

## Press release

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### Basic information

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Department of: Clinical Medicine

Main supervisor: Hans Erik Bøtker

Title of dissertation: Mitochondrial modulation strategies to attenuate ischemia reperfusion injury in non-diabetic and diabetic individuals

Date for defence: 1<sup>st</sup> of February 2019 at (time of day): 14.00 Place: Cardiological conference room, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, Entrance F, DK-8200 Aarhus N

Press release (Danish)

Mitokondrielle moduleringsstrategier til at mindske iskæmi-reperfusionsskade hos ikke-diabetiske og diabetiske individer

I et nyt Ph.D.-projekt fra Aarhus Universitet, Health undersøges effekten af og mekanismerne bag nye behandlingsmetoder til at beskytte hjertet hvis det rammes af en blodprop. Projektet fokuserer på at beskytte hjertet ved at påvirke hjertecellernes stofskifte både i dyr og mennesker med og uden sukkersyge. Projektet er gennemført af Nichlas Riise Jespersen, som forsvare sin PhD-afhandling d. 1. februar 2019.

En blodprop i hjertet er en alvorlig tilstand, som kan medføre svær sygdom eller død. En blodprop i hjertet opstår pludseligt og forårsager iltmangel, som kan medføre celledød i store dele af hjertet og heraf følgende hjertepumpesvigt. Skaden kan forebygges ved at forberede hjertet til at tolerere en længere periode med iltmangel gennem forudgående korte perioder med iltmangel, som ikke i sig selv er skadelige. Denne behandling kaldes konditionering og er den mest effektive måde at reducere skader fra iltmangel på. Det er i midlertidigt vanskeligt at forbehandle hjertet med konditionering da en blodprop i hjertet oftest er uforudsigelig. For at bedre prognosen for patienter med blodprop i hjertet er det derfor nødvendigt at udvikle nye behandlingsstrategier til at reducere skaden.

I denne afhandling viser vi, at direkte påvirkning af cellestofskiftet kan beskytte hjertet mod skade. Studierne er udført i eksperimentelle modeller til at afklare mekanismerne bag hjertebeskyttelsen og senere overført til væv fra patienter for at bevise at behandlingen kan virke i mennesket. Ved forbigående at bremse cellestofskiftet med medicin påviste vi beskyttelse mod iltmangel i hjertet. Behandlingen var lige så effektiv som konditionering, men virkede gennem andre mekanismer. Beskyttelsen kunne også opnås i hjertevæv fra dyr med sukkersyge. Forsøgene i humant væv viste, at medicinen også virkede i væv fra patienter uden sukkersyge, men ikke i væv fra patienter med sukkersyge.

De samlede resultater fra denne Ph.D.-afhandling viser således, at det er muligt at opnå hjertebeskyttelse i forbindelse med iltmangel som følge af en blodprop i hjertet ved at påvirke cellestofskiftet. Dette kan medvirke til udviklingen af nye behandlingsstrategier af patienter med blodprop i hjertet. Der er imidlertid fortsat behov for at afklare, hvorfor behandlingen ikke ser ud til at være tilstrækkelig effektiv hos patienter med sukkersyge.

Forsvaret af Ph.D.-projektet er offentligt. Det holdes på engelsk og finder sted d. 1. februar 2019 kl. 14.00 i kardiologisk konference lokale, Aarhus Universitetshospital, Palle Juul-jensens Boulevard 99, Indgang F, DK-8200 Aarhus N. Titlen på projektet er "Mitochondrial modulation strategies to attenuate ischemia reperfusion injury in non-diabetic and diabetic individuals" .

For yderligere oplysninger kontaktes Ph.D.-studerende Nichlas Riise Jespersen, Kardiologisk afdeling og Institut for klinisk medicin, e-mail: n.riise.jespersen@clin.au.dk, tlf. 30254287, eller hovedvejleder, professor Hans Erik Bøtker, e-mail: Heb@dadlnet.dk.

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Press release (English)

Mitochondrial modulation strategies to attenuate ischemia reperfusion injury in non-diabetic and diabetic individuals

A new Ph.D. project from Aarhus University, Health examines the effects and mechanisms of new treatment strategies to reduce the damage from heart attacks. The project focuses on achievement of protection by modulating the metabolism of cells in both animals and humans with and without diabetes. The project was carried out by Nichlas Riise Jespersen, who is defending his PhD dissertation on the 1<sup>st</sup> of February , 2019.

Heart attack is a serious condition that often causes severe disease or death. Heart attacks are caused by blood clots in the coronary arteries which compromise the bloodflow, causing ischemia and subsequently cell death. Short periods of non-lethal ischemia prepare the heart against a prolonged period of ischemia seen during a heart attack. This treatment is called ischemic preconditioning and is the most effective way to reduce damage from ischemia. However, it is difficult to pre-treat the heart with ischemic preconditioning because heart attacks are most often unpredictable. To improve the prognosis of patients with a heart attack, new treatment strategies to reduce the damage need to be developed.

In this Ph.D. project we show that direct modulation of the cellular metabolism can protect the heart from damage. The studies were conducted in experimental models to clarify the mechanisms of protection and subsequently our findings were transferred to human tissue to clarify whether the treatment works in humans. We found that by transiently slowing the cellular metabolism with medication, the heart can be protected from injury. The treatment was as effective as ischemic preconditioning, but worked through other mechanisms. Furthermore, we found that protection in heart tissue from animals with diabetes can be achieved by treating them with the medication. Finally, we demonstrated that the treatment provides protection in tissue from patients without diabetes, but not in tissue from patients with diabetes mellitus.

The overall results of this Ph.D. thesis demonstrate that modulation of cellular metabolism can be used to achieve cardioprotection. This may contribute to the development of new treatment strategies for patients with an acute heart attack. However, further studies are needed to clarify why the treatment seems less efficient in patients with diabetes mellitus.

The defense is public and takes place on the 1<sup>st</sup> of February 2019 at 14:00 in Cardiological conference room, Aarhus University Hospital, Palle Juul-jensens Boulevard 99, Entrance F, DK-8200 Aarhus N.

The title of the project is "Mitochondrial modulation strategies to attenuate ischemia reperfusion injury in non-diabetic and diabetic individuals".

For more information, please contact PhD student Nichlas Riise Jespersen, Department of Cardiology and Institute of Clinical Medicine, email: [n.riise.jespersen@clin.au.dk](mailto:n.riise.jespersen@clin.au.dk), Phone +45 30254287 or main supervisor Professor Hans Erik Bøtker, e-mail: [heb@dadlnet.dk](mailto:heb@dadlnet.dk)

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