Leukemia-initiating cells of patient-derived acute lymphoblastic leukemia xenografts are sensitive toward TRAIL.

Abstract:
Cancer stem cells represent the most important target cells for antitumor therapy. TRAIL (TNF-related apoptosis-inducing ligand) is a potential anticancer agent that induces apoptosis in a wide variety of tumor cells, but its ability to target cancer stem cells is currently unknown. Here we investigated whether TRAIL targets leukemia-initiating cells. Limiting dilution transplantation assays were performed on xenografts from pediatric patients with precursor B-cell acute lymphoblastic leukemia (pre-B ALL) in NSG mice. In vitro treatment of xenograft cells with TRAIL significantly reduced and delayed their engraftment and procrastinated animal death from leukemia. Systemic TRAIL treatment of mice injected with patient-derived pre-B ALL xenograft cells abrogated leukemia in 3 of 5 mice in 1 sample. In conclusion, our data suggest that TRAIL targets leukemia-initiating cells derived from pre-B ALL xenografts in vitro and in vivo, and hence constitutes an attractive candidate drug for treatment of ALL.