

## Press release

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### Basic information

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Main supervisor: Trine Hyrup Mogensen

Title of dissertation: "A novel innate immunodeficiency predisposing to severe varicella-zoster virus infection"

Date for defence: 17.12.2019 at (time of day): 13.00 pm Place: Eduard Biermann Auditorium (1252-204) Søauditorierne (Lake Side auditorium) Bartholins Allé 3, 8000 Aarhus C

Press release (Danish)  
Overskrift

"Identifikation af immundefekter associeret med varicella-zoster virus infektion i CNS"

Primær infektion med varicella-zoster virus (VZV) er årsag til den almindelige børnesygdom varicella (skoldkopper). VZV kan derudover reaktiveres senere i livet, hvilket kan forårsage herpes zoster (helvedesild). For størstedelen af alle individer er infektionen selvbegrænsende og med få symptomer, men hos et lille antal individer kan VZV-infektionen sprede sig til centralnervesystemet (CNS). Hos disse patienter kan der opstå alvorlige komplikationer såsom encephalitis, meningitis og vaskulitis. Dette studie har fokuseret på genetiske undersøgelser af sådanne patienter, med det formål at identificere mutationer, der kan prædisponere til alvorlig VZV-infektion i CNS. Projektet er udført af Madalina Carter-Timofto, der forsvare sin afhandling den 17.12.2019.

I samarbejde med internationale forskere og klinikere rekrutterede vi børn og voksne med dissemineret VZV-infektion, der involverede CNS. Vi identificerede forskellige mutationer i den immunologiske DNA-sensor, RNA-polymerase III (POL III), der potentielt kunne være årsag til patienternes alvorlige sygdomsforløb. Vi testede mutationerne funktionelt i patienternes immunceller og fandt, at defekter i POL III resulterede i et nedsat antiviralt immunrespons og efterfølgende øget VZV-replikation i patientceller sammenlignet med raske kontroller. Vi forsøgte desuden at belyse, hvordan POL III forhindrer viral reaktivering fra latens, ved at undersøge effekten af POL III-mutationer i en neuronal cellelinje. Dette translationelle studie har resulteret i ny indsigt i sygdomspatogenesen ved VZV-infektion, og kan hjælpe med at guide fremtidige strategier for diagnose, forebyggelse og behandling af patienter med VZV-infektion i CNS.

Forsvaret er offentligt og finder sted den 17.12.2019 kl. 13.00 på Aarhus Universitet, Eduard Biermann Auditoriet (1252-204) Søauditorierne, Bartholins Allé 3, 8000 Aarhus C.

Projektets titel er "Identifikation af immundefekter associeret med varicella-zoster virus infektion i CNS". For mere information, kontakt ph.d.-studerende Madalina Carter-Timofto, e-mail: [m.carter-timofto@biomed.au.dk](mailto:m.carter-timofto@biomed.au.dk), telefon +45 60552114.

Press release (English)

Headline:

"A novel innate immunodeficiency predisposing to severe varicella-zoster virus infection"

Varicella-zoster virus (VZV) causes the common childhood disease of varicella (or chicken pox) following primary infection, and can reactivate later on in life to cause shingles (herpes zoster). Whilst for the majority of individuals infection is self-limiting with few symptoms, in a small number of individuals, VZV infection may spread to the central nervous system (CNS). In these few cases, patients can suffer severe complications such as encephalitis, meningitis and vasculitis. The focus of this study has been carrying out genetic investigations of such patients, with the aim of identifying mutations that may predispose individuals to severe VZV infection. The project was carried out by Madalina Carter-Timofte, who is defending her dissertation on 17.12.2019.

In collaboration with international researchers and clinicians, we recruited both children and adults with disseminated VZV infection involving the CNS. We identified potential disease causing mutations in the immunological DNA sensor, RNA polymerase III (POL III), and functionally tested the mutations in patient immune cells. Here, we identified that defects in POL III confer an impaired antiviral immune response and subsequent increased VZV infection in patient cells, compared to healthy controls. Moreover, we aimed to try and elucidate the role of POL III in preventing viral reactivation, by studying the effects of POL III mutations in a neuronal cell line. This translational study has provided new insights into the disease pathogenesis of VZV infection that may help guide future strategies for diagnosis, prevention and treatment of patients with VZV infection in the CNS.

The defence is public and takes place on 17.12.2019 at 13.00 in Aarhus University, Eduard Biermann Auditorium (1252-204) Søauditorierne (Lake Side auditorium) Bartholins Allè 3, 8000 Aarhus C. The title of the project is "A novel innate immunodeficiency predisposing to severe varicella-zoster virus infection". For more information, please contact PhD student Madalina Carter-Timofte, email: [m.carter-timofte@biomed.au.dk](mailto:m.carter-timofte@biomed.au.dk), phone +45 60552114.

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