

Identification and Characterization of Cross-Reactive HIV-1-Neutralizing Human Monoclonal Antibodies

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Abstract

Human immunodeficiency virus type 1 (HIV-1) has become a global pandemic since its discovery in the early 1980s. Over two decades of intensive effort have yet to produce a viable vaccine candidate. HIV uses various strategies to escape immune responses including the rapid generation of mutants that outpaces the development of neutralizing antibodies. By a variety of mechanisms, HIV also hides some conserved structures of its envelope glycoprotein that are important for replication, including variable loops and extensive glycosylation, transient exposure, occlusion within the oligomer, and conformational masking. As a result, elicitation of cross-reactive neutralizing antibodies in vivo is rare and usually occurs only after relatively long periods and only in a small number of individuals. Therefore, identification and characterization of such human monoclonal antibodies may provide insights into the closely guarded conserved structures that still could serve as epitopes for neutralization. This, in turn, has implications for the development of vaccines, understanding of the mechanisms underlying HIV entry and evasion of immune responses, and the design of entry inhibitors. In this talk, I will introduce our approaches for identification of cross-reactive HIV-1-neutralizing human monoclonal antibodies including various antibody phage display technologies and antibody engineering techniques, and then describe the results from characterization of these antibodies for binding affinity, neutralization activity, epitope mapping, etc.