Autologous Peripheral Blood Lymphocytes Cotransduced with Retroviral Vectors Encoding Inducible IL-12 and Anti-NY-ESO-1 TCR

National Cancer Institute

Source

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Human autologous peripheral blood lymphocytes (PBLs) transduced with two retroviral vectors, one encoding a T-cell receptor (TCR) specific for the cancer-testis antigen NY-ESO-1 and a second that encodes an inducible single chain form of interleukin-12 (IL-12) driven by a nuclear factor of activated T-cells (NFAT)-responsive promoter, with potential immunomodulating and antineoplastic activities. Following isolation of lymphocytes, retroviral vector transduction, and expansion of the cells ex vivo, the inducible IL-12/anti-NY-ESO-1 TCR-expressing autologous PBLs are re-administered into the patient by intravenous injection. As the transduced PBLs traverse the patient's circulation, they can bind to NY-ESO-1-overexpressing tumor cells. This binding activates the TCR signaling pathway in the transduced PBLs, which promotes NFAT-dependent gene transcription and induces expression of the cotransduced IL-12. IL-12 expression activates the immune system by promoting the secretion of interferon-gamma, activating natural killer cells (NKs), and inducing cytotoxic T-cell responses, which may result in both decreased cell proliferation and increased cell death for the NY-ESO-1-overexpressing tumor cells. NY-ESO-1, a tumor associated antigen (TAA), is found in normal testis and on the surface of various tumor cell types. NFAT, a family of transcription factors involved in immune responses, is activated by calcium signaling, which can occur downstream of TCR activation. Use of a retroviral vector to express an inducible IL-12 may remove the requirement for concomitant administration of interleukin-2 (IL-2) as is the case for conventional cell transfer immunotherapies.