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Molecular insights into the inhibition of HIV-1 infection using a CD4 domain-1-specific monoclonal antibody

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The infection with Human Immunodeficiency Virus type 1 (HIV-1) is associated with acquired immunodeficiency syndrome (AIDS). An HIV-1 infection in a host cell occurs through an ordered process that involves HIV-1 attachment to the host's cellular CD4 receptor, co-receptor binding to CCR5 or CXCR4, and the subsequent fusion with the cellular membrane. The natural viral entry pathway into a host cell provides an opportunity to develop agents for the treatment of HIV-1 infections. Several engineered monoclonal antibodies specifically targeting CD4 have shown antiviral activities in clinical trials. Here, we report on an anti-CD4 mAb (15A7) that displays a unique binding specificity for domain 1 of CD4, whose epitope partially overlaps with the gp120 binding region. Moreover, 15A7 displays a much stronger binding affinity to CD4+ cell lines after HIV infection. 15A7 is able to block and neutralize a broad range of primary HIV-1 isolates and T cell-line passage strains. Notably, the bivalent F(ab')2 form of 15A7 is more effective than the Fab form in blocking HIV-1 infection, which is further supported by molecular docking analyses. Together, these results suggest that this novel antibody may exert its antiviral activity by blocking gp120 targeting the CD4 receptor or competing with gp120 for CD4 receptor binding and might present post-attachment neutralization activity. This antibody could provide a new candidate to efficiently block HIV-1 infection or provide new starting materials for HIV treatment, especially when HIV-1-resistant strains against the current CD4 mAb treatments have already been identified.

Biography

Ying Gu, Associate Professor of Molecular Virology, in School of Life Sciences, Xiamen University, China. She leads a group in State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics, and her interests focus on the epitope identification of HIV, Hepatitis E Virus, and Human Papillomavirus. She contributed to the research and development of HIV diagnostics, Hepatitis E vaccine and HPV vaccine. Regarding the HIV research, she endeavors to generate monoclonal antibodies against HIV infection and investigates the assembly of HIV gag protein. She has authored or co-authored a total of 25 papers and 8 patents.

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