Achieving Precision Diagnostics for Cancer using Circulating Biomarkers

av

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Abstract

Each year, nearly 20 million people are diagnosed with cancer worldwide, and over 9.7 million die of the disease. Tumor tissue sampling is essential for diagnosis and treatment, but it poses risks and may not fully represent the tumor due to heterogeneity. Additionally, limited sample sizes can hinder comprehensive testing, affecting precision diagnostics.

Circulating biomarkers offer a non-invasive alternative, as they are easily obtained from body fluids, and reflect tumor activity. These biomarkers include DNA, RNA, vesicles, proteins, metabolites, and whole tumor cells. They hold potential for screening, diagnosis, treatment selection, monitoring, and prognosis. Currently, circulating cell-free DNA (cfDNA) is the only clinically used biomarker for treatment selection and monitoring in cases without available tumor tissue.

The main aim of this thesis was to explore the clinical use of circulating biomarkers in cancer care. Paper I investigated liquid biopsy for variant analysis in lung cancer, finding that plasma cfDNA could predict overall survival and reliably detect variants in advanced cases. Paper II explored glycosaminoglycans (GAGs) as biomarkers for lung cancer, revealing that combining cfDNA and GAG profiles improved diagnostic sensitivity. Paper III developed sensitive assays to detect HPV in plasma, correlating ctHPV-DNA levels with tumor characteristics in oropharyngeal cancer. Paper IV examined methylation patterns in cfDNA, identifying regions that could distinguish cancer from other diseases using machine learning.

Overall, this thesis demonstrates the clinical potential of circulating biomarkers for cancer diagnosis, prognosis, and monitoring, emphasizing the value of multimodal approaches in enhancing detection accuracy.

Keywords: circulating biomarkers, cfDNA, ctDNA, ctHPV-DNA, lung cancer, Next Generation Sequencing, oropharyngeal cancer, severe nonspecific symptoms of cancer, ultrasensitive detection