

Press release

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Basic information

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Department of: Clinical Medicine

Main supervisor: Martin Tolstrup

Title of dissertation: Rethinking ART: Preclinical evaluation of novel antiretroviral nanotherapeutics

Date for defence: 02.12.2019 at (time of day): 10 am Place: Merete Barker auditorium 1253-211
Søauditorierne, Bartholins Allé 3, 8000 Aarhus

Press release (Danish)

Nytænkning af ART: Preklinisk evaluering af nye antiretrovirale nano-terapeutika

Kombinations-antiretroviral behandling (cART) har ændret en hiv-diagnose fra en livstruende sygdom til en kronisk, men håndterbar infektion. Dog er denne hiv-behandling forbundet med dagligt indtag af piller og har visse udfordringer, for eksempel lav lægemiddelkoncentration i væv, såsom lymfeknuderne, der indeholder kronisk smittede celler. Et nyt ph.d.-projekt fra Aarhus Universitet, Health, har undersøgt nye nanoterapeutiske lægemidler, som skal tages mindre hyppigt og samtidig kan trænge ind i de hiv-smittede væv. Projektet er et samarbejde mellem Infektionssygdomme på Institut for Klinisk Medicin og Institut for Kemi på Aarhus Universitet. Projektet er gennemført af cand.scient. Anna Halling Folkmar Andersen, der forsvare det d. 2/12-2019

Afhandlingen er baseret på fem publikationer. I de tre første studier blev kombinationer af godkendte hiv-lægemidler (såsom lamivudine, zidovudine, og elvitegravir) bundet til forskellige polymer-rygrade undersøgt. Fælles for polymerene er en direkte eller indirekte binding til blod-proteinet albumin. Vi fandt en forlænget halveringstid og lokalisering i lymfeknuder efter indsprøjtning i mus under huden med de albumin-bindende polymerer i modsætning til de ikke-bindende polymerer. Samtidig viste kombinationsterapi med forskellige hiv-lægemidler en synergistisk effekt, når de blev leveret på en polymer-rygrad. Disse resultater gav anledning til at udvikle en musemodel for at undersøge anti-hiv effekterne af disse stoffer. I de sidste to studier blev denne model etableret, baseret på indsprøjtning af menneskelige stamceller i immundefekte mus, og dens respons til aktivering af det medfødte immunforsvar blev evalueret. Samtidig blev modellen undersøgt til brug som model for hiv-infektion til prækliniske tests af nye lægemidler. Samlet belyser dette ph.d.-projekt virkningen og potentielle udfordringer med langtidsvirkende polymer-baserede lægemidler mod hiv-infektion og in vivo undersøgelser heraf.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 02/12/2019 kl. 10.00 i Merete Barker Auditoriet (1253-211) Aarhus Universitet, Bartholins Allé, 8000 Aarhus C. Titlen på projektet er "Rethinking ART: Preclinical evaluation of novel antiretroviral nanotherapeutics". Yderligere oplysninger: Ph.d.-studerende Anna Halling Folkmar Andersen, e-mail: ahfa@clin.au.dk, tlf. +4528266946

Bedømmelsesudvalg:

Associate Professor Lene Niemann Nejsum - chairman of the committee and moderator of the defence, Institut for Klinisk Medicin, Palle Juul-Jensens, Boulevard 82, 8200 Aarhus N, Danmark

Associate Professor Alexander Ploss, 110 Thomas Laboratory, Department of Molecular Biology, Princeton University, USA

Associate Professor Joeri Aerts, Department of Pharmaceutical and Pharmacological Sciences, Vrije Universiteit Brussels, Laarbeeklaan 103, 1090 Jette, Belgium

Press release (English)

Rethinking ART: Preclinical evaluation of novel antiretroviral nanotherapeutics

The success of combination Antiretroviral therapy (cART) has changed an HIV diagnosis from a life-threatening illness to a chronic but manageable infection. Despite this, cART is associated with daily administration of pills and several challenges, including suboptimal drug concentration in tissues such as the lymph nodes, where chronically infected cells reside. A new PhD project from Aarhus University, Health, investigated novel long-acting nanotherapeutic compounds, which require less frequent dosing and have the potential to reach lymph nodes. The project is a collaboration between The Department of Infectious Diseases at The Department of Clinical Medicine and The Department of Chemistry, Aarhus University. The project was carried out by Master of Science, Anna Halling Folkmar Andersen, who is defending her dissertation on 2/12-2019.

The dissertation is based on five publications. The first three studies investigated combinations of approved anti-HIV pharmaceuticals (such as lamivudine, zidovudine and elvitegravir) synthesized onto a synthetic polymer backbone. Common for these polymer backbones is a direct or indirect binding to the blood protein albumin. In mice, we found prolonged half-life in the blood as well as lymph node localization after subcutaneous administration of the albumin-associating polymers - which was different than for those without albumin-binding properties. In addition, when cART was delivered via a polymer background, a synergistic antiviral effect was observed. These results led us to pursue the establishment of a mouse model of HIV infection. In the final two studies we established this model based on injection of human stem cells into immunodeficient mice. The response of these mice to innate immune activation was evaluated. In parallel, the model was optimized for modelling HIV infection with the purpose of preclinical testing of novel antiviral compounds. Collectively, these data highlight the effects and potential challenges regarding long-acting pharmaceuticals against HIV infection and the in vivo investigations thereof.

The defence is public and takes place on 02/12/2019 at 10 am in the Merete Barker Auditorium (1253-211) Aarhus Universitet, Bartholins Allé, 8000 Aarhus C. The title of the project is "Rethinking ART: Preclinical evaluation of novel antiretroviral nanotherapeutics". For more information, please contact PhD student Anna Halling Folkmar Andersen, e-mail: ahfa@clin.au.dk, phone +4528266946

Assessment committee: Associate Professor Lene Niemann Nejsum - chairman of the committee and moderator of the defence, Institut for Klinisk Medicin, Palle Juul-Jensens, Boulevard 82, 8200 Aarhus N, Danmark

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