

# Assays to evaluate T cell responses

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# Influenza: Outcomes

## *Catastrophic disability*

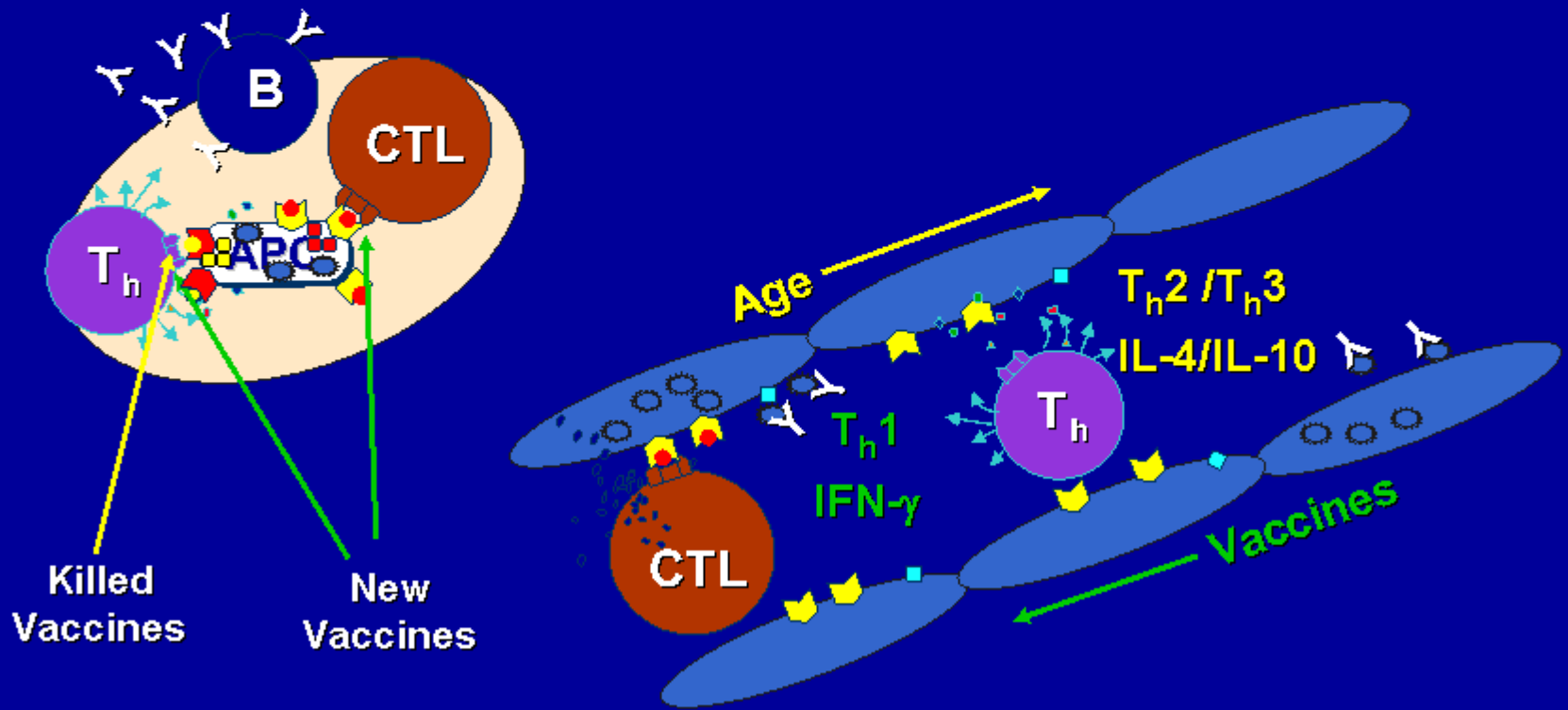
- ❖ Defined as a loss of independence in  $\geq 3$  ADL
- ❖ 72% who experience catastrophic disability have been hospitalized
- ❖ Leading causes of catastrophic disability
  - Strokes
  - CHF
  - Pneumonia and influenza
  - Ischemic heart disease
  - Cancer
  - Hip fracture

