Proteomics
Proteomics and Systems Biology
www.proteomics-journal.com

Spatial Proteomics: A Gateway to Understanding Cell Biology

Georg H. H. Borner

The term "Proteome" is commonly applied to describe the complete complement of proteins present in a given cell type, tissue, or body fluid. Over the last decade, the advent of powerful mass spectrometric approaches has enabled us to define proteomes experimentally with ever-increasing depth. Today it is possible to determine not only the identity of thousands of proteins from nanogram quantities of input material, but also to obtain their accurate and precise quantification and post-translational modification status.[1] Nevertheless, the proteome has yet another, less readily charted dimension: the spatial organization of proteins within cells. Subcellular localization critically affects protein function, since compartments partition cells into environments with distinct molecular compositions (proteins, lipids, nucleotides, metabolites) and chemical milieus (pH, redox potential, ion concentrations). Cells exploit this to regulate protein function, by carefully controlling protein subcellular localization. To capture this dimension, "spatial proteomics" evolved, initially from efforts to determine the proteomes of major organelles. The field has come a long way since; dramatic advances in imaging have revealed that cells have many compartments, membrane-bound and membrane-less, as well as many discrete sub-organellar localizations, domains, and assemblies that need to be accounted for.[2–4] Furthermore, around 50% of proteins are found in multiple subcellular localizations, and their preferred distributions can vary both within a cell population and between different cell types.[2] Linked to this variability are modulated activities or even entirely independent "moonlighting" functions of differentially localized proteins. The spatial proteome is complex.

There are two main experimental approaches to spatial proteomics: high-throughput imaging to visualize all proteins within a cell or within a compartment of interest; and quantitative mass spectrometry, to identify subcellular protein networks by organellar profiling or interactomics (see refs. [5, 6] for recent reviews). Defining the spatial proteome and its dynamics is a challenging task; in return, it offers a rich resource for understanding cell biological phenomena. Most cellular processes involve changes in protein subcellular localization, ranging in scale from individual protein translocations, to transient local assemblies of protein machinery, and whole organellar rearrangements. Prominent examples include events during regulated secretion, autophagy, apoptosis, signaling, mitosis, and many more. Global capture of protein subcellular localization changes upon perturbation identifies proteins involved in the studied process,[7,8] and puts them into spatial context.[9] With sufficient temporal resolution, the sequence of relocalization events may also be delineated.[10] Detailed pictures of cellular process may thus be inferred. Furthermore, many pathological processes upset subcellular organization, and spatial proteomics can be used as a sensitive diagnostic readout.[11] Last but not least, over 150 human disorders are caused by impaired intracellular protein transport;[12] mapping the underlying protein mislocalization events will not only provide a better understanding of the disease mechanisms, but also afford insights into fundamental cell biology.[13,14]

In this Special Issue, several pioneers of spatial proteomics discuss recent findings and key concepts that drive the field. An emerging consensus is the complementary nature of mass spectrometric and imaging approaches, which promises exciting synergies for future explorations of the spatial proteome.

Contributors

Imaging-Based Spatial Proteomics

Emma Lundberg—Spatial Characterization of the Human Centrosome Proteome Opens Up New Horizons for a Small but Versatile Organelle.[15]

Ralf Jungmann—DNA-Barcoded Fluorescence Microscopy for Spatial Omics.[16]

Ron Heeren—MS Imaging-Guided Microproteomics for Spatial Omics on a Single Instrument.[17]

Mass Spectrometric Organellar Profiling

Matthias Mann—The Origins of Organellar Mapping by Protein Correlation Profiling.[18]

Kathryn Lilley—Moving Profiling Spatial Proteomics Beyond Discrete Classification.[19]

Conflict of Interest

The author declares no conflict of interest.

Dr. G. H. H. Borner
Department of Proteomics and Signal Transduction
Max Planck Institute of Biochemistry
Martinsried 82152, Germany
E-mail: borner@biochem.mpg.de

The ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/pmic.201900328

DOI: 10.1002/pmic.201900328

[1] F. Hosp, M. Mann, *Neuron* **2017**, *96*, 558.
[2] P. J. Thul, L. Akesson, M. Wiking, D. Mahdessian, A. Geladaki, H. Ait Blal, T. Alm, A. Asplund, L. Bjork, L. M. Breckels, A. Backstrom, F. Danielsson, L. Fagerberg, J. Fall, L. Gatto, C. Gnann, S. Hober, M. Hjelmare, F. Johansson, S. Lee, C. Lindskog, J. Mulder, C. M. Mulvey, P. Nilsson, P. Oksvold, J. Rockberg, R. Schutten, J. M. Schwenk, A. Sivertsson, E. Sjostedt, M. Skogs, C. Stadler, D. P. Sullivan, H. Tegel, C. Winsnes, C. Zhang, M. Zwahlen, A. Mardinoglu, F. Ponten,

K. von Feilitzen, K. S. Lilley, M. Uhlen, E. Lundberg, *Science* **2017**, *356*, eaal3321.
[3] S. Boeynaems, S. Alberti, N. L. Fawzi, T. Mittag, M. Polymenidou, F. Rousseau, J. Schymkowitz, J. Shorter, B. Wolozin, L. Van Den Bosch, P. Tompa, M. Fuxreiter, *Trends Cell Biol.* **2018**, *28*, 420.
[4] T. Schlichthaerle, M. T. Strauss, F. Schueder, A. Auer, B. Nijmeijer, M. Kueblbeck, V. J. Sabinina, J. V. Thevathasan, J. Ries, J. Ellenberg, R. Jungmann, *Angew. Chem., Int. Ed. Engl.* **2019**, *58*, 13004.
[5] E. Lundberg, G. H. H. Borner, *Nat. Rev. Mol. Cell Biol.* **2019**, *20*, 285.
[6] G. H. H Borner, *Mol. Cell. Proteomics* **2020**, *19*, 1076.
[7] J. J. H. Shin, O. M. Crook, A. Borgeaud, J. Cattin-Ortolá, S. Y. Peak-Chew, J. Chadwick, K. S. Lilley, S Munro, *bioRxiv* **2019**, 841965.
[8] P. Kozik, M. Gros, D. N. Itzhak, L. Joannas, S. Heurtebise-Chretien, P. A. Krawczyk, P. Rodriguez-Silvestre, A. Alloatti, J. G. Magalhaes, E. Del Nery, G. H. H. Borner, S. Amigorena, *Cell Rep.* **2020**, *32*, 107905.
[9] D. N. Itzhak, S. Tyanova, J. Cox, G. H. Borner, *Elife* **2016**, *5*, e16950.
[10] Y. Cai, M. J. Hossain, J. K. Heriche, A. Z. Politi, N. Walther, B. Koch, M. Wachsmuth, B. Nijmeijer, M. Kueblbeck, M. Martinic-Kavur, R. Ladurner, S. Alexander, J. M. Peters, J. Ellenberg, *Nature* **2018**, *561*, 411.
[11] N. Krahmer, B. Najafi, F. Schueder, F. Quagliarini, M. Steger, S. Seitz, R. Kasper, F. Salinas, J. Cox, N. H. Uhlenhaut, T. C. Walther, R. Jungmann, A. Zeigerer, G. H. H. Borner, M. Mann, *Dev. Cell* **2018**, *47*, 205.
[12] R. Yarwood, J. Hellicar, P. G. Woodman, M. Lowe, *Dis. Model. Mech.* **2020**, *13*, dmm043448.
[13] A. K. Davies, D. N. Itzhak, J. R. Edgar, T. L. Archuleta, J. Hirst, L. P. Jackson, M. S. Robinson, G. H. H. Borner, *Nat. Commun.* **2018**, *9*, 3958.
[14] A. K. Davies, M. Ziegler, H. Jumo, W. A. Saber, D. Ebrahimi-Fakhari, G. H. H. Borner, *bioRxiv* **2020**, 353995.
[15] F. Danielsson, D. Mahdessian, U. Axelsson, D. Sullivan, M. Uhlén, J. S. Andersen, P. J. Thul, E. Lundberg, *Proteomics* **2020**, *20*, 1900361.
[16] F. Schueder, E. M. Unterauer, M. Ganji, R. Jungmann, *Proteomics* **2020**, *20*, 1900368.
[17] F. Dewez, J. Oejten, C. Henkel, R. Hebeler, H. Neuweger, E. De Pauw, R. M. A. Heeren, B. Balluff, *Proteomics* **2020**, *20*, 1900369.
[18] M. Mann, *Proteomics* **2020**, *20*, 1900330.
[19] O. M. Crook, T. Smith, M. Elzek, K. S. Lilley, *Proteomics* **2020**, *20*, 1900392.