AARHUS UNIVERSITY

# Press release

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## Basic information

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Department of: Clinical Medicine

Main supervisor: Claus Lindbjerg Andersen, M.Sc., Ph.D., Professor, Department of Molecular Medicine, Aarhus University Hospital

Title of dissertation: Clinical implications of analyzing circulating tumor DNA in colorectal cancer patients

Date for defence: Tuesday the 13th of June 2017 at (time of day): 13.00 Place: Ground Floor Auditorium, Department of Molecular Medicine, Aarhus University Hospital, Skejby - Brendstrupgaardsvej 21, 8200 Aarhus N

Press release (Danish)

## En blodprøve kan afsløre høj risiko for tilbagefald i patienter behandlet for tarmkræft.

Et nyt ph.d.-projekt fra Aarhus Universitet, Health viser, at tilstedeværelsen af tumor DNA i en blodprøve taget kort tid efter den primære behandling af tarmkræft kan identificere patienter med høj risiko for tilbagefald af sygdommen. Desuden er den kliniske anvendelse af en sådan blodprøve i relation til opfølgning af patienter med tarmkræft blevet belyst. Projektet er gennemført af MSc. Lone Vedel Schøler, der forsvarer sin afhandling d. 13/6 - 2017

Tarmkræft er en hyppig kræftform, der hvert år rammer ca. 4000 danskere. To ud af tre patienter der diagnosticeres med tarmkræft opereres med henblik på helbredelse, men alligevel får ca. 30% af dem tilbagefald af sygdommen, hvilket betyder, at de må have rest-sygdom efter operationen, feks. i form af mikrometastaser så små, at de ikke kan ses på scanninger. Patienternes risiko for tilbagefald kan mindskes med kemoterapi. Men da kemoterapi er forbundet med store gener og bivirkninger, så kan behandling kun retfærdiggøres, hvis risikoen for tilbagefald er høj. Riskoen vurderes i dag på basis af undersøgelser af den fjernede tumor. Desværre er denne tilgang suboptimal, bl.a. fordi markørerne kun er løseligt forbundet tilbagefald, men også fordi tilgangen ikke tager højde for, at en stor andel af patienterne rent faktisk blev helbredt af operationen. Det betyder, at mange helbredte patienter behandles unødigt med kemoterapi og desværre, at en del patienter med rest-sygdom, men uden risikomarkører, ikke behandles. For patienter med rest-sygdom efter operationen, er det afgørende at rest-sygdommen opdages så tidligt muligt, idet det øger chancerne for behandling med sigte på helbredelse.

Formålet med det netop afsluttede ph.d.-studie var, at udvikle en ny blodbaseret metode til at identificere rest-sygdom, og at vise at man derved ville få mulighed for at sikre patienterne forbedret behandling.

I løbet af studiet er det lykkedes at udvikle en metode, der kan detektere tumor DNA i blodprøver, og det blev vist at tumorer i tarmen frigiver små mængder tumor DNA til blodet. Tumor DNA kan opfattes som tumorens genetiske fingeraftryk og opdages det i en blodprøve er det et udtryk for, at patienten har kræftceller i kroppen. Studiet har vist, at der kan findes tumor DNA i blodprøver udtaget efter operationen hos patienter der får tilbagefald, men ikke hos helbredte patienter. Tumor DNA er en radikal anderledes markør, end de markører der anvendes i dag, idet tilstedeværelsen i blod er et direkte bevis på, at der er rest-sygdom i kroppen og ikke blot en risiko-markør. Dermed er det muligt at rette behandling mod netop de patienter, der har brug for den. Studiet viser også, at måling af tumor-DNA i blodet kan anvendes til overvågning. På en række patienter blev der efter operationen regelmæssigt udtaget blodprøver, og tumor DNA analysen opdagede sygdomstilbagefald

gennemsnitligt 9.8 måneder tidligere end standard overvågningsprogrammet, som er baseret på scanninger. Dermed er der skabt mulighed for tilbagefaldsbehandlingen kan iværksættes langt tidligere end i dag. Formodentlig tilstrækkelig tidligt til, at andelen af patienter der kan tilbydes helbredende behandling kan øges. Studiet viser også, at mængden af tumor DNA i blodet er tæt forbundet til patienternes tumorbyrde hvilket åbner mulighed for, at bruge metoden til at måle hvor effektiv en given kemobehandling virker. Med blodprøver er det således i princippet muligt at vurdere om den anvendte behandling, har den ønskede virkning, eller om lægerne skal overveje andre behandlinger.
Samlet set giver resultaterne fra dette Ph.d.-studie håb for, at behandlingen af tarmkræft patienter kan forbedres. F.eks. ved at de der har restsygdom efter operationen sikres behandling, mens de der bliver helbredt af operationen ikke udsættes for birkningerne af unødvendig kemoterapi. Sammen med muligheden for tidligere opdagelse af tilbagefald forventes det, at kunne medføre en forbedret overlevelse for patienter med tarmkræft.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 13/06-2017 kl. 13 i auditoriet i stue etagen ved Molekylær Medicinsk Afdeling, Aarhus Universitetshospital, Brendstrupgaardsvej 21, Aarhus N. Titlen på projektet er "Clinical implications of analyzing circulating tumor DNA in colorectal cancer patients". Yderligere oplysninger: Ph.d.-studerende Lone Vedel Schøler, e-mail: lonescholer@msn.com, tlf. 26168834.

