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Increased sensitivity in characterization of proteomes and post-translational modifications in limited samples using CESI-MS

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Informative proteomic profiling of limited samples (e.g., blood-derived isolates, rare cells) to the level of thousands of proteins identified and quantified and especially, characterization of post-translational modifications (PTMs) of such specimens, has been a major challenge. Alterations of proteomes, glycomes, phosphoproteomes, and acetylomes may be associated with a number of pathologies, including immune and oncological diseases, as well as other biological phenomena. To overcome the challenges associated with the analysis of limited biological samples, we developed highly sensitive methods using capillary zone electrophoresis coupled to mass spectrometry (CZE-MS) via the CESI interface. One of the developed CZE-MS techniques for profiling of N-glycans released from human blood-derived isolates resulted in the improved detection sensitivity by ~100-fold in comparison to conventional conditions and allowed the analysis using injected sample amounts equivalent to <500 nL of blood. The optimized CZE conditions increased the resolution ~7-fold in the separation of closely-related and isobaric glycans. N-glycan profiling of OCI-AML5 cancer cells from an injected amount equivalent to ~35 cells demonstrated qualitative and quantitative differences between cells exposed to cytokine treatments used to alter activation and differentiation states of the cells. CZE-MS-based proteomic profiling of ~8 ng of lysed and digested U937 lymphocytes digest (corresponding to ~40 cells) routinely yielded identification of >1,500 protein groups. The impact of CZE-MS interfacing techniques and advantages over LC-MS methods will be discussed.