

CAPILLARY ELECTROPHORESIS-MASS SPECTROMETRY FOR TOP-DOWN PROTEOMICS. **Liangliang Sun**, Department of Chemistry, Michigan State University, 578 S Shaw Lane, East Lansing, MI 48824, USA. (lsun@chemistry.msu.edu)

Capillary electrophoresis-mass spectrometry (CE-MS) has been recognized as a promising analytical tool for top-down characterization of proteoforms since 1980s. We recently showed several cases of applying advanced CE-MS techniques to the delineation of proteoforms. First, we performed the first TDP study of a pair of isogenic human nonmetastatic and metastatic colorectal cancer (CRC) cell lines (SW480 and SW620) using CE-MS/MS.[1] We identified 23,622 proteoforms of over 2000 genes from the two cell lines, representing nearly fivefold improvement in the number of proteoform identifications compared to previous TDP datasets of human cancer cells. We revealed substantial transformation of CRC cells in proteoforms after metastasis. Second, we developed a CE-ion mobility spectrometry (IMS)-MS/MS technique for online multi-dimensional separation of proteoforms for the first time and showed that the technique could substantially improve the identification of large proteoforms (>30 kDa) in complex samples.[2] Third, we applied CE-MS-based TDP to characterize nanoparticle protein corona in a proteoform-specific manner for the first time to advance nanomedicine.[3] Lastly, we developed native CE-MS technique to probe the endogenous protein complexes in complex biological samples with the detection of up to 400 kDa protein complexes from an *E. coli* cell lysate.[4]

[1] McCool EN, Xu T, Chen W, Beller NC, Nolan SM, Hummon AB, Liu X, Sun L. *Sci Adv.* 2022, 8(51):eabq6348.

[2] Xu T, Wang Q, Wang Q, Sun L. *Anal Chem.* 2023, 95(25):9497-9504.

[3] Sadeghi SA, Akbar Ashkarran A, Mahmoudi M, Sun L. *bioRxiv*, <https://doi.org/10.1101/2024.03.22.586273>.

[4] Wang Q, Wang Q, Qi Z, Moeller W, Wysocki VH, Sun L. *bioRxiv*, <https://doi.org/10.1101/2024.04.24.590970>.