Characterizing the role of tumor growth dynamics and proliferation in ctDNA release

Master's Thesis (30 ECTS)

Laura Andersen | 201706497

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Supervisor: Nicolai Juul Birkbak

Associate Professor

Department of Molecular Medicine

Aarhus University

Abstract

Circulating tumor DNA (ctDNA) has become a promising non-invasive biomarker for early detection of cancer throughout all stages of the disease. Studies of ctDNA have focused on its clinical application resulting in great improvement of methods to identify patients with minimal residual disease and high risk of recurrence, as well as surveillance of adjuvant chemotherapy. Limited studies have investigated the biological origin of ctDNA and a better understanding of the cancer-type specific variability in ctDNA release might aid the clinical implementation of ctDNA as a biomarker. Therefore, this thesis aims to investigate the cancer type specific association between ctDNA release and molecular as well as clinical characteristics. By mathematical modelling of ctDNA in lung squamous cell carcinoma (LUSC) and lung adenocarcinoma (LUAD) we found that increased tumor burden, higher cell turnover rate and high expression of proliferative pathways were positively associated with the amount of ctDNA shedding. Furthermore, by characterizing transcriptomic profiles of colon and lung cancer we found that high proliferation distinguishes ctDNA shedding cancers from non-shedding cancers. We show that this pattern potentially scales across multiple cancer types.

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