AARHUS UNIVERSITY

Media release

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Basic information

Name: Rasha Al-Saaidi Email: Rasha.Al-Saaidi@clin.au.dk Phone: 60130788

Department of: Clinical Medicine

Main supervisor: Peter Bross

Title of dissertation: LMNA mutations causing dilated cardiomyopathy: Molecular studies using patient fibroblasts and patient-specific induced pluripotent stem cells

Date for defence: 16/02/17 at (time of day): 13:00 Place: The auditorium in Building E, ground floor, Science Center Skejby, Brendstrupgårdsvej 21, 8200 Aarhus N.

Media release (Danish)

Ny molekylær viden gennem studier af humane bindevævsceller og inducerede pluripotente stamceller

Hjertemuskelsygdommen dilateret kardiomypati kan medføre svigt af hjertets pumpefunktion og alvorlige forstyrrelser af hjerterytmen. Sygdommen er ofte arvelig og forårsages blandt andet af mutationer i LMNA genet der koder for de intermediære filamentproteiner, lamin A og lamin C, udtrykt i hjertemuskulaturens celler. I et nyt ph.d.-projekt fra Aarhus Universitet, Health undersøgte ph.d. studerende Rasha Al-Saaidi forskellige LMNA mutationer for at belyse de molekylære sygdomsmekanismer. Rasha Al-Saaidi forsvarer sit ph.d.-projekt d. 16. februar. Dyrkede bindevævsceller (fibroblaster) fra patienterne blev analyseret ved forskellige metoder. Ph.d.-projektet viste en række interessante observationer blandet andet et ændret lamin A til lamin C-forhold hos patienterne trods forskellige mutationer. Disse nye fund demonstrerer at lamin A og lamin C påvirkes forskelligt af mutationerne. Endvidere tyder resultaterne på signifikante forskelle mellem lamin A og lamin C som hidtil har været overset.
Som et første skridt i retning af studier af kardiomyocytter med LMNA mutationer, genererede Rasha Al-Saaidi inducerede pluripotente stamceller (iPSC) afledt af patienters fibroblaster.
Tidligere forskning har vist at omprogrammering af fibroblaster til iPSC kræver ombygning af mitokondrier og metabolisk skift fra en oxidativ tilstand til en glycolytisk tilstand. I sit ph.d.- projekt undersøgte Rasha Al-Saaidi i samarbejde med anden afdeling den nukleare omprogrammerings effektivitet i forhold til mitokondriefunktion og aktivitet. Resultaterne viste, at normale humane fibroblaster med en lavere respiratorisk reservekapacitet i deres mitokondrier havde højere nuklear omprogrammerings effektivitet.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 16/02 kl. 13 i auditorium i bygning E, stueetagen, Science Center Skejby, Brendstrupgårdsvej 21, 8200 Aarhus N. Titlen på projektet er ” LMNA mutations causing dilated cardiomyopathy: Molecular studies using patient fibroblasts and patient-specific induced pluripotent stem cells”. Yderligere oplysninger: Ph.d.-studerende Rasha Al-Saaidi. E-mail: Rasha.Al-Saaidi@clin.au.dk. Tlf. 60130788.

Media release (English)

New molecular knowledge through studies in human fibroblasts and induced pluripotent stem cells

Dilated cardiomyopathy (DCM) is a disease of the heart muscle which can cause heart failure and serious heart rhythm disturbances. The disease is often inherited and is caused among others by mutations in the LMNA gene encoding the intermediate filament proteins, lamin A and lamin C,

expressed in cardiac muscle cells. In a new PhD project from Health, Aarhus University the PhD student Rasha Al-Saaidi investigated different LMNA mutations to shed light on the molecular disease mechanisms. Rasha Al-Saaidi will defend her dissertation on February 16th. Cultured fibroblasts from DCM patients carrying the mutations were analyzed by different methods. The PhD project showed several interesting observations including altered lamin A to lamin C ratio in patients despite different mutations. These new findings demonstrate that lamin A and lamin C are differentially affected by the mutations. Furthermore, the results suggest significant differences between lamin A and lamin C, which have been largely overlooked.
As a first step towards studies of cardiomyocytes with LMNA mutations, Rasha Al-Saaidi generated induced pluripotent stem cells (iPSCs) derived from patient fibroblasts.
Previous research has shown that reprogramming of fibroblasts into iPSCs requires remodeling of mitochondria and metabolic shift from an oxidative state to a glycolytic state. In her PhD project and in collaboration with another department, Rasha Al-Saaidi evaluated the nuclear reprogramming efficiency in relation to mitochondrial function and activity. The results showed that normal human fibroblasts with a lower mitochondrial respiratory reserve capacity had higher nuclear reprogramming efficiency

The defence is public and takes place on 16/02 at 13:00 in the auditorium in Building E, ground floor, Science Center Skejby, Brendstrupgårdsvej 21, 8200 Aarhus N. The title of the project is" LMNA mutations causing dilated cardiomyopathy: Molecular studies using patient fibroblasts and patient-specific induced pluripotent stem cells" . For more information, please contact PhD student Rasha Al-Saaidi , email: Rasha.Al-Saaidi@clin.au.dk, Phone +45 60130788.

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