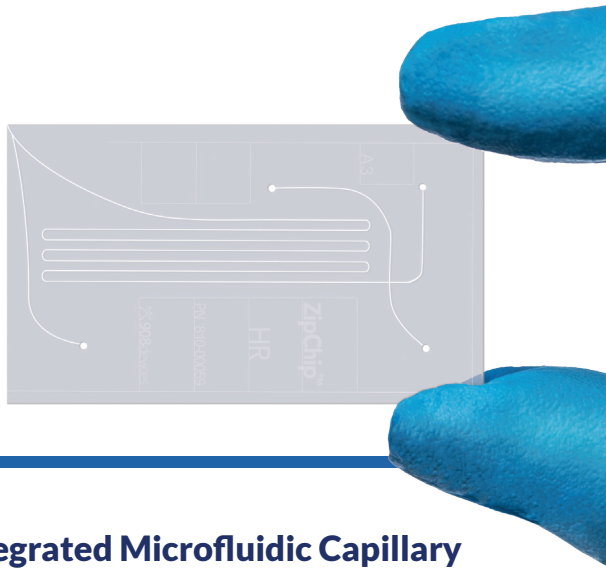
JOURNAL ARTICLE

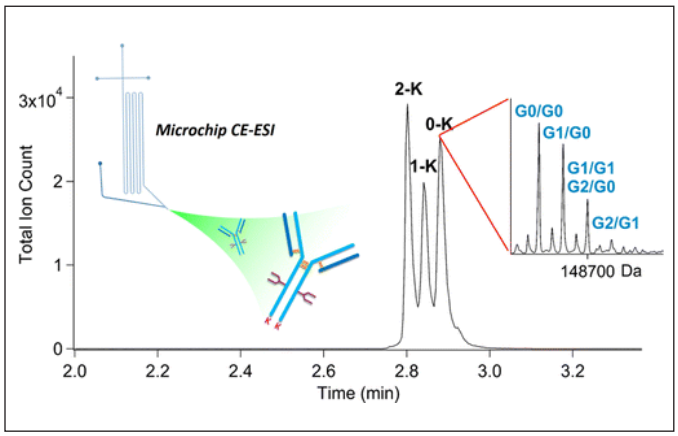
Integrated Microfluidic Capillary Electrophoresis-Electrospray Ionization Devices with Online MS Detection for the Separation and Characterization of Intact Monoclonal Antibody Variants

Published Journal Articles on Microfluidic ZipChip CE-ESI-MS
J.M. Ramsey Group at the University of North Carolina, Chapel Hill, NC



(2) Redman, E. A.; Batz, N. G.; Mellors, J. S.; Ramsey, J. M. Integrated Microfluidic Capillary Electrophoresis-Electrospray Ionization Devices with Online MS Detection for the Separation and Characterization of Intact Monoclonal Antibody Variants. *Anal. Chem.* 2015, *86*, 3493–3500

ABSTRACT: Here, we demonstrate an integrated microfluidic capillary electrophoresis-electrospray ionization (CE-ESI) device for the separation of intact monoclonal antibody charge variants with online mass spectrometric (MS) identification. The need for dynamic coating and zwitterionic background electrolyte (BGE) additives has been eliminated by utilizing surface chemistry within the device channels to control analyte adsorption and electroosmotic flow (EOF) while maintaining separation effciency. The effectiveness of this strategy was illustrated with the separation of charge variants of Infliximab. Three major species corresponding to C-terminal lysine variants were separated with an average resolution of 0.80 and identified by mass difference. In addition to the lysine variants, masses were determined for minor acidic and basic species. The separation of these variants prior to MS analysis facilitated the identification of glycosylation patterns for each of the variants. The general applicability of this method was demonstrated by analyzing two additional monoclonal antibody species: an IgG2 antibody and an IgG1 antibody conjugate. The IgG2 proved to have similar modifications to Infliximab with lower relative abundances of the lysine variants. Analysis of the IgG1 drug conjugate further exemplified the advantages of MS detection; differences in the extent of antibody conjugation were detectable despite limited CE resolution. The CE-ESI-MS methodology described here is a rapid and generic strategy for the separation of intact mAb charge variants and facilitates the identification of variants through MS detection.



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