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Human Immunodeficiency Virus Spreading in Human Peripheral Blood Leukocytes

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As it is well known that human immunodeficiency virus(HIV-1) is a causative agent for CD4⁺ T-cell depletion, resulting in AIDS. However, most of the CD4⁺ T-cells in human peripheral blood are in resting stage in which even CD4⁺ T-cells are not susceptible to HIV-1 infection. Therefore, continuous activation of CD4⁺ T-cells before infected are essential for the AIDS progression. What kind of immune cells are involved in the T-cell activation and HIV-1 spreading in AIDS patients? Recently, several experimental reports have suggested that dendritic cells (DC), having their own distinctive morphology, play an important role in AIDS pathogenesis as virus-carriers and/or reservoirs. DC are terminally differentiated strong antigen presenting cells. Even though the population is less than 1% of total PBL, they are essential in primary immune response together with monocytes/macrophages. DC are highly susceptible to HIV-1 infection.

Highly purified dendritic cells(DC), monocyte and T cells were obtained from peripheral blood by sequential cell fractionation process established recently. Each cell fraction was tested for their susceptibility to primary isolates of HIV-1 from AIDS patients. Also, coculture experiments were performed to investigate HIV-1 transmission in peripheral blood mononuclear cells(PBMC). The results of these experiments show that DC are much more effective than monocyte to transmit HIV-1 to CD4⁺ T cells. Two monocyte-tropic viruses, IH and IIG, did not show the infectivity to purified primary PHA-stimulated CD4⁺ T cells. Nevertheless these viruses were replicated in CD4⁺ T cells when they were transmitted by strong antigen presenting cells(APC) like dendritic cells or monocytes. IH strain replicated in DC, but IIG didn't. Both strain actively replicated in monocytes. However, DC were much more effective than monocytes in HIV-1 transmission to CD4⁺ T cells even in the case IIG transmission. HIV-1 transmission or spreading by APC was not inhibited by an anti-HLA-DR monoclonal antibody, suggesting that HIV-1 transmission may not be quite related to class II antigen. Cytokines were tested for their involvement in HIV-1 transmission in primary immune cells. IL-2 was the only cytokine required for effective transmission and replication of HIV-1 from DC to CD4⁺ T cells, but IL-2 alone was not enough for monocyte to transmit HIV-1 to CD4⁺ T cells.