

Capillary electrophoresis for top-down proteomics of proteoforms and their complexes

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Abstract

The demand for analytical tools that are sufficiently robust for analyzing complex protein samples is steadily increasing, especially for top-down proteomics. Capillary zone electrophoresis coupled to mass spectrometry (CZE-MS) can analyze intact proteins from complex samples in native and denatured modes. Using native CZE-MS, we created a workflow that preserves non-covalent interactions for detection and top-down fragmentation of intact nucleosomes, named nCZE-Nuc-MS. On the other hand, denatured CZE-MS can also be used for top-down proteomics analysis. We coupled CZE and nano LC-MS to create a workflow capable of analyzing primary serous ovarian cancer samples obtained with laser microdissection (LMD). A similar workflow was also used to analyze 5 solid human tissues and increase the number of proteoforms identified per sample. The complete knowledge of proteoform structure and properties is fundamental to deciphering basic and translational research functions. Therefore, CZE and top-down proteomics are powerful new technologies that can be used to reveal human biology's molecular complexity.