass Spectrometry Metabolomics

Data acquisition



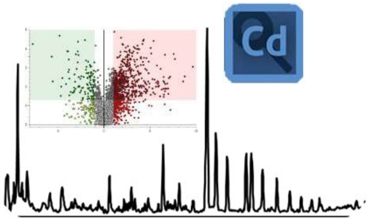


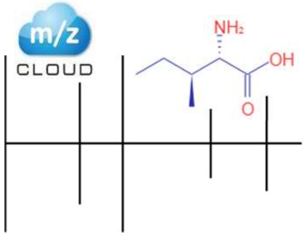
LOQ of 10 femtomole with 5 orders of magnitude linear dynamic range

Targeted Analysis

+

Untargeted Analysis





90% of the MS¹ ions were fragmented using DDA method with Astral

Data analysis

Small Molecule Software for Metabolomics & Lipidomics

Thermo Scientific™ Compound Discoverer™ Software: The Ultimate Toolbox to Analyze **Untargeted Metabolomics** Data

Thermo Scientific™ mzCloud™ Mass Spectral Fragmentation Library: MS/MS and MS^n **Reference Spectra** to Increase Confidence in Unknown Annotation and Identification

Thermo Scientific™ TraceFinder™ Software: To Rapidly Detect **Targeted Knowns** for QAQC, Profiling, and Absolute Quantitation

Thermo Scientific™ mzVault™ Application: To Create, Modify, and **Customize Mass Spectral Libraries** of Accurate Mass Data

Thermo Scientific™ LipidSearch™ Software: **Lipid Specific Untargeted Analysis** for Confident Annotation and Quantitation Using MS/MS and MS^n

Thermo Scientific™ Mass Frontier™ Software: To annotate and build custom libraries of small molecule MS/MS and MSn fragmentation Data

Thermo Scientific™ AcquireX™ Software: **Intelligent instrument control software** for more meaningful fragmentation spectra

Compound Discoverer

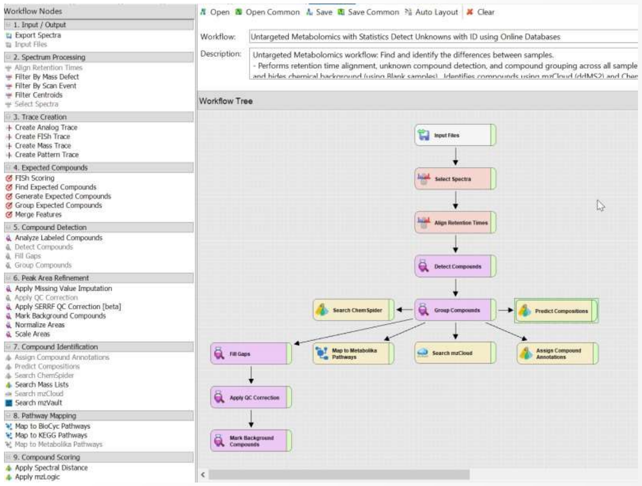
End-to-end capabilities implemented in Thermo Scientific™ Compound Discoverer™ software

Raw mass spectral data → Meaningful data → Meaningful insights into the system under study

RT Correction → Predict Elemental Formula → Feature Detection → Data Reduction → Unknown Annotation → Statistics → Pathway Analysis

- Unknown peak detection
- Advanced statistics
- Interactive data visualization
- Compound annotation tools (Known and unknown)

