



Non-specific immunological effects of vaccines

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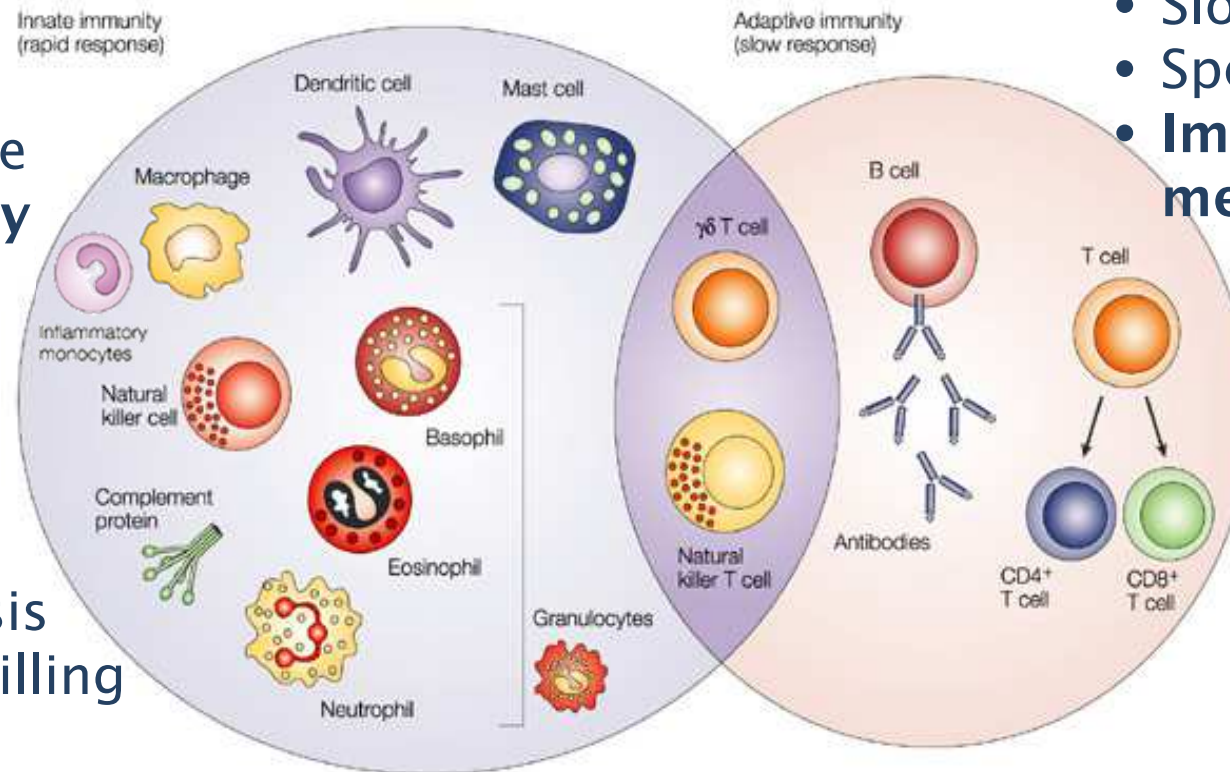
Immune system

