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## HIV-1 Latency in Memory T cells

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**Background:** Central memory, CD4<sup>+</sup> T lymphocytes (TCM) harbor the majority of latent HIV-1 proviruses in vivo. We have developed a latency assay based on cultured TCM cells. We have so far identified two signaling pathways that can reactivate latent viruses in cultured TCM: antigenic stimulation and incubation with IL-2+IL-7. Antigenic stimulation reactivates virtually all latently infected cells, and successfully depletes the reservoir. Despite the potency of antigenic stimulation, anti-CD3/CD28 treatment has been shown to exert deleterious effects in the host. In contrast, IL-2+IL-7 incubation reactivates one tenth of the latently infected population, while inducing homeostatic cell proliferation. Consequently, cells are able to proliferate in response to IL-2+IL-7 stimulation, in the absence of viral reactivation, thus propagating latent proviruses through mitosis. Thus, other signaling pathways need to be identified. This work describes a third pathway that we have recently identified, in which massive viral reactivation is achieved with minimal T cell activation.

**Methods:** We have used a high-throughput variation of our published assay of viral latency in TCM, and identified novel candidate compounds that reactivate latent HIV-1. The biological properties of candidate compounds from the screen were further investigated in order to examine their ability to induce activation markers (CD25 and CD69) and proliferation. This was done in parallel with antigenic stimulation and homeostatic proliferation inducers as a comparison.

**Results:** We have identified a compound ("C7") which, when incubated with latently infected TCM cells at nanomolar concentrations, displays viral reactivation ability that is about 80% of that with anti-CD3/CD28. The activation profile of the C7-treated cells was indistinguishable from that of untreated cells as evidenced by a lack of increase in the expression of CD25 and CD69. C7 induced proliferation although at much lower levels than anti-CD3/CD28 treatment did.

**Conclusions:** We demonstrate the existence of compounds that can reactivate latent HIV in TCM cells with comparable efficiency to antigenic stimulation, but with very limited or no ability to induce the expression of activation markers. These results demonstrate that signaling pathways exist, which can be specifically lead to activation of latent proviruses in primary cells. Key signaling elements controlling these pathways should be considered as novel targets.

### Biography

Vicente Planelles obtained his Ph.D. from the University of California at Davis in 1991 and then conducted postdoctoral studies at UCLA until 1995. Between 1996 and 2002 he was Assistant Professor at the University of Rochester. In 2002 he became Associate Professor at the University of Utah School of Medicine, and in 2008 he became Professor of Microbiology and Immunology. He has published more than 80 papers and reviews on many aspects of HIV-1 and related lentiviruses.

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