AARHUS UNIVERSITY

Press release

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Basic information

Name: Iben Lyskjær Email: iben.lyskjar@clin.au.dk Phone: +45 51330153

Department of: Clinical Medicine

Main supervisor: Claus Lindbjerg Andersen

Title of dissertation: Evaluation of molecular markers of treatment response in metastatic colorectal cancer

Date for defence: 5/11-2018 at (time of day): 12.30 Place: Science Center Skejby, Brendstrupgaardsvej 21, 8200 Aarhus N

Press release (Danish)

Evaluering af molekylære markører til bestemmelse af behandlingsrespons i metastatisk kolorektal cancer.

Behandling af metastatisk kolorektal cancer (mCRC) er udfordrende og nær halvdelen af alle mCRC patienter responderer ikke på den første linje af behandling. For at forbedre behandlingen af mCRC har dette Ph.d-projekt undersøgt potentielle biomarkører som kan være med til at afgøre hvilken behandling den enkelte patient vil have mest gavn af, samt fortælle hvorvidt den anvendte behandling virker. Ph.d.-projektet, som er gennemført på Aarhus Universitet, Health, af Iben Lyskjær bliver forsvaret d. 5. november 2018.
Iben Lyskjær har i sin Ph.d. vist at molekylet, miR-625-3p, giver resistens til oxaliplatin ved at hindre oxaliplatin-associeret celledød gennem hæmning af protein signalvejen (MAP2K6-p38).
Derudover har hun vist hvordan tumor afledte DNA fragmenter (såkaldt cirkulerende tumor DNA, ctDNA) i blodet på mCRC patienter kan bruges som markør for resistens til irinotecan-baseret behandling.
Ydermere har Iben Lyskjær demonstreret at det er muligt at udføre targeteret next generation duplex-sekventering (DS) på celle-frit DNA (cfDNA) isoleret fra plasmaet af mCRC-patienter. DS er en teknik der har meget lav fejl-rate. Dvs. at teknikken er i stand til at finde få kræftDNA molekyler i en stor baggrund af normal DNA molekyler. Det er netop situationen i blodet hos kræft patienter. Årsagen til den lave fejl rate ligger i at metoden mærker begge strenge af de originale dobbeltstrengede cfDNA-molekyler med en unik sekvens. Således kan sekventerings reads spores tilbage til hver enkelt streng i det dobbeltstrengede cfDNA- molekyle og derved bruges til at adskille sande mutationer fra PCR- og sekventerings-fejl.

Forsvaret af Ph.d.-projektet er offentligt og finder sted den 05/11 kl. 12.30 i Auditoriet, nederste etage i Science Center Skejby, Brendstrupgaardsvej 21, 8200 Aarhus N. Titlen på projektet er "Evaluation of molecular markers of treatment response in metastatic colorectal cancer". Yderligere oplysninger: Ph.d.-studerende Iben Lyskjær, e-mail: iben.lyskjar@clin.au.dk, tlf. +45 5133 0153.

Bedømmelsesudvalg:
Associate Professor, PhD, M.Sc. Lise Lotte Hansen (chairman) Institute of Biomedicine, Aarhus University, Denmark
Professor, MD, PhD Klaus Pantel, Director of Institute of Tumor Biology, Center for Experimental Medicine, Hamburg, Germany
Associate Professor, PhD, M.Sc. Jan Stenvang, Department of Drug Design and Pharmacology, University of Copenhagen, Denmark.

Press release (English)

Evaluation of molecular markers of treatment response in metastatic colorectal cancer

Treatment of metastatic colorectal cancer (mCRC) is challenging and almost half of all mCRC patients do not respond to first-line treatment. In order to improve the treatment of mCRC this PhD-project has investigated potential biomarkers that can help determine which treatment the individual patient will benefit the most from, as well as to tell whether the treatment applied is effective. The project was carried out by Iben Lyskjær, who is defending her dissertation on 5th of November 2018.

Iben Lyskjær has in her PhD study investigated potential biomarkers for response to treatment in mCRC. She has shown how miR-625-3p induces resistance to oxaliplatin by preventing oxaliplatin-associated cell death through inhibition of the MAP2K6-p38 signalling pathway.
Additionally, she has described how tumour-derived DNA fragments (so-called circulating tumour DNA, ctDNA) in the blood of mCRC patients can be used as a marker of resistance to irinotecan-based treatment.
Furthermore, Iben Lyskjær has demonstrated how targeted next generation duplex sequencing (DS) can be applied to detect tumour DNA in cell-free DNA (cfDNA) obtained from the plasma of CRC patients. DS is a technique that enables mutational calling with high-confidence by uniquely tagging both strands of original double-stranded cfDNA molecules. Thus, sequencing reads can be traced back to each single strand of the double-stranded cfDNA molecule, and consequently separate true mutations from PCR and sequencing errors.

The defence is public and takes place on 05/11-2018 at 12.30 in the Auditorium, ground floor at Science Center Skejby, Brendstrupgaardsvej 21, 8200 Aarhus N. The title of the project is "Evaluation of molecular markers of treatment response in metastatic colorectal cancer". For more information, please contact PhD student Iben Lyskjær, email: iben.lyskjar@clin.au.dk, Phone +45 5133 0153.

Assessment committee:
Associate Professor, PhD, M.Sc. Lise Lotte Hansen (chairman) Institute of Biomedicine, Aarhus University, Denmark
Professor, MD, PhD Klaus Pantel, Director of Institute of Tumor Biology, Center for Experimental Medicine, Hamburg, Germany
Associate Professor, PhD, M.Sc. Jan Stenvang, Department of Drug Design and Pharmacology, University of Copenhagen, Denmark

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