**BCG & COVID-19**

This webinar, co-hosted by South African Immunology Society (SAIS) and Immunopaedia featured talks by Prof Christine Benn on “BCG for COVID-19 – hope or hype?” & Prof Gerhard Walz on “BCG trials for COVID-19 in SA – progress and promise.”

Studies have shown that in addition to BCG providing protection against Tuberculosis in children, it also have non-specific effects which are associated with a reduction in all-cause infant mortality* (Kristensen et al., 2020) and reduction in upper respiratory tract infections in revaccinated individuals (Nemes et al., 2019; Wardhana et al., 2020). These non-specific responses have been attributed to trained immunity# (Read more: Have you heard of trained immunity?) which are induced upon vaccination and contribute to a decrease in systemic inflammation.

Prof Christine explained two main hypotheses around BCG & COVID-19: (1) BCG-at-birth protects against COVID-19 & Recent BCG protects against COVID-10. Currently, no direct evidence for either is available, however, a plethora of ecological studies have suggested that the first hypothesis is responsible for low COVID-19 prevalence in some countries (Read: BCG & COVID-19). Realistically, this may not be possible because trained immunity is short lived < 2 years, suggesting that it may not be the sole reason for reduced burden in countries where BCG is still give. For hypothesis 2, trials are currently investigating are on-going, in the meantime observation studies provide evidence that recent BCG vaccination is associated with lower the risk of COVID-19 (Moorlag et al., 2020; Amirlak et al., Pre-print)

Prof Gerhard Walzl then presented his talk on “BCG trials for COVID-19 in SA: progress and promise”. He highlighted challenges the SA healthcare system experiences which include high burden of TB, HIV and more recently non-communicable diseases like diabetes, and also inadequate intensive care facilities among others see below. He then described why BCG re-vaccination was “trailed”, and some challenges they experienced which included: funding challenges “poor buy in from govt”, PPE
shortages, lockdown etc.

**Why BCG and why revaccination?**

- Dysregulated macrophages in CoV-2
- Inadequate immune training of CD14+ monocytes
- Transcriptional myeloid bias on human HSPCs
- Enhanced cytokine responses in restimulation but reduced systemic inflammation
- Epidemiological evidence: 10.4% reduction in COVID-19 mortality for every 10% increase in BCG index (Escobar et al., PNAS, 2020)
- BCG efficacy wanes in adolescence (Stowe et al., 1994)

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**...the trial**

- Emergency trial started 4 May 2020: double blind, randomized, placebo controlled trial
- HCW and front line workers
- Baseline BCG vaccination or placebo
- Follow-up for one year
- Primary endpoint: CoV-19 hospitalization or death
- TASK: 1000 participants (780 enrolled)
- UCT: 500 participants (280 enrolled)

**Can we still learn something from the trial?**

- Emergency research not immune from politics (the good, the bad and the ugly of activism)
- Crises can bring competitors together
- Unprecedented rapid SAHPRA approval, WCOH and CoCT permissions and IRB approvals
- Opportunity to investigate the biology of BCG revaccination
  - Single cell ATACseq before and after BCG revaccination to assess chromatin accessibility
Notes:

- *: this is not only associated with BCG but also other live-attenuated vaccines such as measles and polio
- #: Trained immunity is the non-specific resistance to infection that is conferred by innate immune cells. Mechanistic studies have attributed trained immunity to epigenetic reprogramming that occurs when innate immune cells are activated by infection or vaccination (Netea et al., 2016).

Summary by Cheleka Mpande