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Lessons learned in 30 years of HIV vaccine research and the imperative of supporting innovative concepts

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Abstract

Soon after the human immunodeficiency virus (HIV) was isolated and identified as the cause of AIDS in 1983-1984 it was widely expected that an effective vaccine would be rapidly developed. The first paradigm that guided HIV vaccine development was based on the concept that neutralizing antibodies were sufficient to confer protection against HIV infection, and different versions of envelope-based vaccines (mostly gp120) were evaluated. The second paradigm was based on cell-mediated immunity (CMI), resulting in the design of DNA and viral-vectored vaccines. The third and current paradigm is exploring combinations of immune responses and novel approaches. Each paradigm was supported by what was believed at the time to be strong scientific rationale. As we learned more about the complexity of HIV, we recognized that serious judgment mistakes were made because of our incomplete understanding of what constitutes a protective immune response against HIV. In fact, the first two wages (or paradigms) came to an end only with the negative results from large scale efficacy trials (the VaxGen trials in 2003 and the STEP trial in 2007). Paradoxically, a vaccine trial that was opposed by many members of the scientific community (the Thai RV144) was the one that, in 2009, gave the first evidence of vaccine-induced protective immunity. It is essential to explore innovative approaches, and welcome, not dismiss, those that may not conform to current scientific orthodoxy [1]. Innovative concepts, however, lack much of the desirable supporting data, do not have supporting peers and, more importantly, are more likely to fail. In summary, support for innovative research requires a complex “innovation ecosystem” with multiple actors.

Biography

Jose Esparza received his M.D. degree in Venezuela (1968) and a Ph.D. in Virology and Cell Biology from Baylor College of Medicine in Houston (1974). Until 1986, he worked at the Venezuelan Institute of Scientific Research in Caracas, mostly on rotaviruses, becoming the Chairman of the Department of Microbiology and Cell Biology. From 1986 to 2004, he was with the World Health Organization and UNAIDS in Geneva, Switzerland, becoming the Coordinator of their Joint HIV Vaccine Initiative. Since 2004 he has been with the Bill & Melinda Gates Foundation, where he is currently Senior Advisor, Vaccines. He has published over 170 papers.