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# Development of a novel self-adjuvanting mucosal vaccine for TB

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Tuberculosis (TB) predominantly affects the lungs and is caused by Mycobacterium tuberculosis (Mtb). Despite being among the oldest known human pathogens, there is currently only one licensed vaccine against TB, Bacillus Calmette Guerin (BCG), which offers highly variable levels of protection against pulmonary TB in adults. With the increasing burden of drug resistant TB, it is imperative that we continue to test and develop new and more effective vaccine strategies.

We propose that the "next generation" of TB vaccines should be focused on mucosal delivery to offer increased efficacy compared to BCG, in addition to a lower cost and ease of administration in low-middle income settings where TB is most prevalent. In this project, we tested a novel vaccine candidate, TB-PCF, based on our patented single-polypeptide, self-adjuvanting vaccine delivery system that does not require living organisms or exogenous adjuvants for it to induce a robust immune response after respiratory delivery. This can dramatically accelerate quality control and clinical development and testing, by reducing the number of discrete components required in a vaccine candidate, while inducing robust immunity.

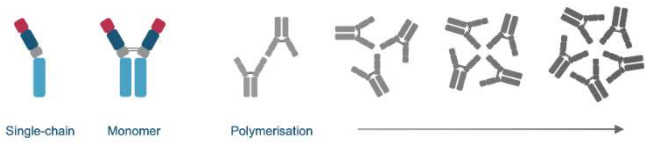
Our proof-of-concept mouse immunisation studies based on systemic prime and mucosal boosting showed strong immunogenicity with induction of mucosal and systemic IgA, IgG and IgM, as well as antigen-specific T cell responses in splenocytes and cell-mediated protection by modified MGIA. Some evidence of protection against aerosol Mtb challenge was also observed, meriting further development and testing of this concept with suitable TB antigens.

## Funding Sources

VALIDATE NetworkBill & Melinda Gates Foundation, CTVD

## Conflicts of Interest

None




Structure and assembly illustration of TB-PCF, showing molecular adjuvant (red), the TB antigens ESAT6 and CFP10 (dark blue), and IgG Fc (light blue). The molecular adjuvant allows for polymerisation of TB-PCF, enabling efficient uptake by antigen presenting cells, while IgG Fc enables Fc-receptor mediated phagocytosis.