

Useful cell lines (PMDC05/11) of plasmacytoid dendritic cell for cellular immunotherapy

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Abstract

Although cellular immunotherapy using antigen-specific CTLs against tumors and severe infections is a promising strategy, one of the problems is hardship in constant supply of efficient antigen presenting cells for generating such CTLs. We established a plasmacytoid dendritic cell (pDC) line (PMDC05) from leukemia cells of pDC leukemia. PMDC05 cells were positive for CD4, CD56, CD33, HLA-DR, CD123 (IL-3Ra) and CD86 in the absence of lineage markers. mRNA of TLR1, TLR2, TLR4, TLR7 and TLR9 were clearly expressed with the prominence of TLR7 expression. Production of IFN- α and IL-12 in PMDC05 was enhanced by stimulation with CpG-A and LPS, respectively. PMDC05 cells were separated into two fractions according to the expression of BDCA1 and CD123. BDCA1-CD123+ cells were found to be pDC-like cells by their morphology, surface phenotypes, TLR expression and IFN- α production. BDCA1-CD123+ cells were demonstrated to have a proliferating capacity and revealed the ability to transform to BDCA1+CD123- cells which showed mDC-like properties. These data

demonstrated the possibility of transformation from pDCs to mDCs in human DC lineage. In addition, we investigated the applicability of PMDC05 for cellular immunotherapy. By stimulation with LPS, PMDC05 showed enhancement in the expression of antigen presentation-associated surface molecules and production of cytokines (IL-12p70 and TNF- α). The antigen presenting ability was markedly increased in PMDC05 stimulated with LPS. By co-culturing of CD8+ T cells with LPS-stimulated and WT1 or CMVpp65 peptide-pulsed PMDC05, WT1 or CMVpp65 tetramer+ cytotoxic T lymphocytes were efficiently generated. PMDC11 cells, which were established by transfecting PMDC05 with CD80 gene by retrovirus-vector, showed an enhanced expression of HLA-DR as well as CD80 and a remarkable antigen presenting ability to allogeneic lymphocytes with an increased stimulation on IFN- γ production by the lymphocytes. These findings reveal the applicability of PMDC05 and PMDC11 in cellular immunotherapy for tumors and severe infections.