Innate immunity

Adaptive immunity

- Fast (minutes)
- Broad range
- **No memory**

- Slower (days)
- Specific
- **Immunological memory**



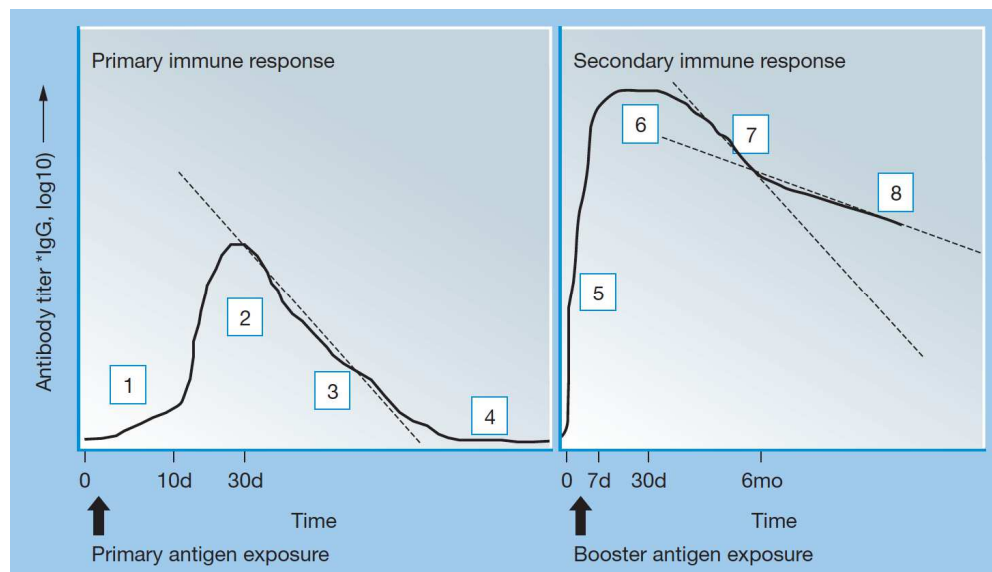
- Phagocytosis
- Microbial killing
- Cytokines:
 - IL-1 β
 - TNF- α
 - IL-6

- Antibodies
- Cytokines:
 - IFN- γ
 - IL-17
 - IL-22

Nature Reviews | Cancer

Classical principle of vaccination

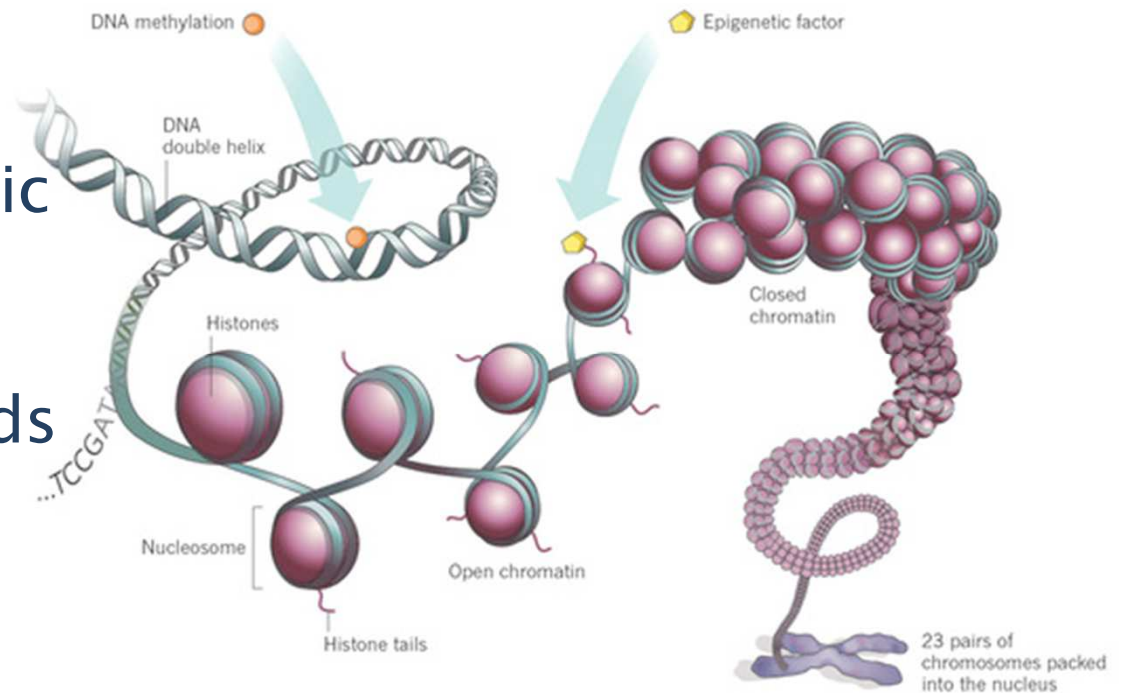
- Vaccine is recognized by adaptive immune system
- Adaptive immunological memory is built
- Stronger antibody response upon infection leads to protection

