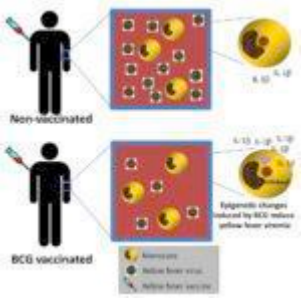
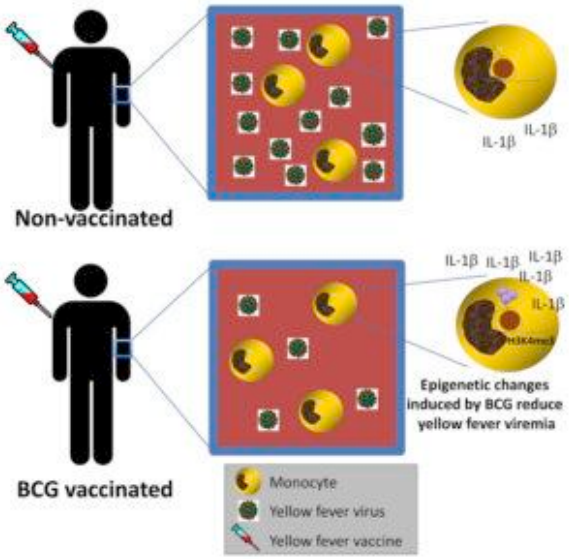
Have you heard of trained immunity?





Arts *et al.*, 2018. Cell Host & Microbes. Graphical Abstract

According to classical immunology, only the adaptive arm of immunity (T and B cells) have the ability to confer immunological memory. However, understanding of immunology memory is being redefined to included *de facto* innate immune memory also known as trained immunity. Trained immunity is the non-specific resistance to infection that is conferred by innate immune cells. Mechanistic studies have attributed trained immunity to epigenetic re-programming that occurs when innate immune cells are activated by infection or vaccination (Netea et al., 2016). This epigenetic reprogramming results

in enhanced inflammatory and antimicrobial properties in innate cells when encountered with secondary stimuli.

Bacillus Calmette-Guérin (BCG) is a live attenuated *Mycobacterium bovis* vaccine strain that protects against Tuberculosis and leprosy. BCG epidemiological studies have shown a protective effect of BCG against non-related infections, where BCG vaccination is associated with reduced infant mortality. Additionally, BCG has been demonstrated to slow tumour progression, when used as a therapeutic agent for bladder cancer. Non-specific effect of BCG has been attributed to induction of histone modifications and epigenetic programming of human monocytes at inflammatory cytokines *TNF-α* and *IL-6* promoter sites.

One of the aims of a study led by Mihai Netea was to examine the effects of BCG-induced trained immunity on viral infection. Using yellow fever vaccination as a model of viral human infections, researchers observed reduced viremia in individuals that received BCG vaccination prior to the yellow fever vaccine compared to cotnrols. Reduced viremia was not associated with reduced levels of yellow fever neutralising antibodies nor yellow fever-specific T cells responses. Illustrating that BCG vaccination did not impair yellow fever induced vaccine responses. Reduced viremia in BCG vaccinated individuals was associated with epigenetic reprogramming of monocytes resulting in increased levels of IL-1β. This study demonstrated a role of IL-1β mediated responses in trained immunity, highlighting the crucial role the IL-1 pathway plays in induction of trained immunity in humans.

Journal Article: Arts *et al*., 2018. BCG Vaccination Protects against Experimental Viral Infection in Humans through the Induction of Cytokines Associated with Trained Immunity. Cell Host & Microbe

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