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Applications of DNA Capillary Electrophoresis in Molecular Cancer Diagnostics: Above and Beyond Sanger Sequencing

Marek Minarik[1,2]

[1]*Elphogene, s.r.o., Prague, Czech Republic, mminarik@email.com*
[2]*Department of Analytical Chemistry, Faculty of Sciences, Charles University, Prague, Czech Republic*

Summary

In the late 1990s the Sanger sequencing of the tumor DNA became a dominant application for capillary electrophoresis, especially after the importance of acquired somatic DNA mutations for cancer initiation and progression was revealed by the work of Bert Vogelstein's group at Johns Hopkins University [1]. However, a decay from the tremendous expansion of the technology started when other non-CE sequencing approaches (termed next-generation sequencing (NGS) or massive-parallel sequencing (MPS)) arrived in the late 2000s [2].

Nowadays, despite to the slow retreat from the DNA sequencing arena, DNA separation by CE still has significant utility in molecular cancer diagnosis. The dominating applications are based on PCR fragment analysis, where capillary CE as well as Chip-CE platforms are widely used. Perhaps the most routine application (sometimes accepted as a golden standard) is the CE detection of microsatellite instability (MSI) with the purpose of (i) revealing hereditary cancer predisposition caused by inherited infidelity of the DNA repair system (Lynch syndrome) and (ii) assessing the tumor mutator phenotype (tumor mutation burden), a major biomarker for prediction of immunotherapy response [3]. In addition to MSI, there is a family of CE-based DNA mutation detection techniques. Using precise temperature settings during the run, they rely on subtle differences in electromigration properties to resolve wildtype (non-mutated) and tumor (mutated) DNA fragments [4].

The last area of CE usage in cancer diagnostics is related to modern sequencing. From the early days, most NGS technologies relied on DNA library preparation workflows that use CE for profiling of the library before putting it onto the sequencer. Although not a separation per se, CE-based NGS library quality control is essential for obtaining quality data and limiting wasteful sequencing runs.

References

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