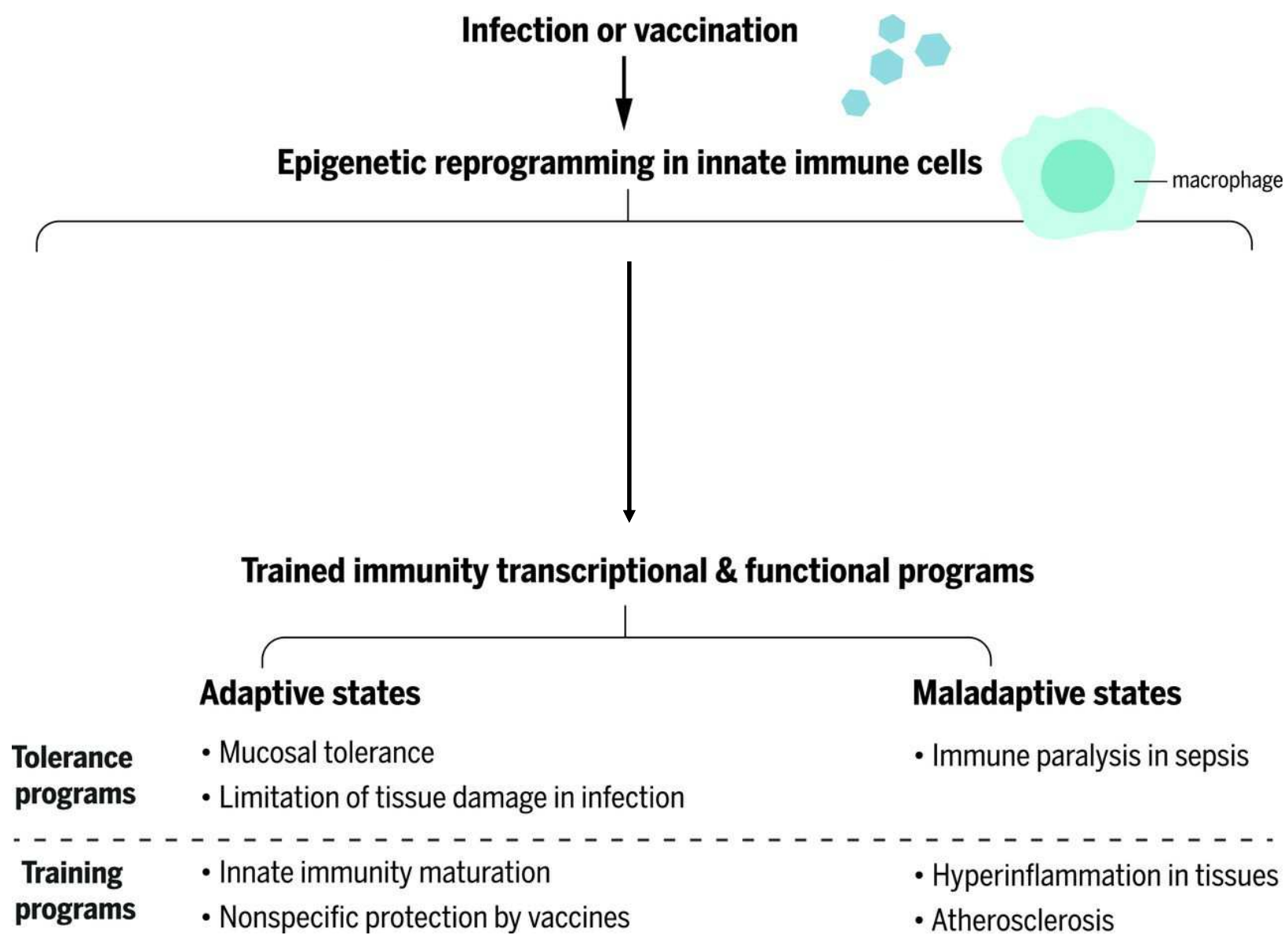


Siegrist CA. Vaccine Immunology 2008

Trained immunity

- Memory of innate immune system
- Mediated by epigenetic changes
- Training stimulus leads to altered immune response upon infection
- Cytokines
 - TNF-a, IL-1b, IL-6

