

Destroying the human immunodeficiency virus before infection

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Human Immunodeficiency Virus (HIV) is the cause of a debilitating disease called AIDS. It poses global health problems and has resulted in approximately 40 million deaths. Apart from that, 39 million people are still living with AIDS, which imparts a significant economic burden and necessitates vaccine development. To date, eight vaccines have been in late-stage clinical trials, and none but one called RV144 (a recombinant vaccine containing gp120) has shown moderate success. HIV envelope (Env) protein is the only protein on the surface of HIV, hence the target of many broadly neutralizing antibodies (bNAbs). However, HIV has evolved a mechanism of immune evasion using multiple strategies, such as concealing the Env through heavy glycosylation and showing different conformational states during its entry into the host cells. Several studies have demonstrated that survivors of chronic HIV-1 infection develop bNAbs with long complementarity-determining region 3 of the heavy chain (CDRH3) that target the state-1 (closed conformation) of HIV-1 Env. We have generated bovine bNAbs with ultra-long CDRH3 regions through sequential immunization of three groups of cows with closed conformations of KNH144 and BG505 gp140 SOSIP and AD8 uncleaved gp140, followed by immunization with the closed conformation of BG505 gp140 SOSIP and the open conformation of AD8 uncleaved gp140, respectively. We have found out that these antibodies are one of the most potent antibodies which targets CD4-binding site on HIV-1 Env. The objective of the study is to structurally characterize the epitopes of these bovine bNAbs on HIV-1 Env, which may inform the design of more effective vaccines and contribute to AIDS prevention.