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DNA Methylation Markers Detected in Liquid Biopsy Specimens Differentiate Pituitary Neuroendocrine Tumors from Other Sellar and CNS Diseases

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Background: DNA methylation abnormalities are pervasive in pituitary neuroendocrine tumors (PitNETs). The feasibility to detect these molecular alterations in circulating cell-free DNA (cfDNA) has been reported for several central nervous system tumors but not across PitNETs.

Hypothesis: PitNET-specific methylation signatures detected in liquid biopsy specimens differentiate PitNETs from other sellar diseases.

Method: We profiled the cfDNA methylome (EPIC array) of 44 serum and 34 plasma liquid biopsy (LB) specimens from patients with PitNETs and other CNS (craniopharyngiomas, other pituitary diseases, gliomas, meningiomas) or nontumor conditions, grouped as non-PitNET.

Results: Our results indicated that, despite quantitative and qualitative differences between serum and plasma cfDNA composition, both sources of LB showed that patients with PitNETs presented a distinct methylome landscape compared to non-PitNETs. In addition, LB methylome captured epigenetic features reported in PitNET tissue. Using LB-derived PitNETs-specific signatures as input into a machine-learning algorithm, we generated a score that distinguished PitNETs from other pituitary and CNS diseases with high accuracy in an independent set.

Conclusions: Our results underpin the potential application of a methylation-based LB as a noninvasive approach to identify clinically relevant epigenetic markers to diagnose and potentially impact the management of patients with PitNETs.

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