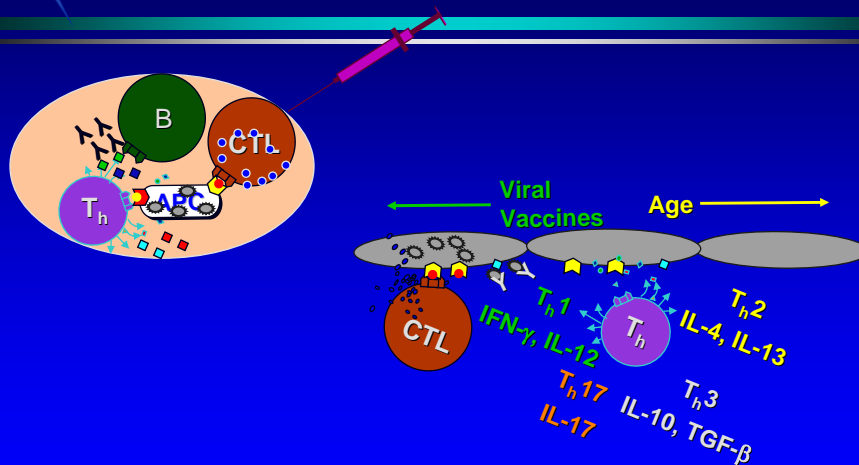


# Cellular Immunity in Aging and HIV: *Correlates of Protection*

Janet E. McElhaney, MD  
Professor of Medicine  
Allan M. McGavin Chair in Research Geriatrics  
University of British Columbia  
Vancouver, BC  
and  
Center for Immunotherapy of Cancer and Infectious Diseases  
Department of Immunology  
University of Connecticut School of Medicine, Farmington, CT

## Immune Senescence



## Correlates of Protection: Targeting the appropriate immune response

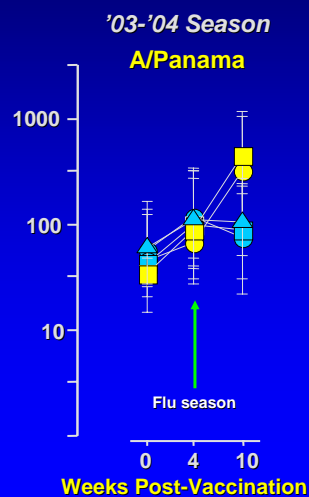
- ❖ **Live-attenuated virus vaccines**
  - Stimulate a response that is similar to natural infection
- ❖ **Killed virus vaccines**
  - Stimulate neutralizing antibodies and CD4+ T helper cells but not CD8+ cytotoxic T lymphocyte responses
- ❖ **Replication defective virus-based vaccines**
  - Stimulate 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?

