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Highlights of Analytical Sciences in Switzerland

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A Complete Mass-spectrometric Map of a Eukaryotic Proteome

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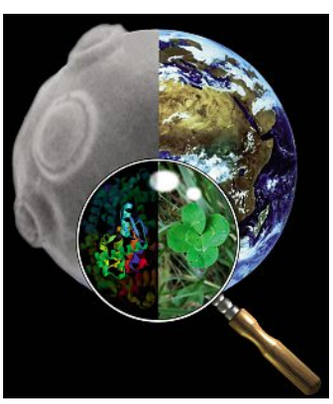
The ability to quantify any protein or set of proteins of interest is an essential task in the life sciences. In terms of total mass, proteins are the second most abundant molecules in human cells, second only to water, and are crucial effectors and regulators of virtually all cellular processes. A eukaryotic cell contains more than 5,000 different proteins, which span a broad range of abundances, and thereby challenge current analytical techniques that aim to reliably measure proteins of interest. Measuring proteins is a crucial requirement in biomedicine, as they can change their abundance in response to stimuli such as an infection or during disease progression (*e.g.* as in cancer). Quantifying proteins is also extremely important in the biological sciences to understand basic cellular processes since proteins directly or indirectly supervise all reactions occurring in cells.



A proteome map enables the extraction of mass-spectrometric coordinates for proteins of interest. The sensitivity of the developed SRM assays enables the reliable detection of low-abundance proteins in yeast (~50 copies/cell), a challenge of dynamic range analogous to finding a four-leaf clover from outer space.

In the analytical sciences, complete gold-standard reference maps or datasets describing the properties of the compounds under study (*e.g.* libraries for the spectroscopic properties of molecules) are commonly used to reliably probe any sample for the presence of the molecule(s) of interest. Attempts to generate such maps for a proteome, the ensemble of all proteins contained in a given organism, have so far failed to reach complete coverage.

To generate a complete (97%) reference map for the proteome of *S. cerevisiae*, a model eukaryotic organism commonly used in biological research, a strategy based on high-throughput peptide synthesis and mass spectrometry (MS) was used. Two versions of this MS map were generated, one supporting discovery experiments and the other hypothesis-driven (targeted) proteomic measurements based on selected reaction monitoring (SRM) assays. As a proof of principle, high coverage of the protein abundance range (~50 – 1E6 copies/cell) was achieved in total cell lysates using SRM assays. The MS map was later coupled to the complete genomic information available for *S. cerevisiae* in a quantitative trait locus (QTL) analysis to unravel the complex relationships that exist between genes and protein abundances in yeast.

This mass-spectrometric proteome map constitutes the first complete set of quantitative proteomic assays for more than 6,000 proteins and can be used to support most contemporary proteomic studies in the model eukaryote, yeast. The same approach can be applied to the human proteome.

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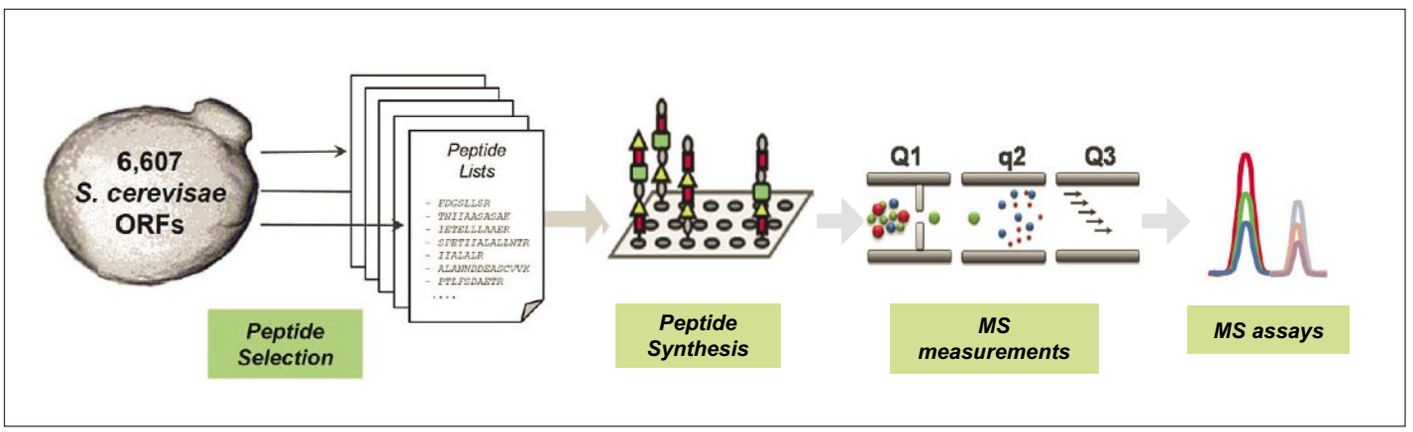

Schematic representation of the workflow used to create a reference mass-spectrometric map of the yeast proteome.

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