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PART VI
IMPLICATIONS FOR THERAPIES

Background

- Current HIV and aging treatment advice: Start ART early and manage traditional risk factors for non-AIDS-related diseases aggressively
- Treatments to reverse poor CD4+ T-cell recovery and inflammation are essential

Interleukin-7 (IL-7)

- Synthetic version of natural cytokine
- Prompts the immune system to generate naive and memory CD4+ and CD8+ T cells
- Unlike IL-2, studied in early HIV trials, IL-7 does not cause serious flu-like symptoms
- Reduces markers of inflammation and immune activation
- Future of development unclear

Levy Y, Sereti I, Tambussi G, et al. Effects of rhIL-7 on T cell recovery and thymic output in HIV-infected patients receiving antiretroviral therapy: results of a phase I/IIa randomized, placebo controlled, multicenter study. Clin Infect Dis. 2012 Jul;55(2):291–300.

Sereti I, Estes J, Thompson W, et al. Gut mucosa T lymphocyte restoration in chronically HIV+ patients treated with recombinant interleukin-7 (Abstract 94). Paper presented at: 19th Conference on Retroviruses and Opportunistic Infections; 2012 March 5–8; Seattle, WA.

SB-728-T

- Gene therapy from Sangamo BioSciences
- Involves extracting CD4+ T cells, modifying them to stop expression of HIV coreceptor CCR5, then expanding and reinfusing them
- Phase I studies in INRs reported sustained CD4+ T-cell count increases and improvements in CD4+ to CD8+ T-cell ratios
- Company now focused on trials aiming to achieve a functional cure of HIV infection

Lalezari J, Mitsuyasu R, Deeks S, et al. Successful and persistent engraftment of ZFN-M-R5-D autologous CD4 T cells (SB-728-T) in aviremic HIV-infected subjects on HAART (Abstract 46). Paper presented at: 18th Conference on Retroviruses and Opportunistic Infections; 2011 February 27–March 2; Boston, MA.

Anti-Inflammatories

- Statins (class of cholesterol drugs)
- COX-2 inhibitors (NSAIDs)
- Angiotensin II receptor agonists (hypertension and heart failure drugs)
- PPAR-gamma agonists (class of diabetes drugs)
- Phosphate-binding agents (sevelamer)
  - Potential to halt “leaky gut” syndrome, a possible contributor to inflammation

Exercise and Diet

- Moderate exercise long established to be beneficial for health and longevity
  - Multiple studies: may lead to declines in levels of senescent T cells
- Mediterranean diet can significantly reduce risk of cardiovascular disease
  - Great potential for PLWHIV

Safer Antiretrovirals

- Role of ART toxicities in aging process remains theoretical
- Nevertheless…
  - Reinforces need for new drugs with improved safety, and clinical trials exploring first-line regimens that don't include NRTIs or PIs
- Ultimate means of eliminating ART—a cure for HIV infection—must remain a major priority

Other Research Goals

- Define safe and effective prevention strategies and treatments for:
  - Coinfections (particularly hepatitis C)
  - Cancers
  - Cardiovascular and pulmonary diseases
  - Liver and kidney impairment
  - Decreasing bone mineral density and increasing bone fracture risk
  - Neurologic and neurocognitive disease

Other Research Goals

- Define interventions to reduce behavioral risk factors of aging-related illnesses
  - Smoking, illicit drug use
- Develop strategies to minimize interactions between ARVs and drugs used to prevent or treat other diseases
- Best practices to overcome barriers preventing older PLWHIV from getting full access to care and services

OAR HIV and Aging Working Group

- Formed by Office of AIDS Research in response to community-driven advocacy effort
  - Coalition for HIV Aging Research and Policy Advocacy (CHARPA) sign-on letter to NIAID highlighting importance of HIV and Aging research
- Working group recommendations for future research published in *JAIDS*

OAR HIV and Aging Working Group

- OAR recommendations encompass all issues described in this presentation and the *Immune System, HIV, & Aging* report
- Crucial for advocates to ensure recommendations are followed

High K, Brennan-Ing M, Clifford D, et al. HIV and aging: state of knowledge and areas of critical need for research. A report to the NIH Office of AIDS Research by the HIV and Aging Working Group. J Acquir Immune Defic Syndr. 2012 Jul 1;60 Suppl 1:S1–18.

Summary

- Treatments for CD4+ T-cell recovery and inflammation being explored
- Diet and exercise important
- Safer ARVs and cure for HIV required
- Research defining prevention and treatment strategies for age-related complications essential
- Need to ensure OAR HIV and Aging Working Group recommendations are being met

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