Ferrucci et al. JAMA 277:728, 1997

Barker et al. Arch Int Med 158:645, 1998

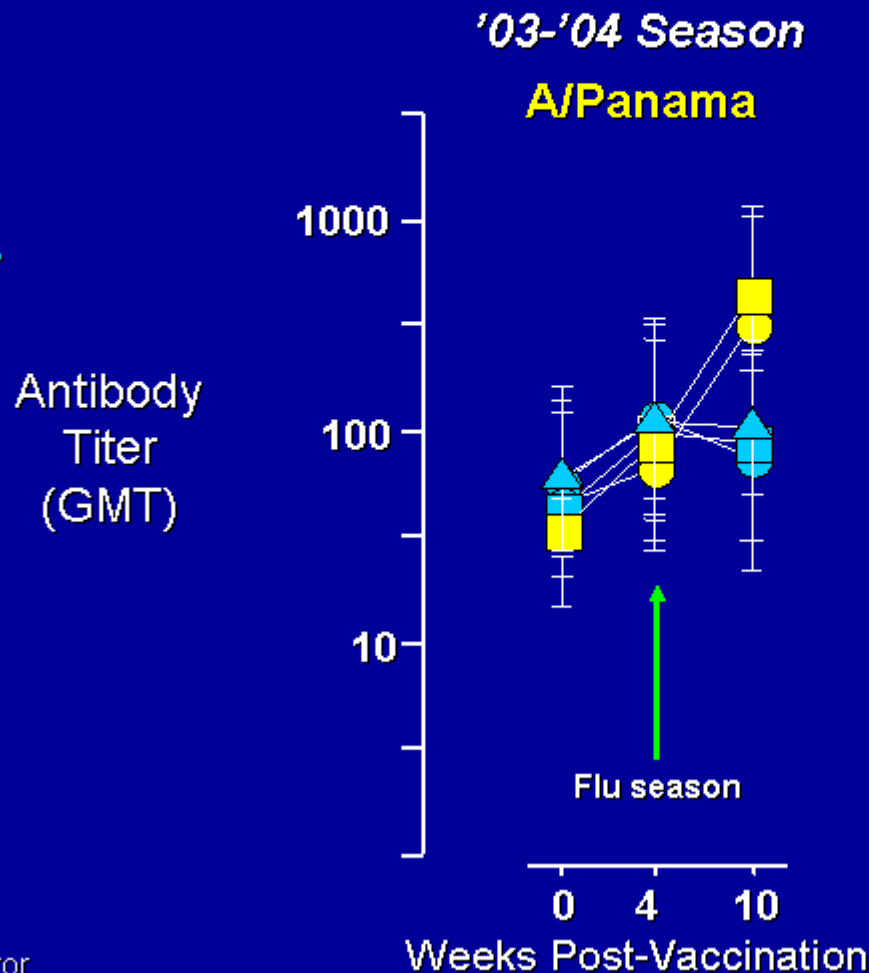
Falsey et al. N Engl J Med. 2005;352:1749

