CTVD
The Collaboration for TB Vaccine Discovery

CTVD Announcements

Gates Foundation News

TB News

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Abstracts for Presentation at the 2nd CTVD Annual Meeting

Congratulations! These abstracts have been accepted for poster presentation at the 2nd Annual Collaboration for TB Vaccine Discovery (CTVD) Meeting which will take place from 23 to 24 June 2016 in Seattle, Washington.

Virtual Forum Recording Available

Speaker: Dr Zhou XING, McMaster University, Canada
Presentation Abstract: Mtb has evolved to counter host defense mechanisms. One way to develop the effective TB vaccination strategies is to identify the immune checkpoints where host defense does not do well in early phases of M.tb infection, and develop vaccination strategies to target these checkpoints. Respiratory mucosal vaccination can most effectively target these checkpoints by accelerating innate immune activation and T cell immunity in the lung upon Mtb exposure. Presentation can be accessed here.

Speaker: Dr Stéphane LEUNG-THEUNG-LONG, Transgene, France
Presentation Abstract: Transgene is carrying an active program aiming at developing candidate vaccines against Mycobacterium tuberculosis. While the developed vaccine candidates have the potential to be evaluated in both a prophylactic and therapeutic settings, priority of the company today is to bring to the clinic a "therapeutic vaccine" or "active-targeted immunotherapeutic" to improve treatment of active TB, in particular linked to DR (drug resistant) strains. The retained platform of Transgene program is the MVA (very high genomic plasticity, safety profile, adapted to multiple administrations as shown in a number of Transgene therapeutic programs). Over the course of the last 5 years Transgene has engineered and tested a collection of different MVA constructs. Today, 6 MVA-TB have been retained, expressing from 6-10 TB antigens covering all 3 phases of the infection (active, latency/dormancy, resuscitation). Those MVA have proven highly immunogenic in mice, capable to induce both CD4 and CD8 T cells, including T cells with lytic activity and producing multiple cytokines as well as specific antibodies (ELISA specific of all selected Mtb antigens have been developed). Presentation can be accessed here.

Virtual Forum

Next Virtual Forum – 11 July 2016

Presenter:	Dr Simone Joosten, Leiden University Medical Center, The Netherlands
Date:	Monday, July 11, 2016
Time:	8h00 PDT | 11h00 EDT
Title:	HLA-E restricted Mycobacterium tuberculosis specific human CD8+ T-cells: novel possibilities for TB vaccine development

Presentation Abstract: Mycobacterial antigens are not only presented to T-cells by classical HLA-class Ia and HLA-class II molecules, but also through alternative antigen presentation molecules such as CD1a/b/c, MR1 and HLA-E. The advantage of these molecules is their low level of polymorphism which makes them interesting donor-unrestricted targets (DURT) for vaccination purposes. We recently described mycobacterial peptides that are presented in HLA-E and recognized by CD8+ T-cells. Using T-cell cloning, phenotyping, microbiological, functional and RNA-expression analyses, we found that these T-cells can exert cytolytic or suppressive functions, inhibit mycobacterial growth, yet express GATA3, produce Th2 cytokines (IL-4,-5,-10,-13) and activate B-cells via IL-4. In TB patients, Mtb specific cells were detectable by peptide-HLA-E tetramers, and IL-4 and IL-13 were produced following peptide stimulation. The frequencies were highest in untreated TB patients and declined following successful treatment. These results identify a novel human T-cell subset with an unorthodox, multifunctional Th2 like phenotype and cytolytic or regulatory capacities, which is involved in the human immune response to mycobacteria and demonstrable in active TB patients' blood. The results challenge the current dogma that only Th1 cells are able to inhibit Mtb growth and clearly show that Th2 like cells can strongly inhibit outgrowth of Mtb from human macrophages. These insights significantly expand our understanding of the immune response in infectious disease.

To join this one hour online event on **July 11th:**

1. Go to: WebEx Meeting
2. Enter your first name, last name, and email address
3. Enter the event password: **CTVD123**

If you have any problems joining, please send an email to brian@regenworks.com (Phone: 425.999.2420)

Research Communities

Research communities aim to address specific areas critical for TB vaccine discovery and development. They are led by persons from outside the foundation and will meet to discuss scientific issues at hand and devise priority areas that have to be addressed. We hope that individuals within these communities would initiate funding applications to major funders, including the foundation.

