

The Current State of HIV Vaccine Research

Mariana Varela*

Inflammation College of Medical, Veterinary and Life Sciences, University of Glasgow, Scotland

The development of a vaccine against HIV is a global health priority and a tremendous scientific challenge that has been hampered by the extraordinary genetic diversity of HIV and the immune evasive properties of the HIV envelope glycoprotein to which neutralizing antibodies target. In 2006, Robert Gallo commented: "...if AIDS had to come, we were lucky (scientifically speaking) it came at a very good time" [1]. He referred to the accumulated knowledge on the retroviral replication cycle and the modern tools in molecular biology that were developed in the seventies which became available in the eighties when HIV was discovered. Although the HIV/AIDS epidemics came at a "good time", HIV has proven to be unique in its transmission, pathogenesis and replication, hampering the way to the discovery of a vaccine and effective therapy. It is unquestionable that the tools, resources and international effort invested to prevent HIV infection and end the global pandemic is unprecedented in the history of infectious agents. Despite the development of antiretroviral therapy that can extend the life of infected individuals, these drugs are not widely available in the underdeveloped world and, thus, a therapeutic vaccine would be of great benefit. Unfortunately, traditional vaccination approaches have failed to confer protection and, thus, complex and rational antigen design approaches have been proposed. These have also proven in most cases ineffective when tested in pre-clinical vaccine trials in non-human primates. There are multiple reasons why it has been so difficult to develop a protective vaccine. From the virus perspective, the extreme genetic diversity within and between hosts with the presence of distinct clades affecting different parts of the world, along with circulating

recombinant forms, complicates the design of antigens that can provide protection across different subtypes. From the host point of view, it is still not clear which are the responses that should be developed to confer protection. And from the experimental point of view, which is the best animal model for pre-clinical trials. The bottom line is that we find ourselves 30 years after HIV was discovered under the light of just a single phase III trial where modest protection was observed [2]. Luckily, as scientists we are not convinced that the raw results of this trial and all the downstream analysis including the dissection of the immune correlates of protection, or the investigation of the breakthrough viral population, among others, will provide all the answers needed to generate the ultimate antigen and immunization strategy that will contain this pathogen. We should take this trial as a new beginning to re-evaluate, think and question antigens, strategies and protocols, but most importantly, to help accelerate the advance of candidates into the clinics. This special issue gathers several articles going from antigen development to HIV animal models that aim at updating the current state of HIV vaccine research. Has HIV come at a good time? We still can turn the answer around.

References

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*Corresponding author: Mariana Varela, Inflammation College of Medical, Veterinary and Life Sciences, University of Glasgow, Scotland, Tel: +44 (0) 141 330 2196; E-mail: Mariana.Varela@glasgow.ac.uk

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