STATENS SERUM INSTITUT (SSI)
Center for Vaccine

STATENS SERUM INSTITUT

Tuesday, 29 August 2017

DIFFERENTIAL RECOGNITION OF MTB-SPECIFIC EPITOPES AS FUNCTION OF TUBERCULOSIS DISEASE HISTORY

PRESENTATION BY CECILIA LINDESTAM ARLEHAMN, PhD, LA JOLLA INSTUTE FOR ALLERGY & IMMUNOLOGY

Individuals with a history of tuberculosis disease are at elevated risk of disease recurrance. The underlying cause is not known, but one explanation is that previous disease results in less effective immunity against Mycobacterium tuberculosis (Mtb). We hypothesized that the repertoire of Mtb-derived epitopes recognized by T cells from individuals with latent Mtb infection (LTBI) differs as a function of previous diagnosis of active tuberculosis (TB) disease. Taking advantage of our comprehensive panel of epitopes we measured T cell responses to peptide pools in samples collected from an adult screening and an adolescent validation cohort. We identified a set of "Type 2" T cell epitopes that were recognized at 10-fold lower levels in Mtb-infected individuals with a history of TB disease <6 years ago (PostTB) than those without previous TB. By contrast, "Type 1" epitopes were recognized equally well in individuals with or without previous TB. The differential epitope recognition was not due to differences in HLA class II binding, memory phenotypes or gene expression in the responding T cells. Instead, 'PostTB sensitive' Type 2 epitopes were significantly ($p<0.0001$) more homologous to sequences from bacteria found in the human microbiome than Type 1 epitopes. Thus, preferential loss of T cell reactivity to Mtb epitopes that are homologous to bacteria in the microbiome in persons with previous TB disease may reflect long-term effects of antibiotic TB treatment on the microbiome.

DEVELOPMENT OF A COMPANION DIAGNOSTIC FOR ESAT-6 BASED VACCINES, THE ESAT-6 FREE IGRA

PRESENTATION BY MORTEN RUHWALD, MD, STATENS SERUM INSTITUT

There is a need for an improved vaccine for tuberculosis. ESAT-6 is a cardinal vaccine antigen with unique properties and is included in several vaccine candidates in development. ESAT-6 is also the core antigen in the IFN-γ release assays (IGRA) used to diagnose latent infection, rendering IGRA tests unspecific after vaccination with ESAT-6 containing constructs. Omission of ESAT-6 from the IGRA antigen cocktail leads to lower sensitivity, which prompted the search for new diagnostic antigens, which are both highly recognized in Mtb infected individuals and specific i.e. not expressed in BCG. This presentation will describe the process from antigen discovery, field-testing of novel antigen cocktails, optimization of a robust and user-friendly test system, and final qualification of the ESAT-6 free IGRA as a reliable primary endpoint in a phase 2 clinical trial.

PROGRAMME

14:00 – 14:05 Welcome to the SSI

14:05 – 14:45 DEVELOPMENT OF A COMPANION DIAGNOSTIC FOR ESAT-6 BASED VACCINES, THE ESAT-6 FREE IGRA
Morten Ruhwald, SSI

14:45 – 15:30 DIFFENTIAL RECOGNITION OF MTB-SPECIFIC EPITOPES AS FUNCTION OF TUBERCULOSIS DISEASE HISTORY
Cecilia Lindestam Arlehamn, La Jolla Institute for Allergy & Immunology

WHERE

Statens Serum Institut, Artillerivej 5, 2300 København S
Jernesalen, building 206, room 125

Please go to the reception upon arrival for sign-up and ID-card.

WHEN

Tuesday, 29 August 2017 at 14:00-15:30.

REGISTRATION

It is not necessary to register for this event. Attendance is free of charge.

If you think that anyone else in your network could be interested in attending this seminar, please feel free to forward this invitation (with cc to: paho@ssi.dk)