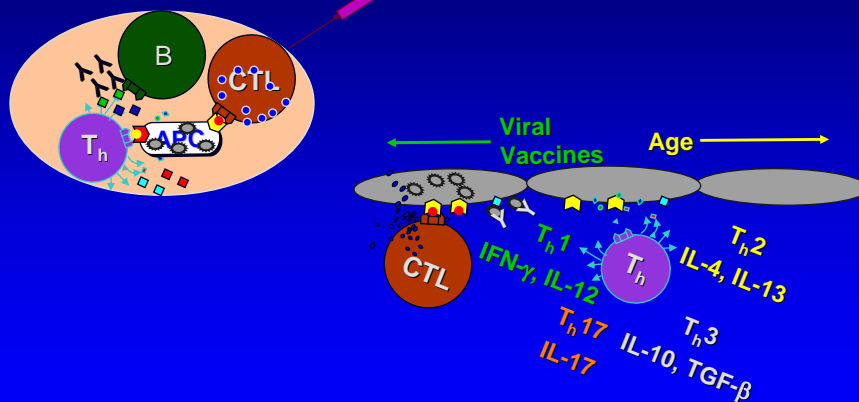


Cellular Immunity in Aging and HIV: *Correlates of Protection*

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Immune Senescence



Correlates of Protection: Targeting the appropriate immune response

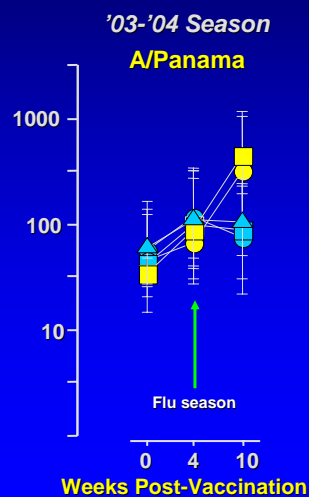
- ❖ **Live-attenuated virus vaccines**
 - Stimulate a response that is similar to natural infection
- ❖ **Killed virus vaccines**
 - Stimulate neutralizing antibodies and CD4+ T helper cells but not CD8+ cytotoxic T lymphocyte responses
- ❖ **Replication defective virus-based vaccines**
 - Stimulate CD4+ T helper and CD8+ cytotoxic T cells responses but poor neutralizing antibody titers
- ❖ **Testing responses to vaccination**
 - Serologic responses - neutralizing antibody titers or equivalent
 - Cellular immune responses
 - ❖ Measure or restimulate virus-specific T cell memory
 - ❖ T-cell proliferative capacity and correlation with serologic response

Pantaleo G and Koup RA. Nature Medicine 10:806, 2004

Antibody Response to Influenza Vaccination: Correlate of Protection?

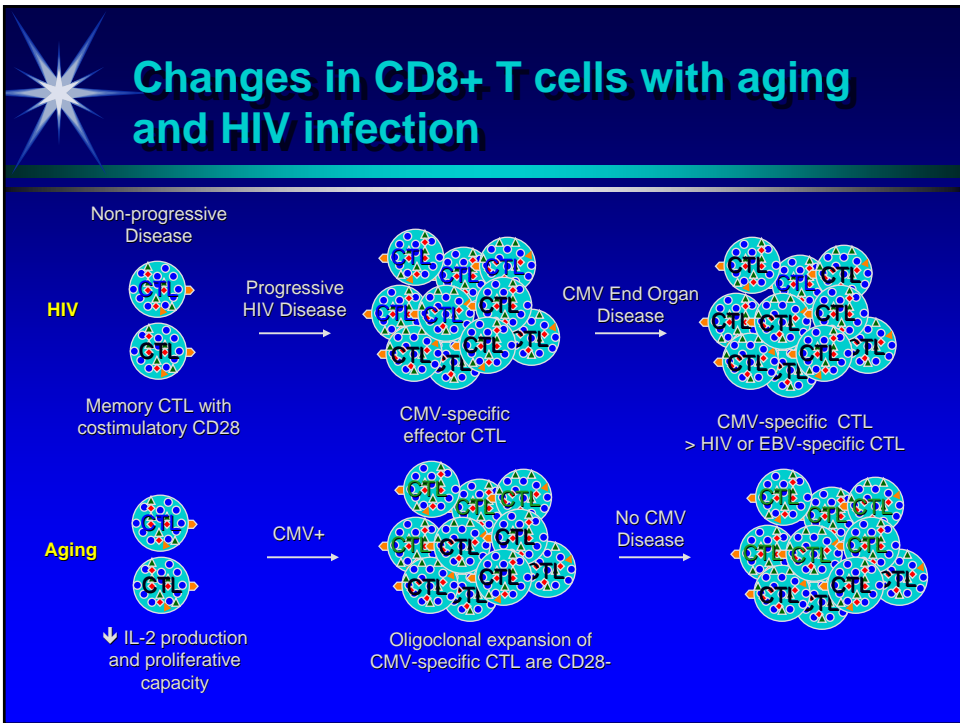
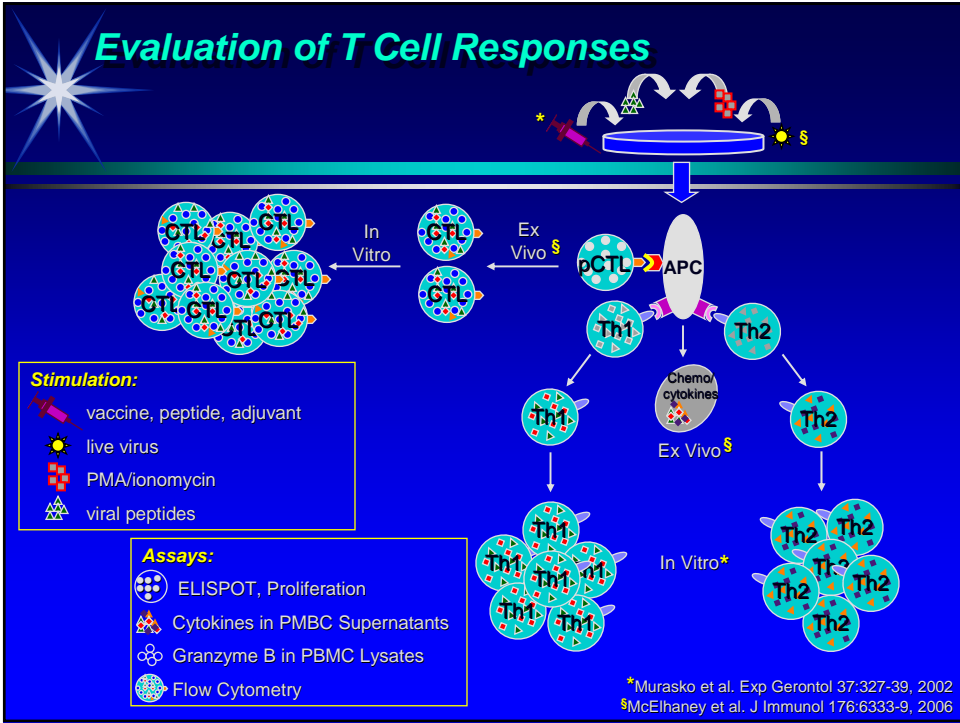
- CHF, flu-
- CHF, flu+
- Old, flu-
- Old, flu+
- ▲ Young, flu-

