AARHUS UNIVERSITY

Press release

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Basic information

Name: Steffen Leth Email: steffenleth@gmail.com Phone: +4525136854

Department of: Clinical Medicine

Main supervisor: Professor Lars Jørgen Østergaard, MD, PhD, DMSc

Title of dissertation: Characterizing viral dynamics during mono- and combinatorial interventions aimed at diminishing the latent HIV-1 reservoir in vivo

Date for defence: Tirsdag d.23 maj 2017 at (time of day): 10.00 Place: Mødelokale 4, indgang G6, G206, Aarhus Universitetshospital, Skejby

Press release (Danish)

Et nyt ph.d.-projekt fra Aarhus Universitet, Health, har undersøgt effekten af immunmodulerende medicin kombineret med en HIV-1 specifik vaccine hos velbehandlede HIV-1 inficerede personer med det formål at mindske mængden af inficerede celler - den såkaldte "Shock and Kill" strategi. Projektet har som det første på verdensplan påvist, at ved at anvende denne form for kombinationstrategi er det muligt at reducere mængden af HIV-1 inficerede celler med op til 40% hos velbehandlede HIV-1 inficerede personer. Projektet er gennemført af Steffen Leth, der forsvarer det d. 23/5 2017

Tidligt i forløbet af HIV-1 infektionen inficeres langlivede hvilende hukommelses CD4+ T celler - det såkaldte latente HIV-1 reservoir. Disse inficerede celler kan undertrykkes af antiviral medicin. Det medfører, at man ikke smitter, når man tager sin medicin. Udfordringen er, at hverken den antivirale medicin eller immunsystemet kan fjerne disse langlivede celler. Disse celler udgør derfor den primære barriere for at kurere HIV.

I øjeblikket er der fokus på adskillige strategier rettet mod at mindske eller ultimativt helt at fjerne mængden af HIV-1 inficerede celler fra kroppen. En af de strategier involverer immunmodulerende medicin, der kan vække de hvilende inficerede celler til live. De bliver på den måde "mærket" for immunsystemet, der efterfølgende registrerer dem som inficerede og slår dem ihjel, mens man stadig tager sin antivirale medicin for at forhindre nysmitte af andre celler.

PhD projektet er bygget op omkring 3 kliniske studier udført med HIV-1 inficerede personer.
Det første studie beskriver den naturlige variation i mængden og aktiviteten af HIV-1 inficerede celler over tid for at skabe et referencemateriale.
Studie 2 beskriver den HIV-1 aktiverende effekt af at anvende immunmodulerende medicin på de hvilende HIV-1 inficerede celler.
Endelig beskriver studie 3 effekten af at booste immunsystemet med en HIV-1 specifik vaccine, inden den immunmodulerende medicin gives.

Resultaterne fra disse studier har været med til at beskrive væsentlige virale dynamikker af det latente HIV-1 reservoir hos HIV-1 inficerede personer - herunder nye immunmodulerende strategier sigtet mod en fremtidig kur imod HIV.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 23/5 2017 kl. 10.00 i Mødelokale 4, indgang G6, G206, Palle Juul-Jensens Boulevard 99, Aarhus Universitetshospital, Skejby. Titlen på projektet er "Characterizing viral dynamics during mono- and combinatorial interventions aimed at diminishing the latent HIV-1 reservoir in vivo". Yderligere oplysninger: Ph.d.-studerende Steffen Leth, e-mail: steffenleth@gmail.com, tlf. +4525136854

Bedømmelsesudvalg:

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Professor David Margolis, MD Director, University of North Carolina HIV Cure Center, IGHID Institute for Global Health & Infectious Diseases 2016 Genetic Medicine Bldg., CB#7042 120 Mason Farm Rd. University of North Carolina at Chapel Hill Chapel Hill, NC 27599-7042 USA

Press release (English)

A new PhD project from Aarhus University, Health, has investigated the effect of immunomodulatory drugs combined with an HIV-1 specific vaccine in well-treated HIV-1 infected persons aimed at reducing the amount of HIV-1 infected cells - the so-called "Shock and Kill "strategy.
The project is the first to show, that by using this form of combination strategy, it is in fact possible to reduce the amount of HIV-1 infected cells by up to 40% in well-treated HIV-1 infected persons. The project was carried out by Steffen Leth, who will be defending his thesis on 23/5 2017.
Early in the course of the HIV-1 infection, long-lived dormant CD4 + T cells are infected - the so-called latent HIV-1 reservoir. These infected cells can be suppressed by antiviral medicine, which means that you are not infectious when taking your medicine. The challenge is that neither the antiviral medicine nor the immune system can remove these long-lived infected immune cells. These cells therefore constitute the primary barrier to a cure against HIV.
Currently, focus on different strategies aimed at reducing or ultimately eliminating the amount of HIV-1 infected cells from the body. One of the strategies involves immunomodulatory drugs that can awaken the dormant infected cells to initiate viral activity and thus "label" them to the immune system, which subsequently detects these cells as infected and kill them, while still taking the antiviral medicin to prevent new cell infection.

The PhD project consists of 3 clinical studies conducted with HIV-1 infected persons. The first study describes the natural variation of the amount and activity of HIV-1 infected cells over time to create a reference material. Study 2 describes the ability of immunemodulating medicine to activate latently infected cells and finally, study 3 describes the effect of boosting the immune system with an HIV-1 specific vaccine before the immunomodulating medication is given.

The results of these studies have helped to describe novel viral dynamics of the latent HIV-1 reservoir in HIV-1 infected persons - including novel immunomodulating strategies aimed at a future cure for HIV.

The defence is public and takes place on 23/5 2017 at meetingroom 4, entrance G6, G206, Palle Juul-Jensens Boulevard 99, Aarhus University Hospital, Skejby. The title of the project is ”Characterizing viral dynamics during mono- and combinatorial interventions aimed at diminishing the latent HIV-1 reservoir in vivo”. For more information, please contact PhD student Steffen Leth, email: steffenleth@gmail.com, Phone +45 25136854.

Assessment committee:

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