Journal Club No. 785 Jan. 30, 2018

トップダウンプロテオミックスでタンパク質のコンプレックスを解析する

室井　誠

MS を使ったタンパク質を解析する方法にはボトムアッププロテオミクスとトップダウンプロテオミクスに分けられる。ボトムアッププロテオミクスではタンパク質をプロテアーゼで分解してフラグメントを詳細に解析するが、トップダウンプロテオミクスではタンパク質をまるのまま解析する手法である。いまだ、サンプルの量が多量に必要なこと、また、サイズにも制約があるが、トップダウンプロテオミクスでコンプレックスの化学量論的解析やその中に含まれるタンパク質の翻訳後修飾の解析もできるようになってきた。最新の技術を紹介する。

紹介論文

Top-down characterization of endogenous protein complexes with native proteomics

Owen S Skinner[1], Nicole A Haverland[1], Luca Fornelli[1,2], Rafael D Melani[1], Luis H F Do Vale[1–3], Henrique S Seckler[1], Peter F Doubleday[4], Luis F Schachner[1], Kristina Srzentić[1,2], Neil L Kelleher[1,2,4*] and Philip D Compton[1,2,4]*

([1]Department of Chemistry, Northwestern University, Evanston, Illinois, USA. [2]Proteomics Center of Excellence, Northwestern University, Evanston, Illinois, USA. 3Brazilian Center for Protein Research, University of Brasilia, Brasilia, Federal District, Brazil. 4Department of Molecular Biosciences, Northwestern University, Evanston, Illinois, USA. *e-mail: n-kelleher@northwestern.edu or philip-compton@northwestern.edu)

Nature Chemical Biology (2018) **14**, 36–41

要旨

Protein complexes exhibit great diversity in protein membership, post-translational modifications and noncovalent cofactors, enabling them to function as the actuators of many important biological processes. The exposition of these molecular features using current methods lacks either throughput or molecular specificity, ultimately limiting the use of protein complexes as direct analytical targets in a wide range of applications. Here, we apply native proteomics, enabled by a multistage tandem MS approach, to characterize 125 intact endogenous complexes and 217 distinct proteoforms derived from mouse heart and human cancer cell lines in discovery mode. The native conditions preserved soluble protein–protein interactions, high-stoichiometry noncovalent cofactors, covalent modifications to cysteines, and, remarkably, superoxide ligands bound to the metal cofactor of superoxide dismutase 2. These data enable precise compositional analysis of protein complexes as they exist in the cell and demonstrate a new approach that uses MS as a bridge to structural biology.