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Liquid Biopsy Metabolomic Profiling of Neuroendocrine Cancer Patients

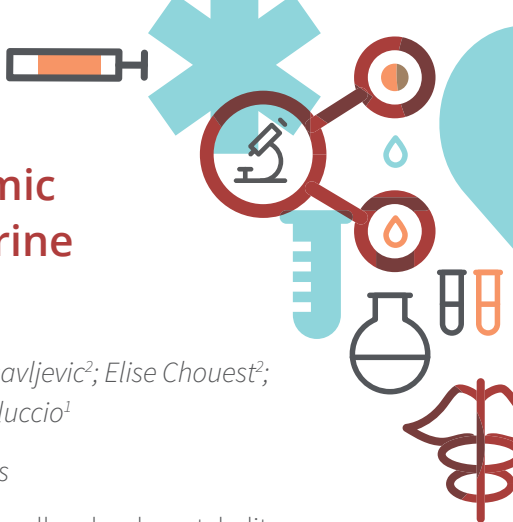
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BACKGROUND: Metabolomics is the study of small molecule metabolites in biofluids and tissue. These small molecules are exquisitely sensitive to different biological states and therefore represent a promising approach to identify changes in biopathology over time and over the course of treatment. Investigating metabolomic signatures associated with NET will highlight unrecognized metabolic aberrancies that contribute to symptoms and performance status. The expectation is that this technique will also identify biomarkers of a response to treatment that will guide the timing and frequency of intervention.

METHODS: Serum samples collected from patients with confirmed neuroendocrine cancer were subjected to high performance liquid chromatography (HPLC) coupled with dual mass spectroscopy to quantitate 309 metabolites spanning multiple metabolomic pathways.

Results: Principal component analysis (PCA) was used to identify key metabolomics differences among NET patients. Living related donor serum was used as controls. Elevated alpha-ketoglutaric acid, tyrosine, and lactate, alongside depressed arginine and adenosine was characteristic of NET patients. Small-bowel primaries displayed elevated cortisol, pyruvate, and glutamine as compared to pancreatic primaries. The three groups were easily distinguished when plotted against eigenvectors 1 and 2 of the PCA. The identified metabolites were used to construct a linear prediction model by partial least squares-discriminant analysis, which identified NET status and primary location with 100% accuracy in jackknife cross-validation.



CONCLUSION: Metabolic aberrancies associated with function identified pathways that likely explain differences in symptoms between pancreatic and intestinal NET. Further Investigation into the metabolic consequences linked to each defect will allow us to better personalize treatment of symptoms.