Allogeneic CD3- CD19- CD57+ NKG2C+ NK Cells FATE-NK100

National Cancer Institute

Source

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A preparation of pharmacologically-enriched, allogeneic natural killer (NK) cells derived from a related but not completely matched human leukocyte antigen (HLA)-haploidentical donor that is seropositive for cytomegalovirus (CMV+), with potential cytolytic and antineoplastic activities. Upon leukapheresis, the donor peripheral blood mononuclear cells (PBMCs) are treated to remove T-lymphocytes (CD3+) and B-lymphocytes (CD19+). The remaining leukocytes are cultured for 7 days with the cytokine interleukin-15 (IL-15) and a small molecule inhibitor of glycogen synthase kinase 3-beta (GSK3beta) to generate the adaptive, CD3- CD19- CD57+ NKG2C+ NK cells FATE-NK100 ex vivo. Upon infusion of the allogeneic CD3- CD19- CD57+ NKG2C+ NK cells FATE-NK100, these cells selectively recognize and bind to tumor cells, and secrete perforins, granzymes, and cytokines, which results in cancer cell lysis. Exposure to CMV induces the expression of the memory-like activating receptor NKG2C and the maturation marker CD57 in the isolated NK cells, making them more potent than those not pre-exposed to CMV. CD57 both enhances the effector function of NK cells and stimulates CD16-dependent signaling. Treatment with IL-15 enhances NK cell proliferation and survival. The GSK3beta inhibitor induces preferential expansion of CD57+ NK cells that exhibit enhanced interferon (IFN)-gamma production.