

Contribution ID: 12 Contribution code: **Tu-I\_1**

Type: **Oral**

## Top-Down Proteomics with FTMS: 1993-2025

*Tuesday, August 26, 2025 9:00 AM (40 minutes)*

Since the early 1990s, FTMS has transformed biomolecular mass spectrometry, but its role in proteomics has been dominated by bottom-up (peptide-based) strategies. Top-down proteomics instead analyzes intact proteins, directly revealing proteoforms (the molecular variants arising from genetic variation, splicing, and post-translational modifications). By capturing the complete biochemical state of proteins, proteoforms provide a more direct link between genotype and phenotype.

FTMS is uniquely suited to this challenge, with unmatched resolution, mass accuracy, and fragmentation capabilities. Advances in ion statistics and single-ion detection now enable routine measurement and sequencing of low-abundance proteoforms and complex mixtures of proteoforms. Building on this, we developed Proteoform Imaging Mass Spectrometry (PiMS), and more recently single-cell PiMS (scPiMS), achieving >20-fold increases in throughput and direct proteoform detection at single-cell resolution.

This talk will trace the evolution of top-down proteomics with FTMS from its beginnings in 1993 to its current state.

**Author:** KELLEHER, Neil (Northwestern University)

**Presenter:** KELLEHER, Neil (Northwestern University)

**Session Classification:** Tuesday

**Track Classification:** FTMS and High Resolution Mass Spectrometry