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RESEARCH ARTICLE

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Combined miRNA and SERS urine liquid biopsy for the point-of-care diagnosis and molecular stratification of bladder cancer

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Abstract

Background: Bladder cancer (BC) has the highest per-patient cost of all cancer types. Hence, we aim to develop a non-invasive, point-of-care tool for the diagnostic and molecular stratification of patients with BC based on combined microRNAs (miRNAs) and surface-enhanced Raman spectroscopy (SERS) profiling of urine.

Methods: Next-generation sequencing of the whole miRNome and SERS profiling were performed on urine samples collected from 15 patients with BC and 16 control subjects (CTRLs). A retrospective cohort (BC = 66 and CTRL = 50) and RT-qPCR were used to confirm the selected differently expressed miRNAs. Diagnostic accuracy was assessed using machine learning algorithms (logistic regression, naïve Bayes, and random forest), which were trained to discriminate between BC and CTRL, using as input either miRNAs, SERS, or both. The molecular stratification of BC based on miRNA and SERS profiling was performed to discriminate between high-grade and low-grade tumors and between luminal and basal types.

Results: Combining SERS data with three differentially expressed miRNAs (miR-34a-5p, miR-205-3p, miR-210-3p) yielded an Area Under the Curve (AUC) of 0.92 ± 0.06 in discriminating between BC and CTRL, an accuracy which was superior either to miRNAs (AUC = 0.84 ± 0.03) or SERS data (AUC = 0.84 ± 0.05) individually. When evaluating the classification accuracy for luminal and basal BC, the combination of miRNAs and SERS profiling averaged an AUC of 0.95 ± 0.03 across the three machine learning algorithms, again better than miRNA (AUC = 0.89 ± 0.04) or SERS (AUC = 0.92 ± 0.05) individually, although SERS alone performed better in terms of classification accuracy.

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