Bedømmelsesudvalg:

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Press release (English)

## A blood sample can reveal high risk of relapse in patients with colorectal cancer

A new PhD project from Aarhus University, Health shows that the presence of tumor DNA in a blood sample drawn shortly after treatment of colorectal cancer identifies patients with a very high risk of having relapse of disease. In addition, the study has assessed different clinical applications of such blood test during follow-up of patients with colorectal cancer. The project was carried out by MSc. Lone Vedel Schøler, who is defending her dissertation on 13/6 - 2017.

Colorectal cancer is a frequent cancer form with ~4000 new cases in Denmark each year. Two out of three patients diagnosed with colorectal cancer undergo surgery with curative intent however, ~30% will experience relapse of disease. Accordingly, residual disease must remain after the initial surgery e.g. in the form of micro metastasis too small to be detected by imaging. The risk of relapse can be reduced by chemotherapeutic treatment however, this is related to serious adverse side effects and should only be given if the risk of relapse is sufficiently high. Currently, the risk of relapse is based on biomarker examinations of the resected primary tumor. However, this approach is suboptimal in part because these biomarkers are only correlated with relapse but also because this approach does not consider the fact that a large fraction of patients are actually cured by the initial surgery. Consequently, many patients cured by surgery alone are inappropriately treated with chemotherapy and unfortunately a fraction of patients actually having residual disease, but with tumors negative for the examined biomarkers, are not offered additional treatment. For patients with residual disease after the initial surgery, early detection of residual disease is essential because it increases the chance of providing relapse treatment with curative intent.

The aim of the recently completed PhD study was to develop a blood based method to identify residual disease in patients with colorectal cancer and to show that this could lead to improved treatment of patients.

During this PhD study a method has been developed, which enables detection of tumor specific DNA in blood samples and it has been shown that colorectal tumors release small amounts of DNA into the blood stream. Tumor DNA can be considered the genetic fingerprint of a tumor and its presence in a blood sample indicates that tumor cells are present in the patient. Tumor DNA is a fundamental different biomarker compared to currently used biomarkers because its presence in the blood is a direct proof that tumor cells are present and not just a risk marker of relapse. The study has shown that tumor DNA is detectable after removal of the primary tumor in patients having relapse of disease but not in patients cured by surgery alone. Consequently, by using tumor DNA as a marker of residual disease it becomes possible to direct treatment towards patients who actually needs it. The study also shows that the method also can be applied for monitoring. On a number of patients, serial blood samples were collected after the initial surgery and tumor DNA analyses detected relapse on average 9.8 months before the conventional follow-up program, which is based on imaging. This will allow initiation of relapse treatment much earlier than today, which expectedly will increase the fraction of patients receiving curative intended treatment. The study also shows that the level of tumor DNA in the blood correlates with tumor burden allowing the method to be used as a measure of efficacy of a given chemotherapeutic treatment. Accordingly, a blood sample can be used to evaluate to what extend the administered therapy is effective or if the clinicians should consider changing the treatment regimen. In conclusion, the results obtained from this PhD study indicate that it is possible to improve treatment of patients with colorectal cancer. E.g. by offering treatment to patients with residual disease and spare patients that was actually cured by the initial surgery, for the adverse side effect of unnecessary chemotherapeutic treatment. Together with earlier detection of relapse this will expectedly lead to improved survival of patients diagnosed with colorectal cancer.

The defence is public and takes place on 13/06-2017 at 13.00 in the ground floor auditorium at Department of Molecular Medicine, Aarhus University Hospital, Brendstrupgaardsvej 21, Aarhus N. The title of the project is "Clinical implications of analyzing circulating tumor DNA in colorectal cancer patients". For more information, please contact PhD student Lone Vedel Schøler, email: lonescholer@msn.com, Phone +45 26168834.

Assessment committee:

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