

A broad rejuvenation

As World AIDS Day approaches, and the thirtieth anniversary year of the isolation of HIV draws to a close, it is timely to reflect on the past, present and future of HIV/AIDS research.

In a Timeline article on page 877 of this issue, Françoise Barré-Sinoussi and colleagues reflect on the past, present and future of HIV research. Along with her colleague Luc Montagnier, Barré-Sinoussi was awarded one-half of the Nobel Prize for Physiology or Medicine in 2008, for the isolation of HIV 25 years previously. The Timeline provides a brief historical overview of some of the major milestones in HIV research, with an emphasis on the ways in which translational, multidisciplinary research has transformed HIV treatment and prevention. As another World AIDS Day is on the horizon and the thirtieth anniversary year of the isolation of HIV is on the wane, we wanted to take this opportunity to take a brief look at how much the field has progressed during the past three decades, in particular, the rejuvenation that has taken place over the past 5 years.

First, the statistics — the headline figures in the latest UNAIDS Report on the global AIDS epidemic¹ are encouraging. In 2012, there were ~2.3 million new HIV infections worldwide, which represents a decrease of 33% since 2001. The number of AIDS-related deaths in 2012 was ~1.6 million, which has reduced from a peak of ~2.3 million in 2005. Although the number of individuals who are infected with HIV/AIDS has reached a high of ~35.3 million, this reflects the success of antiretroviral therapy (ART) regimens, and the increased access to these regimens in low- and middle-income settings.

The increasing success of ART has led to a recent shift in the global landscape of HIV/AIDS research, such that the idea of achieving an AIDS-free world has begun to be mooted with a level of cautious optimism that would have been unthinkable even 5 years ago². This shift is mostly due to recent positive results, such as those of the HIV Prevention Trials Network (HPTN) randomized controlled trial, which proved that early administration of ART can reduce the rate of sexual transmission of HIV-1 (REF. 3). Furthermore, HIV screening and ART as a means to prevent mother-to-child transmission is finally paying off, although there is still much work to do in resource-poor settings. Treatment as prevention is a promising policy strand for the future, although there are still major implementation issues to solve.

In addition to increasing or modifying access to current therapies, many new therapeutic options are also being investigated. Along with eradicating the latent

reservoir and obtaining a ‘functional cure’, one of the most talked about areas is the rejuvenation of research on broadly neutralizing antibodies (bNAbs). bNAbs, which target the HIV envelope glycoproteins, were first identified around 20 years ago. Although they were initially thought to be a promising therapeutic avenue, they proved extremely difficult to isolate and the early optimism faded. However, the combination of new screening and antibody-cloning technologies has led to a renaissance in bNAb research and identification during the past 3 years, and it is now known that potent bNAbs are present at very low levels after ~2–4 years of infection in 10–30 % of HIV-infected individuals⁴. Their presence in naturally infected individuals gives hope for their incorporation into both passive and active immunization regimens, and great progress has been made in characterizing these agents and their viral binding sites and in testing their immunotherapeutic applications. As an example, two very recent papers^{5,6} show that combinations of potent bNAbs can suppress simian–human immunodeficiency virus (SHIV) replication in chronically infected rhesus macaques, and one antibody (known as PGT121) was able to potentially suppress viral replication alone⁵. In addition, the new focus on bNAbs has given the vaccine development field a great deal of food for thought, and there is optimism that the vast amount of data on bNAbs will enable the development of a rationally designed vaccine.

Barré-Sinoussi and colleagues invoke the legacy of Louis Pasteur as a supporter of interdisciplinary research who, they say, “advocated the value of interaction between the laboratory and the public health clinic.” The recent rejuvenation in translational HIV/AIDS research, which involves virologists, structural biologists, immunologists and clinicians — to name just a few — has proven the great value of an interdisciplinary approach.

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1. UNAIDS report on the global AIDS epidemic. [online] http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf (2013).
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4. Kwong, P. D., Mascola, J. R. & Nabel, G. D. *Nature Rev. Immunol.* **13**, 693–701 (2013).
5. Barouch, D. H. *et al. Nature* <http://dx.doi.org/10.1038/nature12744> (2013).
6. Shingai, M. *et al. Nature* <http://dx.doi.org/10.1038/nature12746> (2013).