6.04 An adenoviral COVID-19 vaccine enhances monocyte responses to *Mycobacterium tuberculosis*.

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Background: Trained immunity is a functional reprogramming of the innate immune system which has been put forth as a promising host-directed therapy (HDT) for Tuberculosis. Adenoviral vectors were shown to induce trained immunity in mice, promoting *Mtb* clearance. Therefore, we assessed if the adenoviral vector ChAdOx1 nCoV-19 vaccine could induce trained immunity *in vivo* in humans and its effect on monocyte responses to *Mycobacterium tuberculosis* (*Mtb*).

Methods: Monocytes were isolated from the blood of ten healthy donors pre- vaccination and at day 14, 56 and 83 post-vaccination. The expression of monocyte surface markers was assessed. Metabolic reprogramming was analysed by examining changes in the gene expression of key metabolic enzymes. Finally, monocytes were restimulated *ex vivo* with irradiated *Mtb* and cytokine and chemokine production pre- and post-vaccination was determined.

Results: Expression of HLA-DR, CD40 and CD80 on monocytes was enhanced following vaccination. Monocytes showed evidence of increased glycolysis post-vaccination and produced more IL-1β, IL-6, CXCL1, and MIP-1α upon *Mtb* stimulation.

Conclusions: These data provide evidence for the induction of trained immunity following a single dose of the ChAdOx1 nCoV-19 vaccine, resulting in enhanced monocyte responses to *Mtb*. Trained immunity may be beneficial as a HDT or vaccine platform by promoting early clearance of *Mtb*.

Keywords
Trained immunity, Tuberculosis, Monocytes

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Conflicts of Interest
The authors declare that they have no conflict of interest.