

Honors/Awards

- Institute of Medicine, National Academy of Sciences, Section: Biological and Basic Biomedical Sciences - elected 1996
- Pioneer in NeuroVirology Award, International Society for Neuro-Virology, 2003
- J. Allyn Taylor International Prize in Medicine, 1997
- Biomedical Science Award for Contributions in Autoimmunity, Karolinska Institute, Huddinge, Sweden, 1994
- Rous-Whipple Award for Research Excellence in Investigative Pathology, American Association of Pathologists, 1993
- Abraham Flexner Award for Contributions in Biomedical Research, Flexner Foundation, Vanderbilt University, 1988



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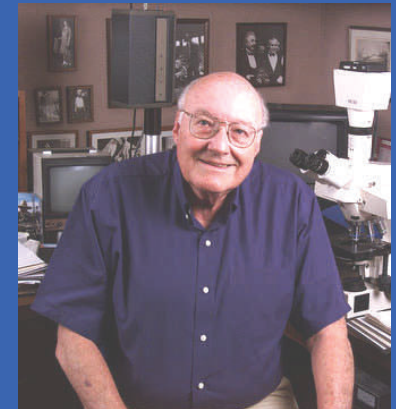
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CCTS ACADEMY DISTINGUISHED SEMINARS

**“Darwin’s Nose
-- How to Cure
a Persistent
Viral Infection:
Role for IL-10”**



Date: 09/20/07
(Thursday)

Time: 4:00 PM

Venue: COMRB auditorium
Following seminar, there will
be a reception in the lobby.
All are welcome!!!!!!

“Darwin’s Nose -- How to Cure a Persistent Viral Infection: Role for IL-10”

Dr. M. Oldstone

Multifunctional antiviral specific T cell responses are associated with control of virus infections but are missing in viral persistence. The cytokine IL-10 induced by viruses that persist is the initial and the master regulator of immunosuppression that characterize persistent infections. Antibody blockage of IL-10 late in infection when antiviral T cells are exhausted result in restoration of effector antiviral T cell response, thus allowing the resurrected T cells to purge the infecting agent. Further, this process is followed by development of immune memory. Interestingly, the constraints imposed by high levels of IL-10 during an established persistent virus infection retards the efficacy of therapeutic vaccination. Alleviation of the immunosuppressive environment coupled with vaccination restores multifunctional antiviral T cell responses thereby permitting such cells to control infection and defines how to successfully use vaccines to treat persistent virus infections.

Select References

1. **Oldstone MB.** A suspenseful game of 'hide and seek' between virus and host. *Nat Immunol.* 2007 Apr;8(4):325-7.
2. Brooks DG, Trifilo MJ, Edelmann KH, Teyton L, McGavern DB, **Oldstone MB.** Interleukin-10 determines viral clearance or persistence in vivo. *Nat Med.* 2006 Nov;12(11):1301-9. Epub 2006 Oct 15.
3. Trifilo MJ, Yajima T, Gu Y, Dalton N, Peterson KL, Race RE, Meade-White K, Portis JL, Masliah E, Knowlton KU, Chesebro B, **Oldstone MB.** Prion-induced amyloid heart disease with high blood infectivity in transgenic mice. *Science.* 2006 Jul 7;313(5783):94-7.
4. Brooks DG, McGavern DB, **Oldstone MB.** Reprogramming of antiviral T cells prevents inactivation and restores T cell activity during persistent viral infection. *J Clin Invest.* 2006 Jun;116(6):1675-85. Epub 2006 May 18.
5. Chesebro B, Trifilo M, Race R, Meade-White K, Teng C, LaCasse R, Raymond L, Favara C, Baron G, Priola S, Caughey B, Masliah E, **Oldstone M.** Anchorless prion protein results in infectious amyloid disease without clinical scrapie. *Science.* 2005 Jun 3;308(5727):1435-9.
6. Hahm B, Trifilo MJ, Zuniga EI, **Oldstone MB.** Viruses evade the immune system through type I interferon-mediated STAT2-dependent, but STAT1-independent, signaling. *Immunity.* 2005 Feb;22(2):247-57.
7. Zuniga EI, McGavern DB, Prunedo-Paz JL, Teng C, **Oldstone MB.** Bone marrow plasmacytoid dendritic cells can differentiate into myeloid dendritic cells upon virus infection. *Nat Immunol.* 2004 Dec;5(12):1227-34.
8. Sevilla N, McGavern DB, Teng C, Kunz S, **Oldstone MB.** Viral targeting of hematopoietic progenitors and inhibition of DC maturation as a dual strategy for immune subversion. *J Clin Invest.* 2004 Mar;113(5):737-45.

In the course of persistent infection, at a time when LCMV-specific CD8+ and CD4+ T cells are 'exhausted', treatment of the mice with a blocking antibody to the IL-10 receptor can restore, in a 'Lazarus-like' way, the function of previously unresponsive T cells and thereby limit or completely cure the infection²⁸. The potential of using antibodies specific for host immunoregulatory molecules involved in immune suppression, such as IL-10 and the IL-10 receptor, suggests a new approach for treating persistent infections.

Nature Immunology 2007