

Title: Cancer Subtyping by CE-Based Technology for Analysis of microRNA Signatures (TAmiRS): from Proof of Principle to a Practical Clinical Technology

Abstract: Cancer is a heterogeneous disease; within each cancer type there are multiple subtypes that exhibit different levels of malignancy and require different management strategies. MicroRNAs

(miRNAs) are very promising molecular markers for discovering and diagnosing cancer subtypes as every cancer subtype is presumably associated with a unique quantitative miRNA signature. Despite all efforts to use miRNA signatures for discovery and diagnosis of cancer subtypes, there is not even a single miRNA signature validated and approved by FDA for clinical use. Discovery and validation of miRNA signatures require a miRNA analysis technology that is (i) quantitative, (ii) highly-sensitive, (iii) rugged, (iv) capable of simultaneously analyzing multiple miRNAs, (v) cost-effective, and (vi) rapid. Such a technology does not exist and this is arguably the major challenge on our way to practical use of miRNA signatures in cancer medicine.

In the last 5 years, we dedicated a significant effort to the development of a Technology for Analysis of miRNA Signatures (TAmiRS), which satisfies the 6 requirements and can facilitate the discovery, validation, and diagnosis of cancer subtypes. The instrumental platform for TAmiRS is CE with LIF detection and the methodological platform is our other invention: CE-based direct quantitative analysis of multiple miRNAs. In this lecture, I will explain the concept of TAmiRS [1], and demonstrate its gradual transition from the proof of principle to a practical clinical technology [2-4]. This transition involves solving a number of fundamental and technical problems

including: (i) ability to quantitate low-abundance miRNAs, (ii) reducing analysis time to less than 1 h, (iii) increasing the number of analyzed miRNAs to 5, (iv) distinguishing miRNAs different by a single nucleotide, and (v) validation with quantitative PCR, which is a current gold standard. Remaining challenges will be finally identified and approaches to their solution discussed.

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