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“Novel strategies for characterizing proteoforms: from targeted to omics analysis”

The research of the Fornelli lab focuses on the study of the proteins present in an organism, or proteomics, using high resolution mass spectrometry. Traditionally, proteomics is carried out by enzymatically digesting the original proteins into short peptides, which are easier to analyze – a process similar to the “shotgun” approach normally used in genomics. This methodology, known as bottom-up proteomics, fails to reconstruct the original complexity of a proteome, as the correlation between different sources of variation – e.g., genetic, such as single nucleotide polymorphisms inducing a single amino acid change, or chemical, such as post-translational modifications – within a single gene product is lost and cannot be inferred starting from proteolytic peptides. Therefore, my research group will apply instead top-down proteomics, a novel approach based on the analysis of intact, undigested protein forms known as proteoforms. We will use top-down proteomics to study the specific modification patterns of proteoforms differentially localized in various sub-cellular compartments, or how different proteoforms derived from the same gene can distinguish between healthy and aberrant phenotypes.