CD workflow editor

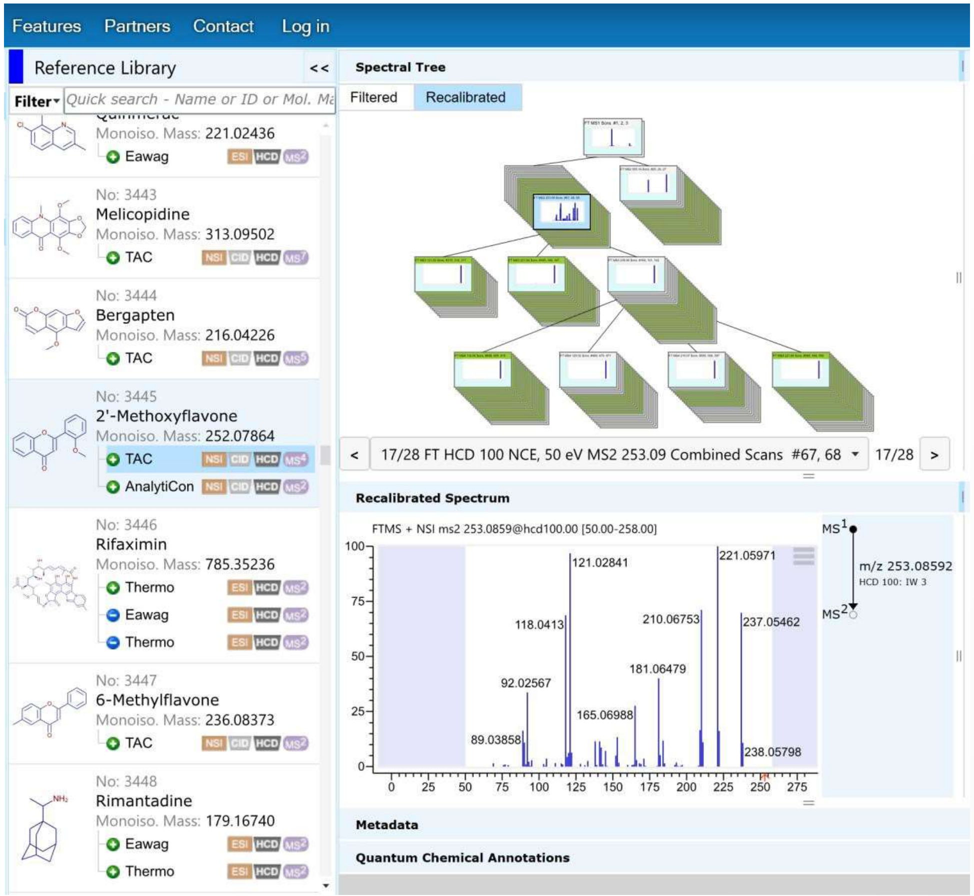


Workflow: Untargeted Metabolomics with Statistics Detect Unknowns with ID using Online Databases

Description: Untargeted Metabolomics workflow: Find and identify the differences between samples.
- Performs retention time alignment, unknown compound detection, and compound grouping across all sample
and hides chemical background (using Blank samples). Identifies compounds using mzCloud (ddMS2) and Chem

- Integrated database and spectral library
- Molecular networks
- Biochemical pathway mapping
- Untargeted stable isotope labeling analysis

mzCloud Library



Monoiso. Mass: 221.02436
Eawag

No: 3443
Melicopidine
Monoiso. Mass: 313.09502
TAC

No: 3444
Bergapten
Monoiso. Mass: 216.04226
TAC

No: 3445
2'-Methoxyflavone
Monoiso. Mass: 252.07864
TAC
AnalytiCon

No: 3446
Rifaximin
Monoiso. Mass: 785.35236
Thermo
Eawag
Thermo

No: 3447
6-Methylflavone
Monoiso. Mass: 236.08373
TAC

No: 3448
Rimantadine
Monoiso. Mass: 179.16740
Eawag
Thermo

< 17/28 FT HCD 100 NCE, 50 eV MS2 253.09 Combined Scans #67, 68 ▾ 17/28 >

FTMS + NSI ms2 253.0859@hcd100.00 [50.00-258.00]

