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Control of infection with human T cell leukemia virus type-1 (HTLV-1) by humanized neutralizing anti-HTLV-1 gp46 antibody

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The number of human T cell leukemia virus type-1 (HTLV-1)-infected individuals in the worldhas been estimated to be ~20 million. However, no prophylaxis vaccines or drugs against HTLV-1 infection have been developed. Thus, for establishing the basis of protective vaccines against HTLV-1,we have humanized a rat monoclonal anti-HTLV-1-neutralizing antibody, LAT-27, that recognizes the HTLV-1 gp46 amino acids 191-196. The humanized LAT-27 (hu-LAT-27) completely blockedboth HTLV-1-infection in vitro at a concentration of 5 microgram/ml as determined by syncytium-formation and transformation inhibition assays. A51Cr-releace assay showed that hu-LAT-27 efficiently lysed HTLV-1-infected cells by ADCC in the presence ofautologous or allogeneic fresh PBMCs. Magnetic cell depletion assays showed that the main effector cells involved in the ADCC were NK cells. The ADCC activity of hu-LAT-27 (human IgG1) was superior to that of original LAT-27 (rat IgG2b). When hu-PBL-SCID mice were pre-infused i.v.with hu-LAT-27, but not a control chimeric human antibody, all the mice were completely protected against HTLV-1 infection. These results indicate that this new humanized anti-HTLV-1 antibody is potent not only in blocking of new infection of human T cells with HTLV-1, but also in surveillance of HTLV-1-infected cells, indicating a possible potential of hu-LAT-27 for passive immunization against HTLV-1 infection.

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