Press release

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Basic information

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Department of: Clinical Medicine

Main supervisor: Lars Østergaard

Title of dissertation: Immunomodulation in diseases characterized by prominent inflammatory aspects

Date for defence: June 20th at (time of day): 14.00 Place: Aarhus Universitets Hosptial, Undervisningslokale 32-33, Indgang D3, Palle Juul-Jensen Blvd. 99, 8200 Aarhus N.

Press release (Danish)

Modulering af immunreponset i HIV og sygdomme drevet af cytokiner fra IL-1 familien.

Patienter med kroniske sygdomme såsom HIV, har en øget forekomst af følgesygdomme heriblandt åreforkalkning. En del af forklaringen på denne tidligere udvikling af følgesygdomme er den sygdoms-associerede betændelse (inflammation) der bl.a. resulterer i at immunsystemet ældes før tid (inflammaging). Således søges der efter mulige interventioner til at mindske denne betændelsesdrevne sygdomsudvikling. Dette kan både gøres ved at angribe sygdommen direkte, som i HIV-kur forskning, eller mere indirekte ved at hæmme de signaleringsproteiner der hjælper med at drive sygdommene. Disse forskellige interventionsmuligheder undersøges nærmere i et nyt ph.d.-projekt fra Aarhus Universitet, Health. Projektet er gennemført af Jesper Falkesgaard Højen, der forsvarer det d. 20/6-2019.

I dette projeket har vi undersøgt hvordan immunsystemet hos deltagere fra et klinisk HIV-eradiaktionsstudie (CLEAR studiet), reponderer på medicin (HDACi (panobinostat)) der påvirker HIV- og genreguleringen i kroppens celler. Tidligere resultater fra dette studie har allerede vist potentielt gavnlige effekter ift. at kunne påvirke den virus der gemmer sig i kroppen, men en mere dybdegående analyse af de øvrige effekter på immunsystemet har manglet. Vi fandt at både den medfødte såvel som den specifikke del af immunsystemet blev påvirket at medicinen, og at medicinen kunne sænke betændelsesniveauet i kroppen uden samtidig at hæmme vigtige signalstoffer der bruges af effektorcellerne når de skal angribe HIV. Således understøtter dette studie videre forskning i brugen af panobinostat til HIV-eradikationsbehandling, samtidig med at dets påvirkning af betændelsesniveauerne vil kunne undersøges nærmere i relation til den betændelsesdrevne udvikling af følgesygdomme hos HIV-patienter.
Projektet undersøgte ligeledes hvordan en specifik gruppe af signalstoffer (IL-1 familie cytokiner) regulerer udviklingen af betændelse på et mere basalt niveau. Denne gruppe af signalstoffer har vist sig at indtage en vigtig rolle i udviklingen af både hjertekarsygdomme og kræft, men også i sygdomme såsom psoriasis og asthma. Fokus har derfor været at undersøge effekterne af blokering af signalstoffernes receptorer, for på den måde at kunne optimere betændelsesbehandlingen. Resultaterne fra disse celle- og musestudier kan dermed bidrage med ny vigtig viden ift en ny terapeutisk tilgang til behandlingen af IL-1 familie drevne sygdomme.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 20/6 kl. 14 i undervisningslokale 32+33, Aarhus Universitets Hospital, Palle Juul-Jensens Blvd. 99, 8200 Aarhus N. Titlen på projektet er ”Immunomodulation in diseases characterized by prominent inflammatory aspects”. Yderligere oplysninger: Ph.d.-studerende Jesper Falkesgaard Højen, e-mail: jesperfh@clin.au.dk, tlf. 40459718.

Bedømmelsesudvalg:
Claus Johansen, Associate professor, Dept. of Clinical Medicine, Aarhus University, Aarhus, Denmark

AARHUS UNIVERSITY

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Press release (English)

Immunomodulation in HIV and diseases driven by the IL-1 family of cytokines

Patients with a chronic inflammatory disease such as HIV, have an increased risk of co-morbidities such as cardiovascular disease. Part of the explanation can be found in the increased level of inflammation, which results in premature-aging of the immune system (inflammaging). The aim is thus to find interventions that can reduce this inflammatory driven disease development. This can be done both by targeting the root of the problem as in HIV-cure research. Or by reducing the signaling molecules that helps drive the disease and development of co-morbidities. Both interventional strategies are investigated in the present PhD project. The project was carried out by Jesper Falkesgaard Højen, who is defending his dissertation on 20/6 2019.

In this project, we investigated how the immune system in participants from a clinical HIV-eradication study (CLEAR study), responded to medication (HDACi (panobinostat)) that alters virus- and gene expression. Previous results from the same trial have already established that this type of medication could have beneficial effects in the path towards a cure. However, a more comprehensive analsysis of the impact on the immune system has been lacking. We found that both the innate as well as the adaptive part of the immune system was impacted by the medication. And importantly, that the medication was able to reduce the level of inflammation without compromising the production of important signaling molecules used by immune effector cells when targeting HIV. These data thus supports further research in the use of panobinostat as a part of an HIV-cure. As well as establishing potential beneficial effects on the levels of inflammation with its known relation to the development of co-morbidities in HIV-infected patients.
This project also had a more basic inflammatory profile, investigating how an important group of signaling molecules (IL-1 family of cytokines) regulates inflammatation in various contexts. This group of molecules are known to be important both in the development of cardiovascular diseases and cancer. But also in diseases such as psoriasis and asthma where it drives disease progression. The aim has thus been to investigate the contribution of the shared signaling receptors in this family. Thus, aiming at optimizing anti-inflammatory interventions. The results from these cell- and mouse experiments thus bring new important knowledge to the field, and hints to a new interventional strategy in the treatment of IL-1 family driven diseases.

The defence is public and takes place on 20/6 at 14.00 in room 32-33, Aarhus University Hospital, Palle Juul-Jensens Blvd. 99, 8200 Aarhus N. The title of the project is "Immunomodulation in diseases characterized by prominent inflammatory aspects". For more information, please contact PhD student Jesper Falkesgaard Højen, email: jesperfh@clin.au.dk, Phone +45 40459718.

Assessment committee:
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