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Meeting Abstract

Lentiviral engineered T cells for tumor therapy: Are we there yet?

Carl June*, Michael Milone, Carmine Carpenito, Jonathon Fish and Stephan Grupp

Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA
**Presenting author*

Abstract

Mesothelin is a tumor-associated antigen that is frequently overexpressed on mesothelioma, non-small cell lung cancer, pancreatic and ovarian cancers. The central hypothesis that we wish to test is that insufficient numbers of CTL with adequate engraftment, persistence and effector function to self antigens have been used in previous trials of adoptive therapy for cancer. Our strategy is the "T-body" approach, which uses genetically reprogrammed, patient-derived lymphocytes transfected with a novel chimeric receptor that contains combinations of the signal transduction domains of 4-1BB (CD137), CD28, and CD3ξ as well as anti-mesothelin scFv (anti-meso-CD28-41BB-ξ). Our recent data has demonstrated the safety and prolonged lentiviral gene transfer with autologous T cells engineered with a lentiviral vector in patients with HIV infection. Therefore, we are planning to test the hypothesis that lentiviral engineered human T cells expressing an anti-mesothelin-CD28-41BB-ξ chimeric receptor will have potent antitumor activity *in vitro* and *in vivo* by: (1) developing and optimizing the anti-meso scFv vector; (2) carrying out *in vitro* experiments to optimize the effector functions of anti-mesothelin scFv CD28-41BB-ξ T bodies. We are currently performing *in vivo* experiments in immunodeficient NOD/SCID/ξ 2null mice xenografted with human tumors that express mesothelin. The present results support the notion that combination immunotherapies with lentiviral engineered T cells hold promise for women with epithelial ovarian cancer.