Adoptive Cellular Immunotherapy in Viral Infection

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Successful adoptive immune cell therapy has been demonstrated for several viral diseases including cytomegalovirus (CMV) and Epstein Bar virus (EBV). However, this innovative therapeutic approach is limited by difficulties to efficiently isolate and expand antigen-reactive immune cells. Since cytokines are major parameters to specific immune cell effector functions, advanced technologies based on effector cytokine secretion have been developed to allow rapid isolation and expansion of Ag-specific immune cells. Interferon (IFN)-gammą is a key effector cytokine in immune cell-mediated anti-viral response. Thus, the methods to isolate and expand IFN-gamma-responding, antigen-specific immune cells have been applied in clinical treatment. CMV reactivation and associated disease is a major cause of mortality after hematopoietic stem cell transplantation (HSCT) due to the compromised host immune response. Although anti-CMV drugs such as foscarnet and gancyclovir are effective in treating CMV infections, these drugs are associated with organ toxicities and a large number of HSCT patients develop drug-resistant CMV diseases. Adoptive immune cell therapy targeting CMV has shown clinical efficacy in many clinical trials. There are two different approaches to obtain virus-specific immune cells for treating CMV diseases. The first approach is to isolate virus-specific immune cells from whole blood-derived mononuclear cells. The second is to amplify virus-specific memory T cells using dendritic cells (DCs) pulsed with specific viral antigen peptides followed by coculture with peripheral blood T cells. The former method uses antibody-labeled magnetic beads to isolate IFN-gamma-secreting T cells after viral antigen stimulation of immune cells. The latter uses viral-peptide-pulsed DCs to activate memory T cells and expand the culture for 10-20 days. Both methods have proven effective in treating CMV and EBV diseases in HSCT patients. Clinical results of these different adoptive cellular immunotherapy methods will be presented and discussed.