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Metabolic Signatures in Blood for Early Detection of Glioma

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Akademisk avhandling

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Abstract

Glioma is the most common malignant primary brain tumor among adults and is often detected at a late stage of the disease. Treatment often include surgical resection of the tumor followed by combined radiochemotherapy. Yet, the prognosis given to glioma patients is often poor, with the median survival for the most common and aggressive glioma subtype glioblastoma being only 15 months. Due to limited treatment options and poor prognosis, an earlier detection of gliomas could potentially improve the outcome and quality of life for patients. Intriguingly, previous studies have shown that the glioma development may actually start several years before clinical diagnosis is given. In this thesis, a search for altered metabolite levels in blood related to glioma development was conducted, to find biomarkers that show potential to be targets in an early detection tool of glioma and to improve the understanding of the mechanism of the disease.

In **Paper I**, pre-diagnostic metabolite levels in blood were analyzed from glioma cases that had been collected several years before they were diagnosed together with matched controls. A panel of 20 metabolites were discovered that could predict glioma development up to 8 years before diagnosis in the discovery cohort and up to 2 years before diagnosis in the validation cohort. The altered metabolites showed indication of an altered energy metabolism and imbalanced redox homeostasis.

In **Paper II**, the altered metabolite levels within 8 years to glioma diagnosis related to an altered energy metabolism was replicated. Longitudinal blood metabolite analysis from years before diagnosis to the time of surgery revealed an altered amino acid metabolism. A set of metabolites with diagnostic potential at surgery and years before diagnosis was presented.

In **Paper III**, a discovery analysis was conducted on altered metabolite levels at the time of glioma surgery compared to years before diagnosis. A large set of metabolites was significantly altered at surgery, with several metabolic pathways altered including the amino acid metabolism. The pre-diagnostic 20-metabolite panel discovered in **Paper I** was revisited and their levels was analyzed at surgery, were 8 metabolites showed further significantly elevated levels at surgery than years before, indicating early detection and diagnostic potential for those metabolites.

Keywords

Glioma, glioblastoma, liquid biopsy, blood, metabolites, early detection, surgery, N-lactoyl-amino-acids, N-lactoyl-phenylalanine

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