HRAM MS/MS and MS^n

HCD and CID fragmentation

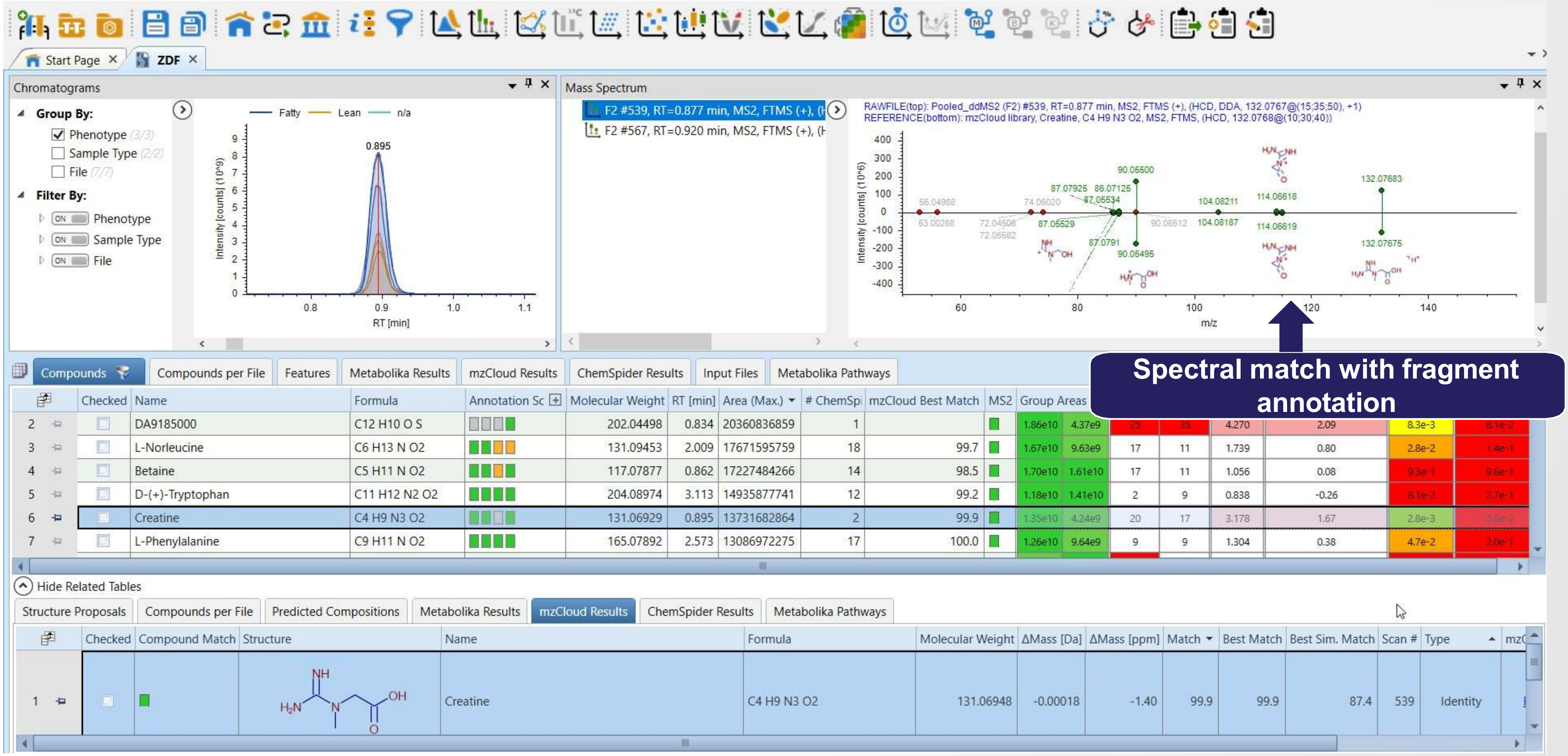
Multiple Energy Levels

100% Professionally Curated

>21,000 Compounds

>10M fragment structures

mzCloud batch search in Compound Discoverer



Group By:

☑ Phenotype (3/3)

☐ Sample Type (2/2)

☐ File (7/7)

Filter By:

ON Phenotype

ON Sample Type

ON File

F2 #539, RT=0.877 min, MS2, FTMS (+), (H

F2 #567, RT=0.920 min, MS2, FTMS (+), (H

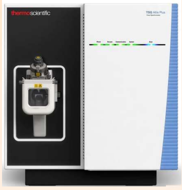
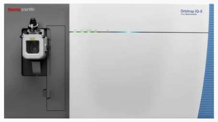
RAWFILE(top): Pooled_ddMS2 (F2) #539, RT=0.877 min, MS2, FTMS (+), (HCD, DDA, 132.0767@(15;35;50), +1)
REFERENCE(bottom): mzCloud library, Creatine, C4 H9 N3 O2, MS2, FTMS, (HCD, 132.0768@(10;30;40))

