

## **Basic Science and HIV/AIDS: Perspectives from the Past and Prospects for the Future**

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From 25 to 26 years ago (1983-84) HIV was first isolated at the Institute Pasteur (IP) by the Montagnier group, and by our group then at the National Cancer Institute (NCI) and shown to be the cause of AIDS. Several of our isolates of HIV were grown in continuous culture making an accurate global blood test possible as well as enabling HIV genomic analysis, cellular tropism, body distribution, modes of transmission, and variability (1984-85) by contributions from both groups. Other major advances soon followed, including the beginning of effective anti-viral therapy (a first in medicine) by another NCI group by 1986, and ultimately (by 1995) the huge advances in treating HIV and preventing mother to child transmission.

The lessons from this early period center on preparedness. In this report I will argue that despite the fact that the pace of discovery between 1982-85 was perhaps the fastest in medical history from the time of inception of a new complex disease and that basic science achieved two major practical advances (the blood test and effective anti-HIV therapy), nonetheless (1) we were far from prepared for the HIV epidemic; (2) most of the individuals or groups who made the early contribution did so almost by chance; (3) society regularly forgets the lessons of past major epidemics after an absence of some 20-30 years; and (4) we need multiple centers of excellence in virology that cover the breadth of human viral pathogens.

Three great needs remain: (1) drug delivery to developing nations (although this has been greatly aided by the U.S. PEPFAR program); (2) a "cure" so as no further therapy is needed by complete viral eradication or in the absence of a cure the continued development of new approaches to therapy because therapy is life-long and consequently can lead to side effects and HIV drug resistant mutants; and (3) a successful vaccine. I will specifically describe the difficulties in HIV vaccine development but some important recent progress made at our Institute with a novel concept. To summarize: the special challenges for a successful HIV vaccine are due to HIV DNA integration, HIV variation, and its early harm to the immune system. Though easy to describe, the challenge is uniquely difficult compared to past successful vaccines. However, most if not all current and past vaccine candidates have not taken these features of HIV into account. What is needed and has been needed for over two decades are: (1) far more availability of primates and to a broader number of scientists; (2) an immune response which is sustained; (3) an immune response which is broad and results in sterilizing immunity or close to sterilizing immunity. Finally, I will describe the characteristics and progress, and remaining problems with a candidate vaccine developed at the Institute of Human Virology.