Barna Dey, J Antivir Antiretrovir 2011, 3:4
doi: http://dx.doi.org/10.4172/1948-5964.S1.4

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
VIROLOGY
5-7 September 2011 Baltimore, USA

A bifunctional anti-HIV protein: Delivering a 1-2 punch based on the sequential dual receptor virus entry mechanism

Barna Dey, Laurel A. Lagenaur, Vadim A. Villarroel, Virgilio Bundoc and Edward Berger

Laboratory of Viral Diseases, NIAID, NIH, USA

Viral entry inhibitors have been a major focus of research on HIV prevention and treatment strategies, with the HIV envelope glycoprotein (Env) being the main viral target. Despite the structural variability of the gp120 subunit of Env, its binding surfaces for the primary receptor (CD4) and co-receptor (CCR5 or CXCR4) are highly conserved among diverse HIV-1 isolates. During HIV entry, CD4 interaction exposes the conserved bridging sheet that is critically involved in co-receptor binding, which triggers Env to promote virus entry by direct fusion between the virion and cell membranes. Antibodies against this region are poorly neutralizing due to inacessibility of the corresponding epitopes on the free virus prior to engagement of CD4 on the the target cell. Based on this sequence of receptor interactions, we designed a novel chimeric bifunctional protein called sCD4-17b, consisting of the first two domains of CD4 linked to the single chain Fv region (ScFv) of the 17b human monoclonal antibody whose epitope resides on the conserved, masked gp120 bridging sheet. We hypothesized that upon gp120 interaction with the sCD4 moiety of the bifunctional protein, the 17b ScFv moiety will bind to its epitope, thus blocking coreceptor interaction and viral entry. As predicted, the bifunctional protein neutralized all HIV-1 isolates tested from diverse genetic subtypes, with very high potency compared to previously described broadly neutralizing antibodies. Utility of the sCD4-17b bifunctional protein for HIV prevention is currently being evaluated.

Biography

Dr. Barna Dey completed her PhD in 1994 from Wayne State University in Detroit, Michigan and received post-doctoral training at NIH in the laboratory of Dr. Edward Berger. She then spent 7 years at the NIH Vaccine Research Center as a Staff Scientist, and currently holds a Staff Scientist position in the Laboratory of Viral Diseases, NIAID. She has published 15 papers in highly reputed journals and serves as an Associate Faculty member of Faculty 1000.