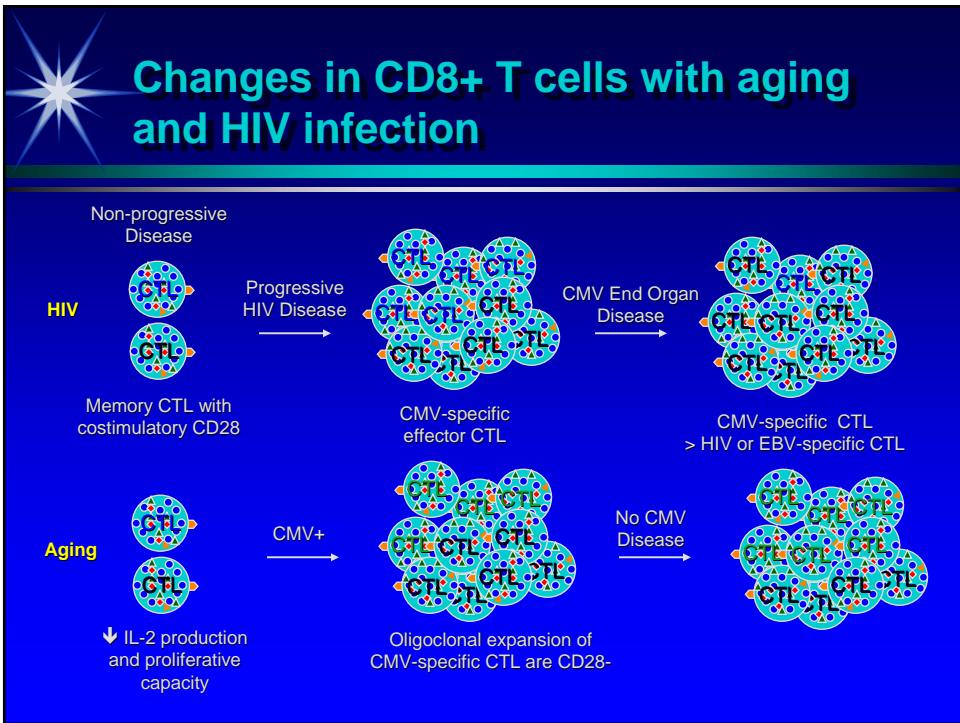
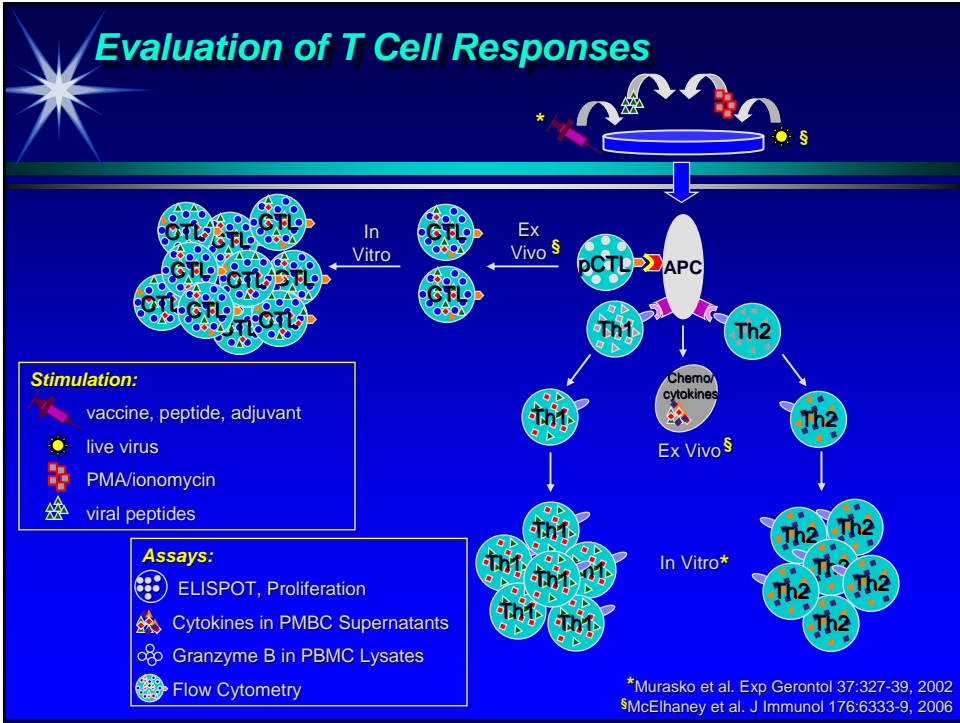
- CHF, flu-
- CHF, flu+
- Old, flu-
- Old, flu+
- ▲ Young, flu-

Antibody  
Titer  
(GMT)

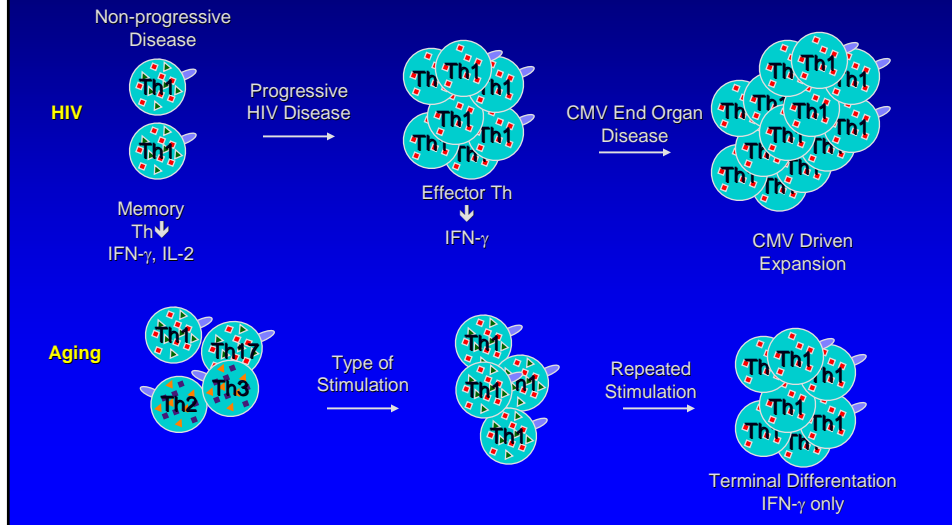


Error Bars = Std Error

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

