The Mucosal Immune System
Gut-Associated Lymphoid Tissue (GALT)

Effect of aging
Effect of HIV

Rita B. Effros

UCLA MACS
UCLA AIDS Institute
David Geffen School of Medicine at UCLA
Los Angeles, California, USA

The mucosal immune system

Blood contains ~ 2% of total body lymphocytes
Gut is the site of high antigenic exposure
What do we know about the effect of aging on the human gut?
Data from mouse studies

- the gut immune changes appear at younger ages than those in the blood
- frequencies of CD4 T cells and dendritic cells in Peyer's patches decreases with age
- decreased responses to mucosal vaccines
- reduced responses to cholera toxin and E. coli enterotoxin
- decreased helper T cell and cytotoxic T cell activity

The gut and HIV: I

- Regardless of route of transmission, at initial infection, HIV selects CD4+ T cells that also express CCR5
- Most CCR5+ cells are in the gut
- Calculated # of lymphoid cells containing potentially replication-competent HIV-1 DNA
  PBMC 70,000; GALT 100,000
  (Poles et al. JAIDS, 2006)
- Different regions of gut have different “infectibility”
  (P. Anton, unpublished)
The gut and HIV: II

• even if treat early (during acute phase) and blood CD4+ T cells rebound normally, gut remains depleted (Markowitz and colleagues)

• After 3 yrs of therapy that fully suppressed HIV replication, most had only 50% of normal CD4+ T cell number in gut

• Once the infection has become chronic, the CD8+ T cell response in the gut is “too little, too late”: <5% of that seen in any other lymphoid organ

• Long-term non-progressors: prolonged maintenance of mucosal T cells, enhanced virus-specific reponses

The gut and HIV: III

• Successful vaccine must stimulate mucosal immunity

• Mucosal tissue readout to evaluate vaccines

• HIV and colorectal cancer:
  present with more advanced case at younger age
  more adenomas found at younger age

• start screening at younger age
HIV and bone loss: are immune cells involved?

- Activated T cells secrete factors that affect osteoclasts
- Immune activation associated with bone loss
- Osteoporotic fractures correlate with increased proportions of senescent CD8 T cells
- Oxidized LDL stimulate T cells