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Bioanalytical characterization of HIV gp120 vaccine antigens and its relation to vaccine-induced antibody response

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Abstract

The viral envelope glycoprotein (Env) has been a key target for antibody-mediated vaccine development against Human Immunodeficiency Virus type 1 (HIV 1). Although several recombinant Env-based immunogens have been evaluated in clinical trials, only gp120 proteins (Subtype B, MN, and Subtype A/E, A244) used in ALVAC prime-AIDSVAX gp120 boost RV144 Phase III HIV vaccine trial have contributed to protective efficacy, although modest and short-lived. Therefore, as we selected gp120 protein candidates from Subtype C isolates for a post-RV144 proof-of-concept (POC) Phase I/II trial in Southern Africa, we used a rational selection approach based on several pre-set criteria that included protein productivity, homogeneity, antigenicity, and immunogenicity. This approach led to the identification of two gp120 antigens. Detailed analytical analysis of the two CHO-produced gp120 proteins revealed glycan profiles and occupancy, monoclonal antibody binding and extent (and impact) of heterogeneity during expression. Additional in vitro analysis of the two gp120 protomers (gp120 monomer and dimer) highlighted the disulfide 'scrambling', particularly in V1V2-C1 region, leading to the generation of gp120 dimers. These gp120 dimers not only lacked binding to certain key epitope-directed monoclonal antibodies but also elicited little to no antibody response directed to those epitopes, when immunized in rabbits, in contrast to monomeric gp120. In summary, we highlight the rationale for overall selection of gp120 vaccine antigens based on thorough bioanalytical characterization to assist antigen production for pivotal clinical trials in Southern Africa.

Biography

Antu Dey is Senior Scientist (in Exploratory and Early Clinical Development group) at Novartis Vaccines & Diagnostics. Antu Dey completed his DPhil. in Biochemistry from University of Oxford followed by his post-doctoral training at Weill Cornell Medical College in New York City. His deep interest in biochemical and biophysical characterization of vaccine antigens and rationale vaccine design led him to join Novartis Vaccines in 2008, and since then he has been in positions of increasing responsibility. He has published several patents and peer-reviewed papers and has been serving as an ad hoc reviewer and editorial board member for several journals..