INFORMAL SEMINAR
MOLECULAR STRUCTURE AND FUNCTION PROGRAM

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The structure and conformational landscape of the HIV-1 envelope glycoprotein

Abstract: The HIV-1 envelope glycoprotein is displayed on the virus membrane, projecting outwards to interact with cellular surface receptors, and thereby mediate viral infection. The protein has an extensive carbohydrate coat, variable structural features, and sterically shielded conserved epitopes. These structural features are hurdles to elicitation of full-size IgG antibodies (~150 kDa), which has motivated the engineering of smaller antibody derivatives (~15 kDa) that retain the ability to bind envelope and neutralize the virus. To further understand the mechanisms by which these novel molecules neutralize HIV-1, cryo-electron tomography was used to study the interaction of two such antibody derivatives, A12 and m36, with native envelope displayed on the virus surface. It was found that these molecules mimic the effects of full-size, virus-neutralizing IgG antibodies on the quaternary conformation of trimeric envelope. Because these small neutralizing proteins are less sterically hindered than full-length antibodies at zones of virus-cell contact, the finding that their binding has the same structural consequences as that of other broadly neutralizing antibodies highlights their potential for use in therapeutic applications. Furthermore, by virtue of probing envelope structure with molecules that share features with cellular receptors, this study also sheds light on the conformational landscape accessible to HIV-1 envelope during infection.

Date : Friday, April 25, 2014
Time : 2:00 - 3:00 pm
Location : Room 03.9320, Multi-Media Room, PGCRL
Peter Gilgan Centre for Research and Learning, 686 Bay Street

Host: Dr. John Rubinstein

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