Editorial for "Advances in Biological Mass Spectrometry and Proteomics"

Article

Accepted Version

Editorial for “Advances in Biological Mass Spectrometry and Proteomics”

Biological mass spectrometry has been a key tool in deciphering the post-genomic molecular complexity of life. Together with its applications in proteomics it has pushed the bioanalytical limits further in order to satisfy the ever increasing demand for greater sensitivity, accuracy and throughput. Although proteomics had to undergo a period of disappointing progress after its initial ‘hype and hope’ phase, it is difficult to ignore the fact that it is the proteins which are the crucial task force and response units of biological organisms, and thus advances in protein analysis will be an essential part of learning more about their mode of (inter)action. However, many beginners’ mistakes have been made in proteomics and it has become clear that just more and faster is often not the right analytical strategy if the important aspects of accuracy, precision and validity are not considered.

Thus, it is timely that after a period of six years another special issue on mass spectrometry and proteomics is now published in *Methods*. It can be seen that both the progression to more thoughtful approaches in analyzing proteins and the development of improved methods, increasingly towards the rather difficult subjects of low-abundant proteins and protein interactions, are becoming well established in the proteomic researcher’s mindset. It is also evident that in addition to protein identification, accurate quantification is now of prime concern, something that has often been ignored despite its fundamental importance. Finally, six years is sufficient time for new instrumentation, techniques and concepts to emerge.

This issue starts with some key ideas and thoughts on quantification in proteomics [Brownridge and Beynon] followed by three articles applying different quantification approaches to the analysis of the serum proteome and phosphoproteome, for which optimal fractionation (enrichment) and dynamic range are pivotal as low-abundant proteins are the target [Sinclair and Timms; Montoya et al.; Dephoure and Gygi]. The next contribution provides a review discussing the various steps in deciding upon an analytical strategy for quantitative protein-protein interaction (PPI) analysis by mass spectrometry and includes an example protocol for quantitative PPI analysis using SILAC and mass spectrometry [Paul et al.]. This is followed by two contributions addressing the specific purification of membrane proteins and protein-binding partners, respectively [Mathias et al.; Rees and Lilley]. These and the subsequent articles are less concerned about quantification than about new methods and technologies for the identification and characterisation of proteins, often under conditions that – due to the subject protein(s), the cellular environment, or the lack of pre-analytical data (e.g. from protein databases) – are challenging and typically demand novel tools of analysis. Here, the first article addresses a topic that has been on the proteomic agenda for some time, single-cell analysis [Koroleva and Cramer]. It is shown that current proteomics tools are well capable of detecting cell-specific protein sets from single-cell samples. The emerging concept of peptide identification by searching MS/MS spectral libraries is described next and compared to MS/MS data searching using sequence databases, critically evaluating its advantages and drawbacks [Lam and Aebersold]. Following this article two emerging issues that require *de novo* gene and structure annotation are addressed. As next-generation sequencers facilitate the sequencing of an increasing number of new genomes, tools that improve gene annotation and enable function prediction of novel gene products also need to be established. Proteogenomics in combination with *in silico* structure prediction using proteomic data is certainly one avenue that could

effectively fill this wide gap in knowledge with respect to the expression of unknown gene products [Bindschedler et al.]. Finally, the last two articles focus on a technique that has recently entered the proteomics arena, ion mobility. While ion mobility has been around for some time it was only in the last five years that the technology matured to the point of providing sufficient performance for proteomic analyses and its availability through commercial instrumentation. The first of these two articles describes the hyphenation of ion mobility with MALDI mass spectrometry imaging, another techniques that has undergone an enormous development in proteomics in the last five years [Cole et al.], while the second article provides a review of ion mobility for peptide analysis [Harvey et al.].

As can be seen from the variety of topics covered by this issue, proteomics is an active and flourishing research field and well aware of the challenges ahead – from the fundamental aspects of quantification and accuracy to the challenges of the hidden proteomes and the proteomes of newly sequenced organisms. Clearly, biological mass spectrometry and proteomics still have a long way to go and likewise have the capacity to contribute enormously to the life sciences. Whether there will be real alternatives to biological mass spectrometry providing equally high sensitivity, fast analysis and analytical versatility remains to be seen. In any case, proteomics will remain essential in understanding the molecular processes of cells and organisms, and biological mass spectrometry will certainly play a crucial role in this endeavour for the foreseeable future.