

Potential anti-ATL therapeutic vaccine using short-term cultured autologous peripheral blood mononuclear cells: preclinical evidence in vitro and in vivo

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Background:

A recent clinical study of Tax peptide-pulsed dendritic cell vaccine suggests that activation of Tax-specific CTL can be a new therapeutic concept for adult T-cell leukemia (ATL). Here, we aimed to develop another immunotherapy for ATL to activate Tax-specific CTL without HLA limitation by using short-term cultured patients' own PBMCs as a vaccine that contain HTLV-1 expressing cells.

Methods:

In in vitro system, mitomycin C (MMC)-treated HTLV-1-infected T-cells from ATL patients were co-cultured with antigen presenting cells (APCs), and the APC function to evoke CTL response (e.g. antigen cross-presentation, expression of co-stimulatory molecules and cytokine production) was examined. In in vivo system, Japanese macaques naturally infected with simian T-lymphotropic virus type 1 (STLV-1), closely related to HTLV-1, were vaccinated with short-term cultured own PBMCs following MMC-treatment.

Results:

The APCs co-cultured with short-term cultured PBMCs or HTLV-1-infected T-cell lines derived from ATL patients could cross-present Tax antigen on the MHC-I to activate CD8+ Tax-specific CTL. This effect was not a result of de novo infection in the APC, as it was not affected by a reverse transcriptase inhibitor. The co-cultured APCs also expressed IL-12 and CD86, while the levels of expression varied. Pre-treatment of the HTLV-1-infected cells with HDAC inhibitors improved these APC functions.

In naturally STLV-1-infected Japanese monkeys, STLV-1 antigens were undetectable in fresh PBMCs but inducible following culture as observed in humans. We inoculated short-term cultured autologous PBMCs into STLV-1-

infected monkeys that had exhibited low CTL response, and found that STLV-1-specific CTLs were markedly activated.

Conclusion:

Short-term cultured autologous PBMCs from ATL patients expressing HTLV-1 antigens potentially act as a therapeutic vaccine to activate CTL responses.

Disclosure of Interest Statement:

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