HIV Cure Research: An example of successful advocacy by scientists for science

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Following medical school and an internal medicine residency in Toronto, and infectious diseases training at the New England Medical Center/Tufts University in Boston, Jonathan joined the Division of Infectious Diseases, Department of Medicine at the Ottawa General Hospital in 1995. His research focuses on understanding how HIV damages the immune system and how these insights may lead to new therapies. Jonathan is currently Professor of Medicine, University of Ottawa and Senior Scientist, Ottawa Hospital Research Institute. He was Editor-in-Chief of CIM from 2010–2015.

Since the start of my career as an Infectious Diseases specialist in Ottawa in 1995, nothing has had a greater influence than the discoveries and progress made in addressing the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic. Since the initial reports of cases of AIDS in New York and San Francisco in 1981, and the eventual recognition of the disease's devastating global impact, unprecedented research efforts soon followed. The discovery in 1983 of the virus that causes AIDS, ultimately named the human immunodeficiency virus, and the development of an assay to detect antibodies to HIV as a diagnostic test, quickly led to rapid expansion of HIV clinical research and the execution of a great many clinical trials of treatments for HIV and its complications.

In Canada, 1990 saw the launch of the National AIDS Strategy and the announcement of the Canadian HIV Trials Network (CTN) with the commitment of tens of millions of dollars to HIV research. The CTN, created to support the development and conduct of clinical trials, facilitated access to life-saving drugs to hundreds, if not thousands of Canadians suffering from the complications of HIV disease. As my early introduction to HIV research, this was a clear and first-hand example of how clinical research saved lives.

While major efforts have been made over the past three decades in the development of biomedical preventative strategies, and in particular in the areas of vaccines and microbicides, successes have not been realized as rapidly as initially hoped or anticipated. On the other hand, advances in the discovery and evaluation of antiretroviral therapies have occurred at an unprecedented pace. By the late 1990s, "triple drug therapy" had dramatically decreased the morbidity and mortality associated with HIV infection, and today, almost everyone with access to care and treatment can be effectively treated with a relatively non-toxic, well tolerated single tablet regimen and expect to live a normal or near-normal life expectancy.

With the availability of easy-to-take, lifesaving medications, and the apparent diminished need for addition-

al or novel antiretrovirals or immune-based therapies, there was a sense that opportunities for research into newer therapies would shrink. In addition, there was a concern that the basic studies of HIV pathogenesis were in less demand (i.e., less likely to be funded) as the widespread use of near perfect antiviral agents reduced the perceived need to understand the mechanisms by which HIV caused progressive immunodeficiency. With a sense that future investments in HIV research could be drying up, HIV scientists would not be resigned to see this happen.

In the late 1980s and early 1990s, it was largely the HIV community that drove the federal governments to support (i.e., fund) HIV policy, programming and research. This was, in part, a result of ongoing demand for improved access to HIV drugs. More recently, it has been researchers who have influenced major funding commitments in HIV research.

In 2009, the case of Timothy Brown, "the Berlin patient", was published in the New England Journal of Medicine. After receiving a stem cell transplant for acute myeloid leukemia from a donor who was homozygous for the CCR5 delta 32 mutation, Timothy Brown became the first person (and only one so far) to be effectively cured of HIV infection. Based on the possibility that a cure for HIV was an achievable goal, a number of high profile scientists, under the auspices of the International AIDS Society, guided the development of a global scientific strategy, "Towards an HIV Cure". Launched in 2012, the aim of the global scientific strategy is "to contribute both to maximizing resources and strategic investment in the most promising strategies in search of a cure, and to the establishment of an international research alliance and/or expansion and global collaboration of existing consortia. Within the Global Scientific Strategy, the international group of scientists identified seven priority research areas, spanning basic science in virology and immunology, preclinical science and clinical trials. The seven priority research areas are:1) Cellular and viral mechanisms that maintain HIV persistence, 2) Tissue and cellular sources of persistent SIV/HIV [simian immune deficiency virus, SIV] in animal models and long term ART-treated individuals [antiretroviral therapy, ART] in animal models and long term ART-treated individuals, 3) Immune activation and dysfunction in the presence of ART, 4) Natural models of HIV/SIV control, 5) Assays to measure persistent infection, 6) Therapeutic and immunological approaches for eliminating persistent HIV infection, and 7) Enhancement of immune response to control viral replication".

Most, if not all, of the scientists behind the Towards a Cure strategy, have had successful research careers in the area of HIV viral and immune pathogenesis. These seven priority research areas largely represent a "repackaging" of HIV pathogenesis work–now with the ultimate aim of "curing" HIV infection. This is, perhaps, a unique example of how scientists have rapidly, collectively and in an organized fashion, dictated the direction of an entire field of research and did so with overwhelming success.

This effort from these scientists, with support from research stakeholders, funders and leading advocates, including people living with HIV, has reinvigorated biomedical and clinical HIV research and has lead to major new investments in HIV research. Locally, this included a $10 million commitment from the Canadian Institutes of Health Research in partnership with the Canadian Foundation for AIDS Research and the International AIDS Society to support large research teams focused on HIV cure research; a program from which my own research career has directly benefited. Much larger commitments have been made in the United States and elsewhere around the globe. In addition to successfully maintaining high levels of HIV funding, widespread support for HIV cure research is also reflected in the creation of scientific journals dedicated to this line of investigation and the occurrence of multiple conference that have evolved or been created to address this topic.

Whether or not the existing enthusiasm for HIV cure research has given unrealistic hope to people living with HIV will only be determined with time. While the scientific community may understand that sustained viral remission and viral eradication represent two distinct types of HIV cure, this is not necessarily the case for individuals living with HIV or the general public for whom the term "cure" is typically equated with eradication of every last bit of virus from the body. As there is considerable scepticism as to whether a sterilizing cure will ever be found, it will be important for the HIV community and funders to understand that the discovery of an effective

and scalable approach that results in viral remission will demonstrate that the time and money dedicated to find an HIV cure has been a worthwhile investment. And that advocating for increased and dedicated research dollars is not (as it may appear) self-serving, but rather serves the community at large.

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