mass produce these treatments for use in low-income countries at a cost close to the cost of production, with a small royalty paid back to the pharmaceutical companies. This is the same mechanism used to sell vaccines in low-income countries. In some countries, reductions in the price of HIV-1 treatments were only achieved after long legal battles with pharmaceutical companies. In some cases, countries overturned company patents on drugs and started importing generic drugs at lower costs—so-called compulsory licensing—which is permitted in cases of national medical emergencies.

Creating a new funding mechanism for poor nations is difficult in the current economic climate, but HIV has left a legacy of structures ready to adapt to hepatitis C to complement government and private-sector efforts. UNITAID, the United Nations agency created in 2006 to overcome market barriers for treatments of HIV, tuberculosis, and malaria, recently announced its first funding for hepatitis C, with an aim of reducing treatment costs to $500 to $1000 per patient (14). It plans to scale up treatment through a multinational group of HIV programs run by Médicins Sans Frontières, the international medical humanitarian organization. The Global Fund, which addresses HIV/AIDS, tuberculosis, and malaria, has funded treatment programs with old-generation HCV drugs in several developing countries for the past 3 years.

If we can learn from the lessons of HIV/AIDS, mass production of generics can save millions of lives. This has been an inspiring medical success story which need not stand alone but can be repeated, even more rapidly, for hepatitis C.

REFERENCES AND NOTES


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HIV/AIDS

Persistence by proliferation?

Latently HIV-infected cells driven to proliferate may raise a further challenge for eradication strategies

By David Margolis* and Frederic Bushman

The persistence of HIV-1 infected cells in individuals on antiretroviral therapy (ART) presents an obstacle for cure of infection. ART is the best available remedy for millions of infected people, but treatment must be lifelong because HIV establishes latent infection that is unaffected by antiretrovirals and is invisible to immune surveillance. Because decades of treatment may be unsustainable, there is intense interest in reverting latency. If quiescent HIV in CD4+ T cells can be identified and activated without enhancing new infection, HIV-targeted immune response might be able to control or even clear infection. On page 179 in this issue and in this week’s Science Express, Maldarelli et al. (1) and Wagner et al. (2), respectively, raise a new challenge for these efforts suggesting that proliferation of latently infected cells may be a key factor in sustaining this durable viral reservoir.

Latent HIV proviruses (viral genome integrated into the host cell DNA) are found most often in resting CD4+ T cells within the central memory arm of the immune system (3–5), although other T cell subpopulations have been implicated (6, 7). The latent pool shows minimal or absent decay (8), which is not fully understood. One possible explanation is that ongoing low-level HIV replication during ART replenishes the pool. However, viral genetic diversity does not increase over time in individuals during ART (9), at odds with this view.

Other evidence suggests that virus emerges from the pool of latently infected cells periodically. Even patients whose viral load is well suppressed show intermittent bursts of viremia (“blips”), and in many patients viremia is detectable in specialized assays (10, 11). Given that the pool of latently infected cells must be primarily established before ART, it is difficult to understand why such periodic induction of the pool does not lead to it running dry.

Homeostatic proliferation of infected transitional memory T cells (6) has been proposed as a source that could maintain the pool, but this does not explain persistence in the dominant central memory reservoir. Latently infected stem cell–like memory T cells could proliferate (7), and it will be of great interest to compare integration patterns seen in these cells and in more differentiated cell populations.

Maldarelli et al. and Wagner et al. harvested DNA from the blood cells of HIV-infected individuals after a decade of successful ART, and analyzed the distribution of sites of proviral integration in the human genome. Typically, HIV favors integration in regions of the genome that are transcriptionally active (12), but a unique pattern was seen in rare proviruses from well-suppressed patients. Both groups found expanded proviral clones that were enriched for proviruses in or near a limited set of cellular genes, some of which

REFERENCES
