

Supplementary Table 1. Chromatography and MS instrument acquisition settings for DDA

Sample Volume	5 μ L	MS² Acquisition	Data dependent, 3 s cycle time, Centroid
Stationary Phase	PicoChip; C ₁₈ 75 μ m \times 10.5 cm	MS² Fragmentation	HCD
LC Solvent A	100% H ₂ O, 0.1% formic acid	MS² Detection	Orbitrap
LC Solvent B	80% ACN, 0.1% formic acid	MS² fixed first mass	110 <i>m/z</i>
Gradient Ramp	6-36% B	Isolation Window	1.6 <i>m/z</i>
Duration	95 minutes		
Flow Rate	300 nL/min		
Mass Spectrometer	Thermo Orbitrap Fusion Lumos	MS² AGC Target	5e4
Spray Voltage	2.0 kV	MS² Maximum IT	100 ms
In-Source CID	0.0 eV	Normalized Collision Energy	30
MS¹ Scan Range	375-1500 <i>m/z</i>	Minimum Intensity Req.	5e4
MS¹ Resolution	120,000 @ 200 <i>m/z</i>	Dynamic Exclusion	60.0 s
MS¹ AGC Target	4e5	MS² resolution	30,000 @ 200 <i>m/z</i>
MS¹ Maximum IT	50 ms		

Supplementary Table 2. Chromatography and MS instrument acquisition settings for DIA

Sample Volume	5 μ L, Microliter Pickup	MS² Acquisition	Data independent, Profile
Stationary Phase	PicoChip; C ₁₈ 75 μ m \times 10.5 cm	MS² Fragmentation	HCD
LC Solvent A	100% H ₂ O, 0.1% formic acid	MS² Detection	Orbitrap
LC Solvent B	80% ACN, 0.1% formic acid	MS² scan isolation windows	400-600 <i>m/z</i> by 20 <i>m/z</i> windows 600-1000 <i>m/z</i> by 40 <i>m/z</i> windows
Gradient Ramp	6-36% B	MS² scan range	120-1200 <i>m/z</i>
Duration	95 minutes		
Flow Rate	300 nL/min		
Mass Spectrometer	Thermo Orbitrap Fusion Lumos	MS² resolution	30,000 @ 200 <i>m/z</i>
Spray Voltage	2.0 kV	MS² AGC Target	1e5
In-Source CID	0.0 eV	MS² Maximum IT	100 ms
MS¹ Scan Range	375-1500 <i>m/z</i>	Normalized Collision Energy	30
MS¹ Resolution	120,000 @ 200 <i>m/z</i>	Max Cycle Time	3s
MS¹ AGC Target	4e5		
MS¹ Maximum IT	50 ms		

Supplementary Table 3. Chromatography and MS instrument acquisition settings for PRM

Sample Volume	20 μ L, full-loop Injection	MS² Detection	Orbitrap
Stationary Phase	Thermo Acclaim PepMap C ₁₈ 75 μ m \times 25 cm	MS² m/z range	120-1200 m/z
LC Solvent A	100% H ₂ O, 0.1% formic acid	Isolation Window	1.6 m/z
LC Solvent B	80% ACN, 0.1% formic acid	MS² AGC Target	5e4
Gradient Ramp Duration	2-28% B in 52 minutes	MS² Maximum IT	54 ms
Flow Rate	28-40% B in 7 minutes 300 nL/min		
Mass Spectrometer	Thermo Orbitrap Fusion Lumos	Normalized Collision Energy	Variable
Spray Voltage	2.0 kV	MS² resolution	30,000 @ 200 m/z
In-Source CID	0.0 eV	MS² Detection	Orbitrap
MS¹ Scan Range	325-1500 m/z	MS² m/z range	120-1200 m/z
MS¹ Resolution	120,000 @ 200 m/z	Isolation Window	1.6 m/z
MS¹ AGC Target	4e5		
MS¹ Maximum IT	50 ms		

Supplementary Table 4. DDA search parameters

Platform	ProteomeDiscoverer 2.2	Quantitation	Precursor Ions Quantifier, Peak Area
Search Algorithms	SequestHT	Normalization	Total Peptide Amount
Validation	Percolator Peptide Validator Protein FDR Validator	Scaling	On All Average (to value of 100)
Database	UniProt; Rabbit; created 10/03/2017 MaxQuant Contaminants Database; 10/03/2017	Ratio Calculation	Summed Abundance Based
Digest	Trypsin (full) 2 Missed Cleavages Allowed	Hypothesis Test	ANOVA (Individual Proteins)
Precursor mass tolerance	10 ppm	Target FDR (Strict) for PSMs:	0.01
Fragment mass tolerance	0.02 Da	Target FDR (Relaxed) for PSMs:	0.05
Static Modifications	Carbamidomethyl (C)	Target FDR (Strict) for Peptides:	0.01
Dynamic Modifications	Oxidation (M), Acetylation (protein N-terminus)	Target FDR (Relaxed) for Peptides:	0.05