# Targeting Immune Responses



# Antibody Response: Vaccination and Infection

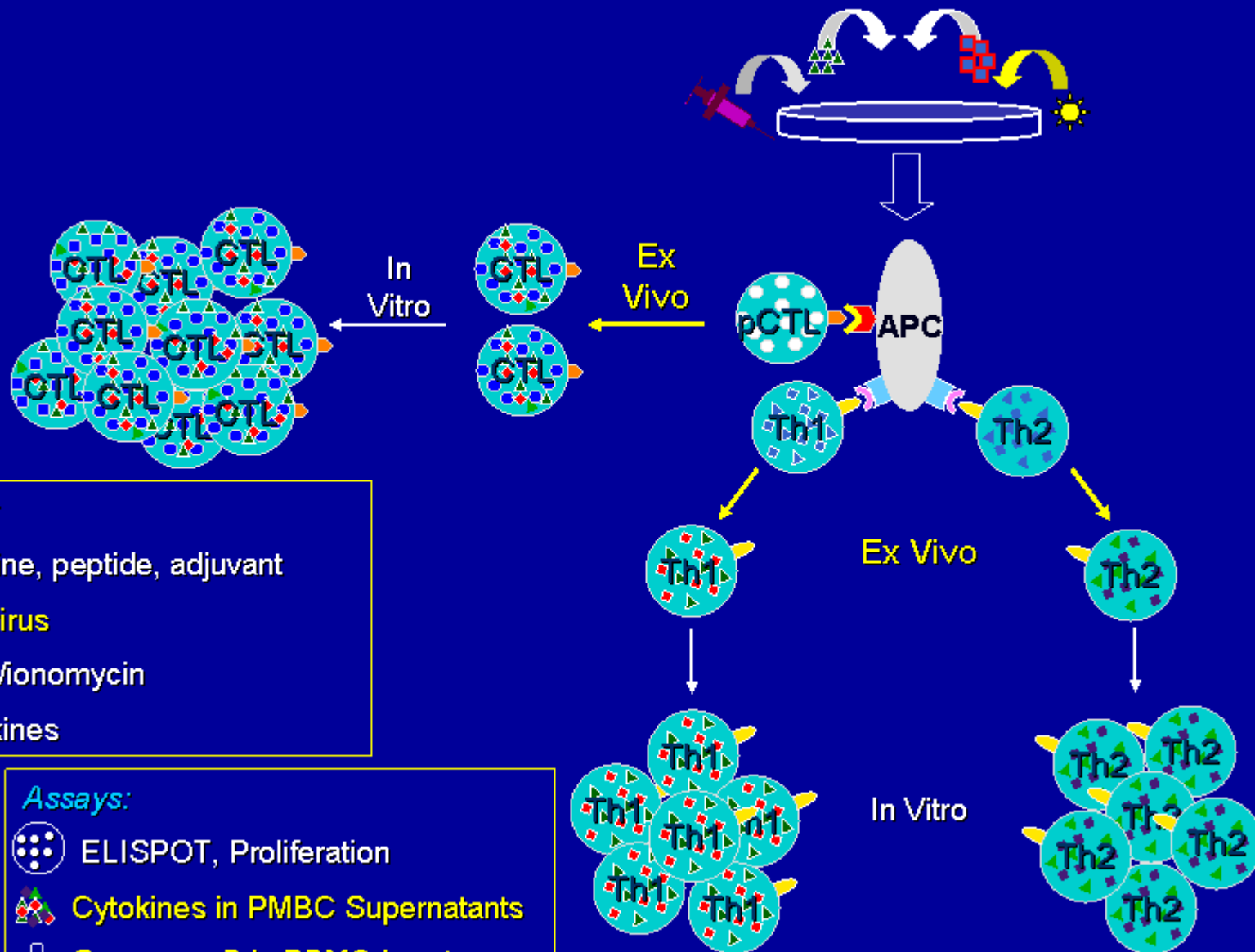
- CHF, flu-
- CHF, flu+
- Old, flu-
- Old, flu+
- ▲ Young, flu-







Error Bars = Std Error

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





# Cell-Mediated Immune Assays



## Stimulation:

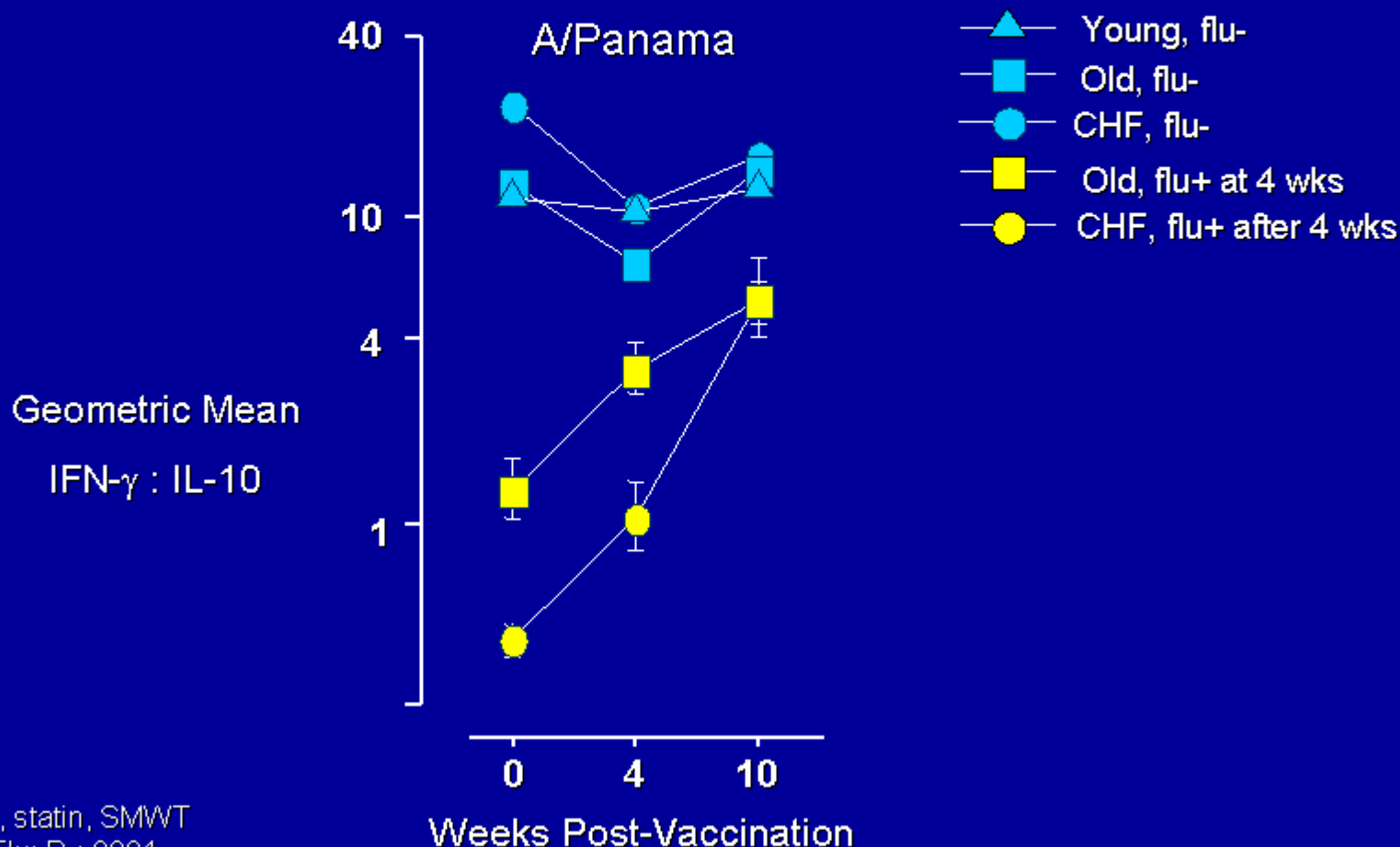
-  vaccine, peptide, adjuvant
-  live virus
-  PMA/Ionomycin
-  cytokines