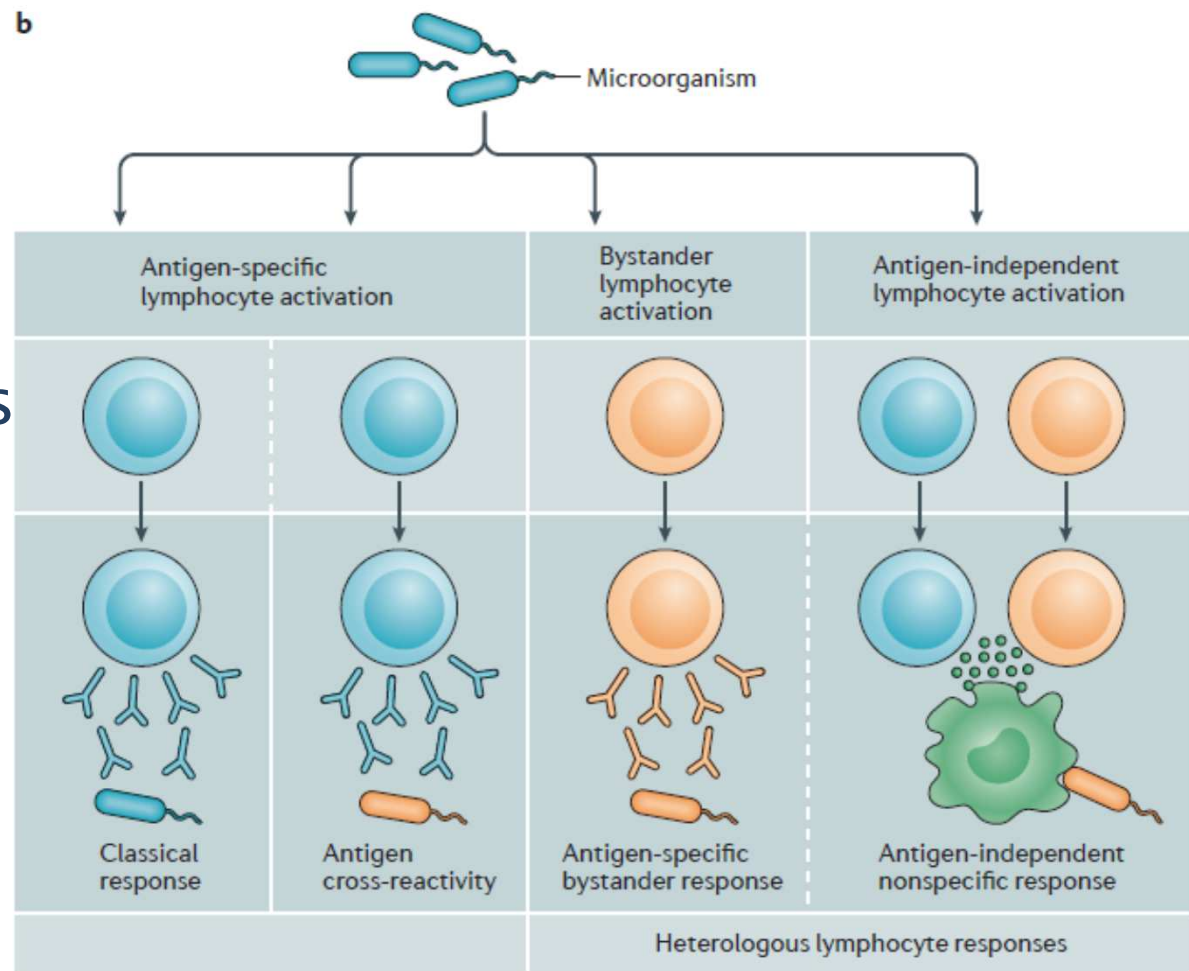




Adapted from: Netea et al. Science 2016

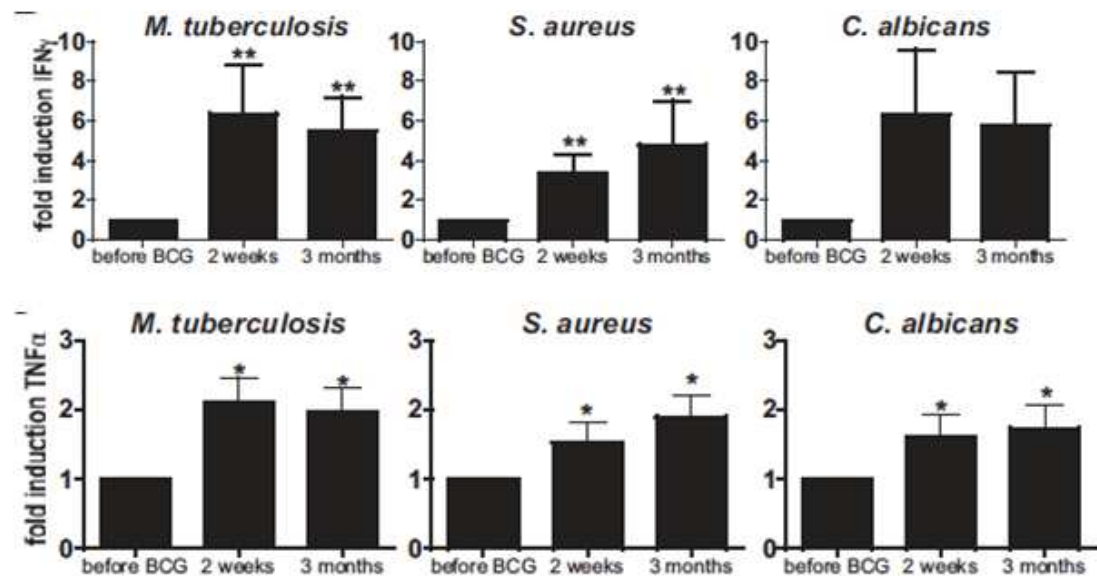
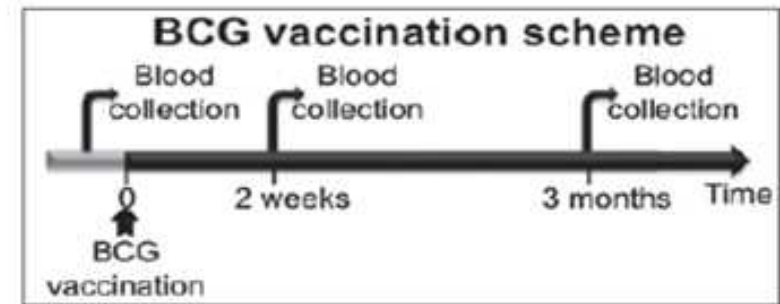
Heterologous adaptive immunity

- Adaptive immune cells respond to unrelated pathogens
 - Cross-reactivity
 - 'Bystander activation'
- Cytokines
 - IFN- γ , IL-17, IL-22