Aerosol vaccination: Aurelio Bonavia | Steffen Stenger
DURTs: Dave Lewinsohn | Branch Moody
NHPs: Mario Roederer | Bob Seder
Whole cell vaccines: Olivier Neyrolles | Tom Scriba

NEW communities:
Conventional T cells: Helen Fletcher | Kevin Urdahl
B-cells and Antibodies: Bryan Charleston | Richard Frothingham

Publications of Interest

Drug-resistant TB: deadly, costly and in need of a vaccine.
Transactions of the Royal Society of Tropical Medicine and Hygiene | 3.2016
Manjelievskaia J, Erck D, Piracha S, Schrager L

Vaccination against tuberculosis with whole cell mycobacterial vaccines
The Journal of Infectious Disease | 5.2016
Scriba TJ, Kaufmann SHE, Lambert PH, Sanicas M, Martin C, Neyrolles O.

Mycobacterium tuberculosis infection and vaccine development
Tuberculosis | May 2016
Tang J, Yam WC, Chen Z.

TB/HIV pleurisy reduces Th17 lymphocyte proportion independent of the cytokine microenvironment
Tuberculosis | 7.2016
Korb V, Phulukdaree A, Lalloo UG, Chuturgoon AA, Moodley, D

Expression of nuclear factor, erythroid 2-like 2-mediated genes differentiates tuberculosis
Tuberculosis | 7.2016
Qian Z, LV Jingzhu, Kelly GT, Wang H, Zhang X, Gu W, Yin X, Wang T, Zhou T

Another acronym, but an important one! GTBVP

The Global Tuberculosis Vaccine Partnership (GTBVP) is a collaboration between the European Commission, the European and Developing Countries Trials Partnership (EDCTP), the European Investment Bank, Aeras, TBVI, the South African Department of Science and Technology and the French Ministry for Research which aims to introduce global portfolio management for clinical trials of new TB vaccines. In short, we cannot afford to test candidates that have not passed gating criteria that suggest success. GTBVP hopes to create an independent global portfolio assessment committee (GPAC), which could be contacted by funders when individual candidates are considered for funding – to give input. All funders that operate in the global TB vaccine space will meet soon to discuss this initiative (as well as outcomes of CTVD research communities).

Gates Foundation News

Open letter from Sue Desmond-Hellman, CEO BMGF

On May 23, 2016, Sue Desmond-Hellman published an open letter to Foundation partners and followers, intended to give further clarity to "who we are, what we do, and how we do it". The current letter presents three of the many areas where the Foundation is investing, based on the belief that all lives have equal value: tobacco control, sleeping sickness, and U.S. education. The CEO letter is to be an annual tradition, as a component of an ongoing dialogue with partners and the public.

Controlled Human Infection Models as a new resource under GH-VAP

In a Controlled Human Infection Model (CHIM), a selected strain of a pathogen is administered to healthy adult volunteers at a defined dose and by a specific route of administration. Volunteers are cared for and closely monitored for evidence of infection and the symptoms of disease that develop, and the pathogen is cleared from volunteers prior to study completion. Such models, while not available for HIV, currently exist a range of enteric, respiratory, and vector-borne diseases, and have played a key role in the development of some of the vaccines we use today. GH-VAP now provides the opportunity to do studies with the CHIM Consortium, a network of clinical research sites and investigators skilled in the conduct of CHIM, with centralized support and coordination through PATH and The Emmes Corporation. As a platform technology within the Global Health Vaccine Accelerator Program (GH-VAP), the CHIM Consortium will provide opportunities for greater integration of the immune monitoring technologies available through the GH-VAP into CHIM studies. You can learn more regarding the CHIM Consortium on the GH-VAP Portal.

TB News

Canada announces major contribution for Stop TB Partnership's TB REACH Initiative

The Government of Canada today announced a renewed investment of CA$ 85 million for the Stop TB Partnership's TB REACH initiative over the next five years. This new injection of funding will help the Partnership to reach, treat and cure many of the 3.6 million people affected by TB who every year go without proper care. TB REACH will continue to test innovative, daring and fresh strategies for improving TB detection, service delivery, roll-out of new tools and policies.

FDA Issues Warning Letter to Qiagen for TB Test

Qiagen received a warning letter from the US Food and Drug Administration (FDA) last week detailing repeated complaints for high false positive rates for Qiagen's QuantiFERON-TB Gold (QFT) test device—its blood test used for diagnosing tuberculosis.

Six Reasons Why It's Critical to Invest in the Deadliest Disease You Probably Never Think About

Current investments in TB vaccine research and development (R&D) are consistently quite low compared to other diseases. In fact, in 2014 HIV vaccine R&D received six times the amount of funding that was invested in TB vaccine R&D($652 million compared to $112 million). It's particularly important to support R&D for a new, effective, and affordable TB vaccine. Here's 6 reasons why.

We Need to Inject Some Funding Into Tuberculosis Research

The funding needed to research and develop a TB vaccine is a small fraction compared to the financial burden caused by TB. The WHO calculates that the TB epidemic costs the world US$8 billion per year.