Antibody
Titer
(GMT)

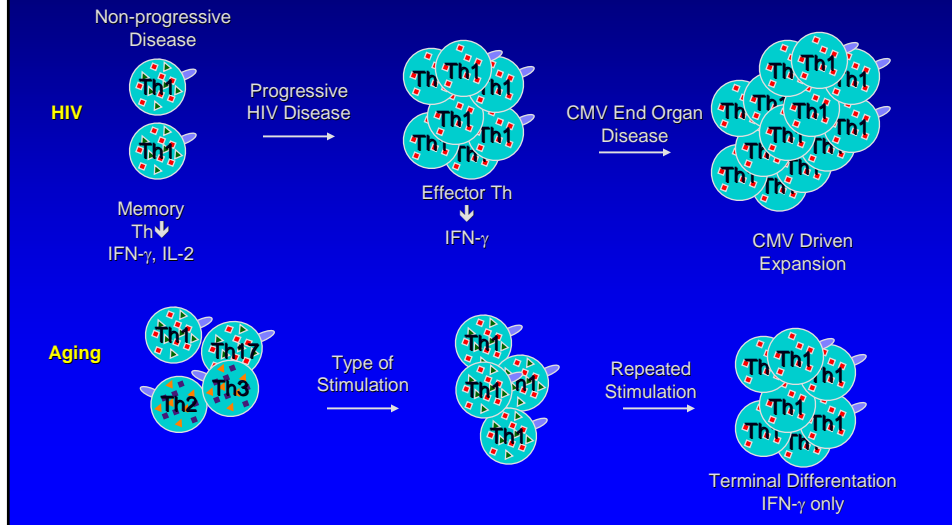


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McElhaney et al. J Immunol 176:6333-9, 2006



Changes in CD4+ T cells with aging and HIV infection



Correlates of Protection: Comparisons of HIV and Aging

- ❖ **CD4+ T-cell responses in non-progressive disease**
 - HIV-specific similar to EBV- and CMV-specific responses
 - IFN-γ and IL-2 production associated with non-progressive disease but decline with aging
- ❖ **CD8+ T-cell responses**
 - HIV-specific similar to EBV- and CMV-specific responses
 - IL-2 production and proliferative capacity maintained with non-progressive disease but decline with aging
- ❖ **Chronic progressive HIV infection**
 - Monofunctional T-cell response with high frequencies of virus-specific CD4+ and CD8+ T cells that secrete IFN-γ; this also occurs with aging
- ❖ **Effectiveness of the virus-specific immune response**
 - Depends more on the quality rather than quantity of CD4+ and CD8+ T cells
 - ❖ HIV-specific CD8+ responses in individuals exposed to HIV remain uninfected
 - ❖ HIV-specific CD4+ responses associated with virus control
 - ❖ Depletion of CD8+ results in loss of virus control and restored with repletion of CD8+ T cells
 - ❖ HIV-specific CD4+ and CD8+ preserved in long-term non-progressors

Pantaleo G and Koup RA. Nature Medicine 10:806, 2004

