

Press release

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Basic information

Name: Trine Block Mattesen Email: trinemattesen@clin.au.dk Phone: +45 24663351

Department of: Clinical Medicine

Main supervisor: Claus Lindbjerg Andersen

Title of dissertation: Molecular subtyping for improved prognostication of colorectal cancer

Date for defence: 24/3-2020 at (time of day): 13:00 Place: Grundet COVID-19 vil forsvaret blive afholdt som et web-forsvar via Zoom. Kontakt venligst Trine Block Mattesen for online deltagelse.

Press release (Danish)

Inddeling af tarmkræft i undertyper for at forbedre forudsigelsen af prognose

Tarmkræft er den tredje hyppigste kræftsygdom på verdensplan og den anden hyppigste årsag til kræft-relaterede dødsfald. Tarmkræft behandles først og fremmest med operation og ved fremskreden sygdom tilbydes patienterne kemoterapi efter operation. Desværre oplever 30-40% af dem, som er blevet opereret for tarmkræft, tilbagefald af sygdommen. Dette tyder på at tarmkræft er en heterogen sygdom, hvor både prognose og den mest optimale behandlingsstrategi kan være svær at forudsige. Ny molekylær forskning viser, at tarmkræft kan inddeles i kræftundertyper med forskellig biologi og prognose. Inddeling af sygdommen i undertyper har vist sig at være lovende i forhold til bedre at kunne forudsige prognose samt den mest optimale behandlingsstrategi.

Et nyt ph.d.-projekt fra Aarhus Universitet, Health har haft til formål at inddele tarmkræft i undertyper, etablere en klinisk anvendelig metode til dette formål, samt anvende disse strategier til at forbedre forudsigelsen af tarmkræftpatienters prognose. Projektet har vist, at en udvidet strategi, som kombinerer inddeling af tarmkræft i undertyper med undertype-specifikke markører kan forbedre forudsigelsen af patient prognose sammenlignet med de retningslinjer, der anvendes i klinisk praksis. Yderligere er der blevet etableret en DNA-baseret metode, som hjælper den kliniske anvendelse af disse lovende resultater på vej, da metoden er forenelig med det tumor vævs materiale, som indsamles i klinikken. Projektet er gennemført af Trine Block Mattesen, der forsvare det d. 24/3-2020.

Ph.d forsvaret er offentligt og finder sted den 24/3-2020 kl. 13. Grundet COVID-19 vil forsvaret blive udført som et web forsvar via Zoom. For online deltagelse i forsvaret kontakt venligst Ph.d.-studerende Trine Block Mattesen, e-mail: trinemattesen@clin.au.dk, tlf. +4524663351. Titlen på projektet er "Molecular subtyping for improved prognostication of colorectal cancer".

Bedømmelsesudvalg:

Professor Eigil Kjeldsen, MD, DMSc
Department of Clinical Medicine, Department of Haematology,
Aarhus University Hospital, Denmark

Associate Professor Anita Sveen, MSc, PhD
Institute of Clinical Medicine, Faculty of Medicine,
University of Oslo, Norway

Professor Henrik Ditzel, MD, PhD, DMSc
Department of Cancer and Inflammation Research Unit, Institute of Molecular Medicine,
University of Southern Denmark, Denmark

Press release (English)

Molecular subtyping for improved prognostication of colorectal cancer

Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of cancer-related deaths. The standard treatment is radical surgery and adjuvant therapy when patients present with pathologically advanced tumors. Unfortunately, 30-40% of CRC patients experience disease recurrence. This reflects that CRC is a heterogeneous disease and that pathologically similar tumors differ in treatment response and patient survival. Recently, several studies have confirmed that pathologically similar tumors are indeed very different at the molecular level and that molecular subtyping of tumors shows promise to improve both prognostication and treatment strategies of the disease.

The overall aim of this PhD project was to perform molecular subtyping of CRC, facilitate clinical exploitation of CRC subtyping, and ultimately improve patient prognostication using these strategies.

We have established an extended framework for molecular stratification of CRC that combines stratification of fresh-frozen CRC cohorts into homogeneous transcriptional subtypes with subtype-specific prognostic biomarkers. This strategy allowed identification of subtype-specific prognostic biomarkers that provided prognostic information beyond and independent of subtypes alone and clinical prognostic guidelines. Furthermore, we have developed a method called MethCORR, which infers gene expression from DNA methylation. We used the inferred gene expression to perform uniform molecular subtyping, characterization, and subtype-specific prognostication of both fresh-frozen and clinically collected formal-fixed paraffin-embedded (FFPE) tissue samples. These results are promising as they allow transcriptional analysis of clinical FFPE tissue samples, which normally can be challenging due to impaired RNA quality. Additionally, we have shown that the method can be used to infer gene expression in cancer types other than CRC.

In summary, the PhD project demonstrate that subtype-specific biomarkers improve prediction of prognosis superior to subtypes alone and that the clinical exploitation of CRC subtyping may be helped along by shifting to a DNA-based approach that is more compatible with clinically collected FFPE tissue samples.

The project was carried out by Trine Block Mattesen, who is defending her dissertation on 24/3-2020.

The defence is public and takes place on 24/3-2020 at 13:00. The defence will be held as a web defence (due to COVID-19) via Zoom. Please contact Trine Block Mattesen to gain access to the defense. Email: trinemattesen@clin.au.dk, Phone +45 24663351.

Assessment committee:

Professor Eigil Kjeldsen, MD, DMSc
Department of Clinical Medicine, Department of Haematology,
Aarhus University Hospital, Denmark

Associate Professor Anita Sveen, MSc, PhD
Institute of Clinical Medicine, Faculty of Medicine,
University of Oslo, Norway

Professor Henrik Ditzel, MD, PhD, DMSc
Department of Cancer and Inflammation Research Unit, Institute of Molecular Medicine,
University of Southern Denmark, Denmark

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