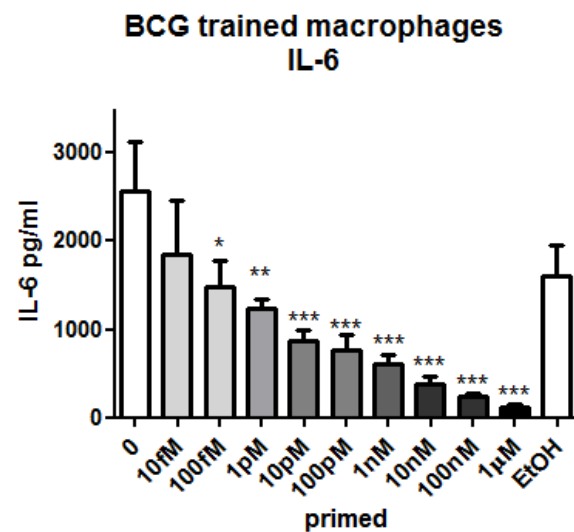
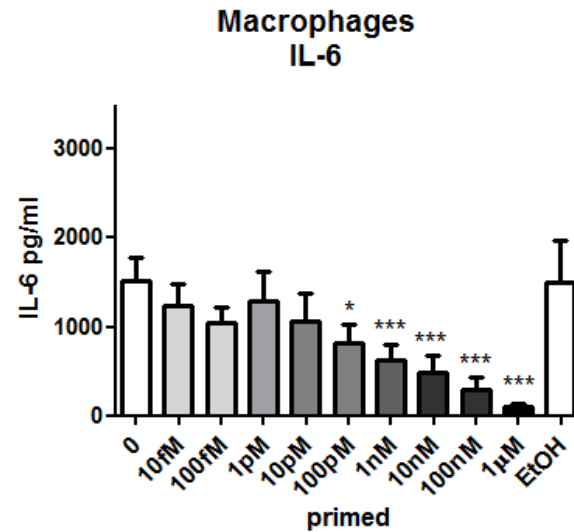
Non-specific effect of BCG

- BCG vaccination leads to increased cytokine responses to unrelated antigens
- Associated with increased active epigenetic marks
- Also shown in neonates



Vitamin A modulates trained immunity

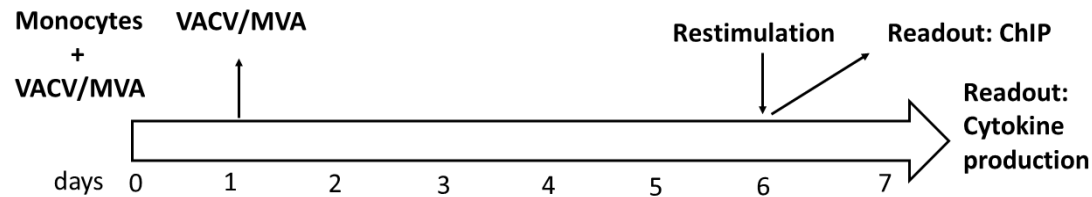
- Vitamin A inhibits cytokine production
- Vitamin A inhibits BCG-induced trained immunity
- Different interventions can interact



