Call for ideas for identifying M72/AS01E vaccine-elicited correlates of protection against TB disease

The Problem
Tuberculosis (TB) is a major cause of death and morbidity in low- and middle-income countries, negatively impacting human health and the global economy and serving as one of the top drivers of antimicrobial resistance (WHO 2018). A critical gap in the development of a globally efficacious vaccine against tuberculosis is the lack of identified vaccine-induced correlates of protection (CoP) against TB disease. Identification of these CoP has the potential to accelerate clinical vaccine development by enabling early triaging of novel vaccine candidates, greatly accelerating evaluation in expanded populations and of alternate regimens, and may illuminate mechanistic underpinnings of immune protection, further spurring innovations in therapeutic and prevention strategies. Potential identification of CoP has recently become feasible because the novel vaccine candidate M72/AS01E showed 50% efficacy at 36 months in preventing TB disease in latently infected participants in a phase IIb trial (Tait, Hatherill et al. 2019), and samples were collected prospectively from 99% of trial participants in a substudy (NCT02097095).

Toward correlates of protection
The Bill & Melinda Gates Foundation and the Bill & Melinda Gates Medical Research Institute are coordinating planning activities to identify M72/AS01E-induced CoP against active TB disease. The National Institute of Allergy and Infectious Diseases (NIAID), GSK, IAVI, the South African Tuberculosis Vaccine Initiative (SATVI) and Fred Hutch, among others, are collaborating in this effort. The process will be based on the assessment of vaccine-induced responses in samples from participants who developed TB disease (cases) and participants who remained disease free (matched controls).

What We Are Seeking
We are seeking input from the broader community in the form of novel ideas for the analysis of potential immune correlates of M72-induced protection against TB disease. Available samples include 6 vials of PBMC (~ 5 million cells each) and 2 vials of plasma per participant from each of study days 0, 37 and 180 (vaccine was administered on days 1 and 30). Additionally, 1 Paxgene vial and 2 vials of lysed whole blood (~250 µL) are available from days 0, 37, 180 and 365. Proposals will undergo scientific review as well as review by funding agencies. Proposals should address a pre-specified hypothesis based on preliminary data from non-clinical or clinical studies. We are specifically seeking ideas to discover potential correlates of protection mediated by the M72/AS01E vaccine, in addition to correlates of risk associated with development of TB disease independently of vaccination. There will be an opportunity to run pilot studies to address submitted ideas using non-case/control samples from the M72/AS01E trial to assess whether the proposed assays are fit-for-purpose, i.e., they fulfill the following criteria:
a) The required sample type is available, and the assay can be run on limited sample volumes
b) The assay covers a unique immunological niche in the immune space or maximizes potential knowledge to be gained compared to other assays addressing the same immune space
c) The assay directly addresses a pre-specified hypothesis and/or is supported by scientific rationale
d) Measured with validated, qualified or standardized assays
e) Broad, biologically relevant dynamic range across vaccinees
f) Different distribution (i.e., quantity of the marker) among vaccine vs. placebo recipients (i.e. evidence of vaccine-induced response)
g) Low technical measurement error (informed by technical replicates)
h) Low intra-individual temporal variability among placebo recipients

Proposals covering the entire immunological space, including adaptive cellular and humoral responses, “innaptive” responses (i.e. those bridging innate and adaptive immunity including non-classical T cells, NK cells and trained immunity), as well as the immune milieu will be considered.

Submission Requirements
Submit up to a 2-page pdf document of narrative (11-point font, single spaced) that includes the following sections:
1) Scientific rationale and specific hypothesis to be tested
2) Brief description of the assay including readout
3) Supporting data generated in your laboratory
4) Sample requirements (sample types, volumes, and timepoints required, including both minimum and optimal volumes)
5) Current level of assay standardization and existing plans for further qualification/validation (see http://miataproject.org/miata-guidelines/guidance-on-module-5/ for a description of different levels of standardization)

Governance
For evaluation of submissions to this Call for Ideas we have established a Scientific Advisory Committee (SAC). This group of scientists and other stakeholders have substantial experience in the fields of identification of CoP and Mtb/TB vaccine research and will advise on the scientific merit, and how the proposed approach would/could feature within a broader plan for analysis of available samples. The SAC will propose this plan to the Bill & Melinda Gates Foundation, other interested funders, and to a committee that governs the use of samples collected during this M72/AS01E Phase IIB trial, for final approval and funding. Any chosen project would be implemented in close collaboration with...
with the Gates Medical Research Institute, who will lead the effort to identify CoP and a leadership team, consisting of key members from the SAC, who will also have an ongoing, central role.

Feedback and Communication
The submissions will be considered confidential and feedback on the submitted proposals will be provided after SAC deliberations and funding commitment. Priority for advancement will be based on scientific support for the proposed hypotheses and level of compliance with criteria a) – h) outlined above. Note that further distribution of this Call for Ideas to additional potential investigators is encouraged.

Deadline for Submissions
All submissions are requested by Friday, January 31, 2020.
Click here (or type https://tinyurl.com/Correlates-M72 into your browser) to submit your response to this Call for Ideas.

Questions
If you have any questions about this Call for Ideas or the TB Immune Correlates Program, please contact Dr. Nicole Frahm and team at tbcorrelateslt@gatesmri.org.

References