		Checked	Name	Formula	Annotation Sc	Molecular Weight	RT [min]	Area (Max.)	# ChemSpi	mzCloud Best Match	MS2	Group Areas							
2		☐	DA9185000	C12 H10 O S		202.04498	0.834	20360836859	1		🟩	1.86e10	4.37e9	25	35	4.270	2.09	8.3e-3	8.1e-2
3		☐	L-Norleucine	C6 H13 N O2		131.09453	2.009	17671595759	18	99.7	🟩	1.67e10	9.63e9	17	11	1.739	0.80	2.8e-2	1.4e-1
4		☐	Betaine	C5 H11 N O2		117.07877	0.862	17227484266	14	98.5	🟩	1.70e10	1.61e10	17	11	1.056	0.08	9.3e-1	9.6e-1
5		☐	D-(+)-Tryptophan	C11 H12 N2 O2		204.08974	3.113	14935877741	12	99.2	🟩	1.18e10	1.41e10	2	9	0.838	-0.26	8.1e-2	2.7e-1
6		☐	Creatine	C4 H9 N3 O2		131.06929	0.895	13731682864	2	99.9	🟩	1.35e10	4.24e9	20	17	3.178	1.67	2.8e-3	5.6e-2
7		☐	L-Phenylalanine	C9 H11 N O2		165.07892	2.573	13086972275	17	100.0	🟩	1.26e10	9.64e9	9	9	1.304	0.38	4.7e-2	2.0e-1

		Checked	Compound Match	Structure	Name	Formula	Molecular Weight	ΔMass [Da]	ΔMass [ppm]	Match	Best Match	Best Sim. Match	Scan #	Type	mzC
1		☐	🟩		Creatine	C4 H9 N3 O2	131.06948	-0.00018	-1.40	99.9	99.9	87.4	539	Identity	

Spectral match with fragment annotation

Metabolomics and Lipidomics workflow guide LC-MS

Workflow	Application	LC	MS Instrumentation	Data Processing
Targeted Quant	Absolute quantitation of known metabolites	 Thermo Scientific™ Vanquish Horizon/Flex/Duo	 Thermo Scientific™ TSQ™ Altis Plus Triple Quad MS  Thermo Scientific™ Orbitrap Exploris MX/120/240	Targeted Quan Spectral Library
Simultaneous Quant and Discovery (SQUAD)	Accurate quantitation of known metabolites with ability to discover unknown	 Thermo Scientific™ Vanquish Horizon/Flex/Duo	 Thermo Scientific™ Orbitrap Exploris 120/240  Thermo Scientific™ Orbitrap Astral MS  Thermo Scientific™ Orbitrap IQ-X™ Tribrid™ MS	Targeted Quan QA/QC Ultimate Untargeted Toolbox Lipid Spectral Library
Untargeted Discovery & Lipidomics	Identification and comparison of all metabolites/lipids in multiple samples without prior knowledge	 Thermo Scientific™ Vanquish Horizon/Flex/Duo	 Thermo Scientific™ Orbitrap Exploris 120/240  Thermo Scientific™ Orbitrap Astral MS  Thermo Scientific™ Orbitrap IQ-X™ Tribrid™ MS	Ultimate Untargeted Toolbox Lipid In-house Custom Library Spectral Library