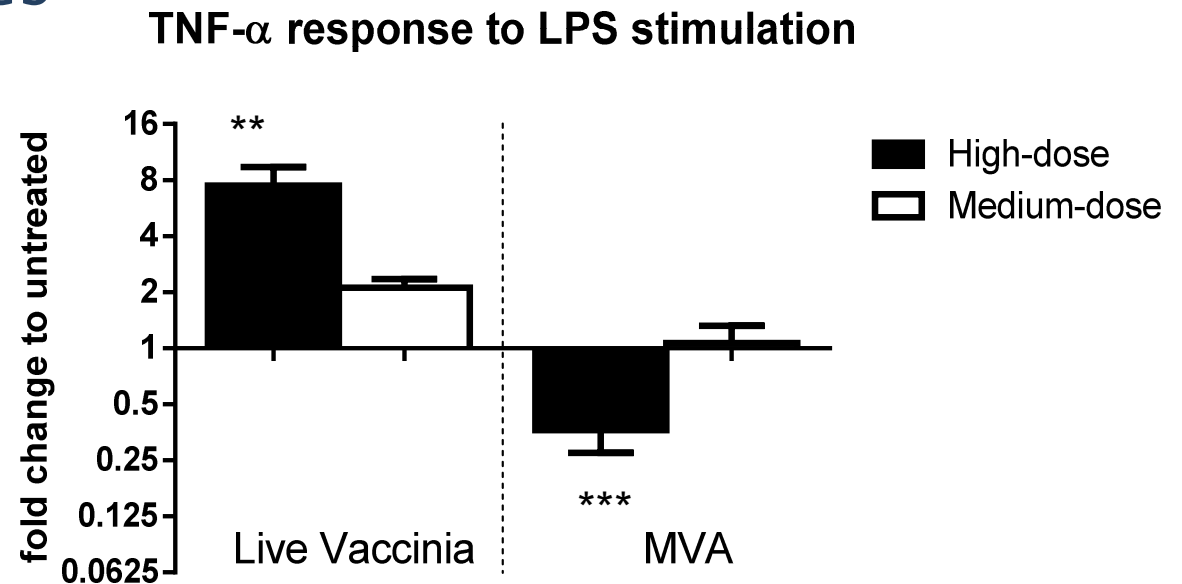
Arts et al. JLB, 2015

Arts & Benn, Sight and Life, 2015

Not all vaccines are equal

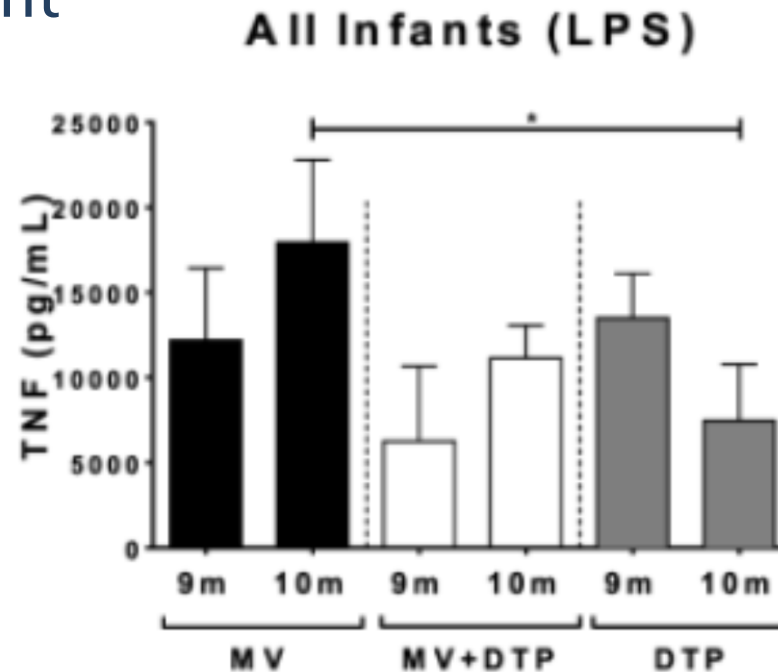


- Live Vaccinia induces trained immunity
- Non-replicating Vaccinia induces immune tolerance



Negative heterologous effects - DTP

In children DTP reduces innate immune response to unrelated stimuli – different for boys and girls



Concluding

- Vaccines confer specific protection against disease through adaptive immune memory
- Vaccines also modulate the immune response to unrelated pathogens, i.e. have non-specific effects
 - Trained immunity
 - Heterologous adaptive immunity
- This can lead to enhanced or reduced immune responses depending on vaccine
 - Enhanced by live vaccines: **BCG, Vaccinia**
 - Decreased by inactivated vaccines: **MVA, Salmonella, DTP**