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Immune correlates of protection in individuals immunized with HIV cannot help to solve the inverse problem of inducing a protecting anti-HIV immune response in humans

Most solvable scientific problems are downstream; direct problems which involve determining what are the effects that follow certain causes. In contrast, upstream, inverse problems involve determining what the causes of observed phenomena are and these are more difficult to solve because they may have several solutions or none at all. Medical diagnosis, for instance, is an inverse problem that consists in guessing the disease from some of its symptoms, while developing an HIV vaccine is an inverse problem which requires the identification of the multiple causes that sometimes allow a limited number of human immune systems to produce antibody (Ab) or cellular responses that protect against HIV infection. When the epitopes of antigens present in HIV Env glycoproteins are used for immunization, they are given the label "immunogens" which suggests that they are able to generate immune responses, in spite of the fact that they only trigger in the immunized host a series of reactions with B-cell receptors while it is actually the immune system (IS) that produces Abs. Many properties of the IS control the types of Abs that are produced, for instance the host Ab gene repertoire, the presence of helper and suppressor T cells, self-tolerance and numerous other immunoregulatory mechanisms in the host . Unfortunately, vaccine designers using the structure-based reverse vaccinology approach tended to ignore these factors because they focused their attention only on the recognition process between a single HIV epitope and one neutralizing MAb, expecting that an antigenic epitope would also be a good immunogen. As a result, they never succeeded in developing an effective HIV vaccine. Subsequently, a major research effort was undertaken to determine the innumerable antibody maturation pathways that lead from germline Abs to neutralizing Abs, but this also did not solve the inverse problem. In recent years, it has become widely believed that *in vivo* empirical immunogenicity experiments could be the only way to try to solve the inverse problem of how to induce protective immunity against HIV infection by vaccinating humans.

Biography

Marc H V Van Regenmortel has been an Emeritus CNRS Research Director at the University of Strasbourg in France since 2001. He previously held professorship appointments at several Universities in South Africa and France and was the Director of the Immunochemistry department of the CNRS Molecular Biology Institute in Strasbourg for 22 years. He is currently the Editor-in-Chief of *Archives of Virology*, *J. Molec. Recognition* and *J. AIDS & Clin. Res.*, *Associate Editor of Analytical Biochemistry, Frontiers in Immunology, J Immunol Methods* and *Bionomina* .He has published 17 books in Virology and Immunochemistry, 400 research and review papers and co-edited with Brian Mahy for the third edition of the "*Encyclopedia of Virology*" published by Elsevier.

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