

INVITED LECTURE H13

Mapping the sub-cellular location of organelles and complexes

Kathryn S. Lilley

Cambridge Centre for Proteomics, Department of Biochemistry, University of Cambridge, UK

Cells are organized functionally and spatially into sub-cellular compartments. Changes in sub-cellular localization of proteins are involved in regulation of interactions, stability and activity, and thus the study of global changes in protein localization provides useful insights into cellular functions.

Assignment of proteins to many sub-cellular compartments is challenging as they cannot be purified to homogeneity. Proteins from the same organelle however, co-sediment and hence exhibit similar distributions in a density gradient. Sub-cellular localization can therefore be assessed by comparing distributions of unknown proteins to those of known organelle markers. To enable this process, robust quantitative proteomics methods need to be applied to accurately quantify distributions of proteins within density gradients.

We have developed LOPIT (localization of organelle proteins by isotope tagging), a high-throughput proteomics technique enabling protein localization to sub-cellular organelles. In this approach, organelles are partially separated by density gradient centrifugation and protein distribution patterns quantified using differential stable isotope labeling.

We have applied LOPIT technique to different biological systems and have assigned hundreds of proteins to different sub-cellular locations. More recently we have extended LOPIT to dynamically map protein redistribution upon a given perturbation as well as mapping the sub-cellular location of members of protein complexes.

References:

1. Dunkley TP *et al* , *Proc Natl Acad Sci* 103(17):6518-23.
2. Sadowski PG. *Proteomics*. 8(19):3991-4011