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Antigen-specific Immunotherapy of Cancer with Genetically Modified Fibroblasts

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To induce efficient antitumor immune responses, mouse fibroblasts were genetically modified to secrete interleukin-2 (IL-2) and interferon-gamma (IFN- γ) along with the expression of tumor antigens (IL-2/IFN- γ -secreting cells). As controls, mouse fibroblasts were modified to express tumor antigens and secreted either IL-2 or IFN- γ alone (IL-2- or IFN- γ -secreting cells). Cytokines secreted from the genetically modified fibroblasts were biologically active. The survival period of B16 melanoma-bearing mice treated with the IL-2/IFN- γ -secreting cells was significantly longer than that treated with the IL-2- or IFN- γ -secreting cells. The IL-2/IFN- γ -secreting cells induced higher antitumor cellular response than the IL-2 or IFN- γ -secreting cells. Both natural killer(NK) cells and cytotoxic T lymphocytes(CTLs) were major effector cell-types involved in the antitumor responses. This results suggest that immunization with IL-2/IFN- γ -secreting cells stimulated multiple antitumor effector mechanisms.