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IMMUNOTHERAPY

Novel approach for universal adoptive cell transfer therapy with improved outcome

Adoptive cell transfer is a promising treatment, with advances seen in patients with melanoma and neuroblastoma. The generation of tumor-specific T cells for patients, however, is technically and economically challenging. Zelig Eshhar and his team, who pioneered the use of redirected T cells with antibody-based non-MHC restricted chimeric antigen receptors, have developed a novel universal adoptive therapy approach for treating disseminated disease with no need for MHC matching between the donor cells and patient. Eshhar explains, "we hypothesized that low-dose irradiation would delay the host-versus-graft (HvG) effect allowing allogeneic T cells time to destroy the tumor, but that the allogeneic T cells would ultimately be rejected preventing graft-versus-host disease (GvHD)."

Mice with metastatic tumors were lymphodepleted by irradiation and treated with mismatched HER2 redirected T cells. The lymphocyte-sequestering agent, FTY720, allowed the HvG and graft-versus-host (GvH) responses to be inhibited to a far greater extent than graft-versus-tumor response. This approach cured a significantly higher proportion of mice compared with syngeneic T cells, with a striking median survival time of over 1 year in mice treated with the novel therapy. Eshhar adds, "our work conclusively demonstrates that GvH exploited to enhance the response of allogeneic tumor-specific T cells does not cause GvHD." Allogeneic adoptive therapy may become the treatment of choice as it provides greater efficacy and cost advantages, although clinical validation is needed.

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Original article Marcus, A. *et al*. Redirected tumor-specific allogeneic T cells for universal treatment of cancer. *Blood* doi:10.1182/blood-2011-02-334284