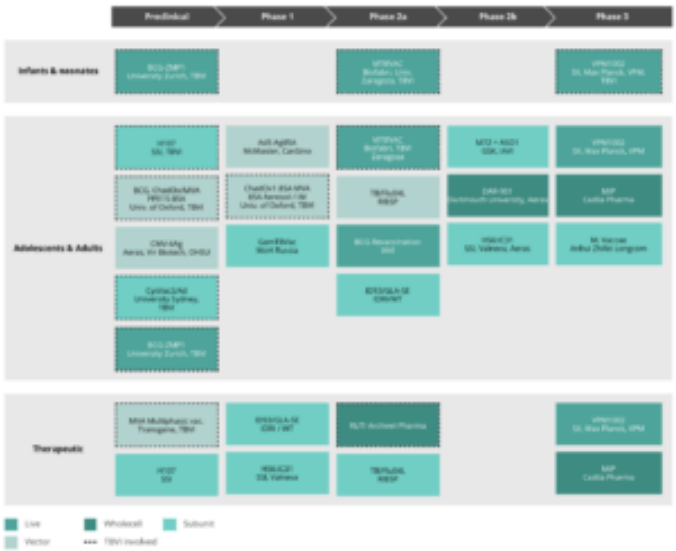
IDA Highlight: Immune responses to TB vaccines



The current TB vaccine pipeline (last update September 2019). Source: TuBerculosis Vaccine Intitiative (TBVI) [tbvi.eu/what-we-do/pipeline-of-vaccines/]

Bacille Calmette-Guerin (BCG) the only vaccine against Tuberculosis (TB) was developed in 1921, and for the past [almost] 100 years, it has predominantly been used to immunize children. Despite this vaccination strategy adults are still susceptible to TB, thus it remains a global health burden. There are currently 14 vaccine trials being investigated in various parts of the world, of which the South African Vaccine

Trials Network (SATV) has tested 9/15 in vaccines in clinical trials. These various vaccine trials aim at exploring different vaccination strategies to induce immune response that can prevent development of TB disease and in some cases prevent or clear *Mycobactierum tuberculosis* (M.tb) infection (Reviewed in Andersen and Scriba, Natural Reviews Immunology 2019).

Dr Elisa Nemes from SATVI presented on the current status of TB vaccinology, where she primarily focused immunological aspects of tested vaccine strategies. Immunoprofiling of TB-vaccine induced immunity, still primarily focuses on determining T helper (Th) 1 specific CD4 T cell responses and how those responses contribute to protection or clearance. This is because Th1 CD4 T cells are needed to activate macrophages, the primary host cells for M.tb replication. However, studies have shown these cells are necessary but not sufficient to clear infection (Nunes-Alves *et al* Nat Rev Micr 2014). Highlighting the need to cast wider net for vaccine induced immunoprofilling to include other Th CD4 subsets, B cells, as well as non-conventional T cells and innate immune responses.

Dr Nemes gave a brief summary of some the recent pre-clinical research. Pre-clinical TB vaccine studies in M.tb infected mice that have been vaccinated with different strategies e.g before or after TB infection have been reported to show different immune profiles compared to post-exposure vaccine induced responses. It is known that M.tb infection alters immunological profiles of antibody (Ab) and T cell responses. This is important to consider in vaccine trials especially when they target different stages of TB infection and diseases, thus suggesting that we may need different strategies for pre-exposure and post-exposure populations. ID-93 immunogenicity trial in has been shown to boost/induce immune responses in M.tb-infected vaccinees, thus warranting testing in phase 2/3 clinical trials. MTBVAC is another

vaccine in clinical trials which aimed to look at immunogenicity in infants and adults. These trials tested different doses of MTBVAC and reportedly induced higher responses compared to BCG vaccine induced responses. These responses appeared to be more polyfunctional. Using tSNE analysis researchers were able to scrutinize the cells responsible for cytokine production in response to BCG vaccination/stimulation or other vaccines. Results presented by Dr Nemes showed that natural killer (NK) cells and NK T-like cells release cytokines in response to stimulation. Suggesting a potential role of NK and NKT cells in vaccine induced immunity.

The TB vaccine field is also investigation the impact of route of vaccination of systemic and organ specific immunity. Data presented at the IDA showed that changing the delivery of the BCG vaccine delivery changes the magnitude and type of vaccine induced T cell immunity of the vaccine, where aerosol vaccine induces changes in Th1 and Th2 profiles in the lungs, but not in the blood. Dr Nemes also discussed challenges the TB vaccine field is experiencing, where in spite of testing 14 vaccines there is a minimal diversity of vaccine-induced functional profiles. There are also documented immune response differences between individuals who are TB unexposed and those who have been exposed. Thus, strategies need to be implemented for both pre-exposure and post-exposure populations.

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