Multi-Omics Workflow

MULTI-SCALE DATA ACQUSITION

METADATA

DNA SEQUENCING

TRANSCRIPTOMICS

PROTEOMICS

METABOLOMICS

STAGE 1 **STAGE 2** **STAGE 3** **STAGE 4**

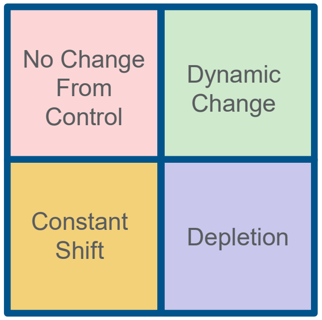
Multi-Omics Workflow

MULTI-SCALE DATA ACQUSITION

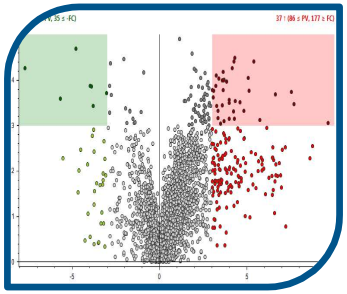
- METADATA
- DNA SEQUENCING
- TRANSCRIPTOMICS
- PROTEOMICS
- METABOLOMICS

STAGE 1

UNDERSTANDING BASIC DIFFERENCES



No Change From Control	Dynamic Change
Constant Shift	Depletion



STAGE 2

STAGE 3

STAGE 4

Multi-Omics Workflow

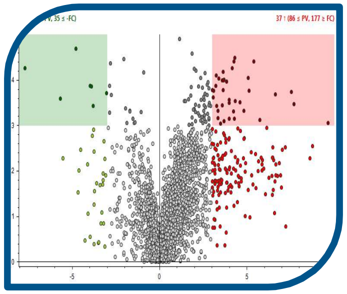
MULTI-SCALE DATA ACQUSITION

- METADATA
- DNA SEQUENCING
- TRANSCRIPTOMICS
- PROTEOMICS
- METABOLOMICS

STAGE 1

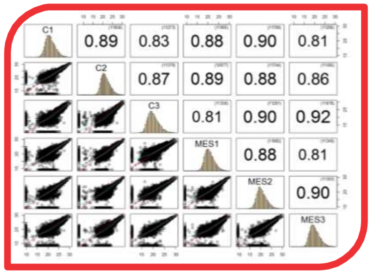
UNDERSTANDING BASIC DIFFERENCES

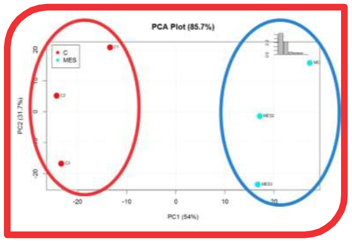
No Change From Control	Dynamic Change
Constant Shift	Depletion



STAGE 2

UNDERSTANDING CORRELATION IN DATA





STAGE 3

STAGE 4

Multi-Omics Workflow

MULTI-SCALE DATA ACQUSITION

METADATA

DNA SEQUENCING

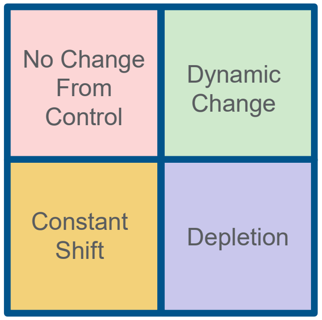
TRANSCRIPTOMICS

PROTEOMICS

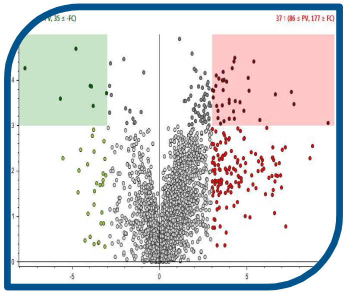
METABOLOMICS

STAGE 1

UNDERSTANDING BASIC DIFFERENCES

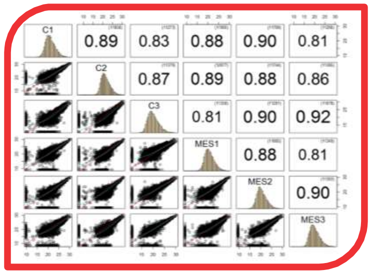


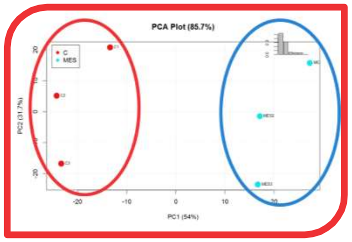
No Change From Control	Dynamic Change
Constant Shift	Depletion



STAGE 2

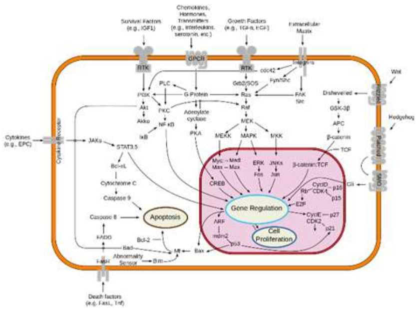
UNDERSTANDING CORRELATION IN DATA

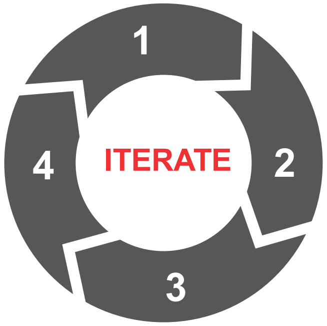




STAGE 3

UNDERSTANDING METABOLIC OR SIGNALING MECHANISMS





STAGE 4

JA1

Thank you

Slide 129

JA0 Believe we need to have more detail in the boilerplate on this last slide.
Johnson, Ann; 2024-04-29T03:12:22.240

JA1 Per Corporate from the first review: The logo on the thank you slide looks quite small -- please use something similar to the Thermo Fisher bumper and add the copyright/legalese to the bottom

https://thermofisher.frontify.com/document/56#/videography/video-elements/bumpers
Johnson, Ann; 2024-04-29T03:14:11.106

AR1 0 [@Johnson, Ann] This is the corporate template not something Duarte created
Robitaille, Aaron; 2024-04-29T22:39:03.048