## Assays:

-  ELISPOT, Proliferation
-  Cytokines in PMBC Supernatants
-  Granzyme B in PBMC Lysates
-  Flow Cytometry

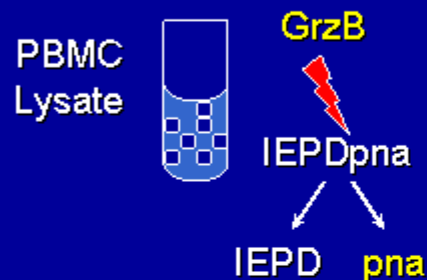
# IFN- $\gamma$ : IL-10 Ratio

## Vaccination and Infection

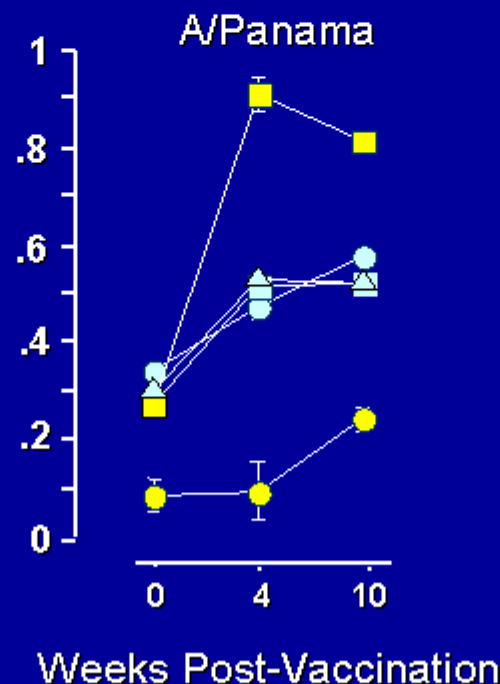


\*Adjusted for ACEI, statin, SMWT  
A/Pan: Flu vs. No Flu:  $P < .0001$   
Error bar: std dev

# Granzyme B Level: Vaccination and Infection\*



Mean Log Grz B  
U/mg protein



- CHF, flu-
- CHF, flu+ after 4 wks
- Old, flu-
- Old, flu+ at 4 wks
- ▲— Young, flu-

\*Adjusted for ACE, statin, SMWT

A/Panama: H3N2 vaccine strain

A/Wyoming: H3N2 circulating strain

# *Unpublished observations*

- After adjustment for baseline antibody titers:
  - antibody responses by hemagglutination inhibition assay do not change with aging
- In ex vivo PBMC stimulated with live influenza virus
  - granzyme B is largely produced by T cells that express degranulation markers consistent with their effector function
  - NK cells are not stimulated to produce granzyme B under these ex vivo conditions



# *Summary*

## *In older adults:*

- HI antibody titers as a sole measure of vaccine efficacy may not predict protection
- Cytokine and granzyme B responses to influenza may complement antibody titers in the evaluation of vaccine efficacy
- There remains a significant margin for improvement of both pandemic and seasonal influenza vaccines - the aging immune system may senesce but memory is not lost!

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