CMV promoter,8 and analyzed by X-gal staining. As shown in Figure 1C, transduction efficiency is dose-dependent.

To determine whether intravenous administration of mMSCs genetically modified with ECSOD has a therapeutic effect for radiation damage, 5-week-old female BALB/c mice were given 9 Gy total body y irradiation from a 137Cs source. Twenty-four hours later, the animals were given a tail vein injection of phosphate-buffered saline (PBS), Ad5CMVnlacZ-transduced mMSCs, or Ad5CMVECOSD-transduced mMSCs. As shown in Figure 1D, 52% of animals in the ECSOD gene-modified mMSC treatment group survived for 35 days, whereas only 9% of animals in the nlacZ gene-modified mMSC treatment group and 10% of animals in the PBS treatment group survived for 35 days. Furthermore, all mice that survived for 35 days also survived for 5 months. These findings demonstrate for the first time that intravenous administration of MSCs genetically modified with ECSOD improves survival in irradiated mice, highlighting its clinical potential for the treatment of radiation damage resulting from a radiation accident, nuclear terrorism, and other radiologic emergencies.

Mice given 9 to 10 Gy total body irradiation die a hematologic death 10 to 14 days after exposure.9 It has been found that MSCs migrate to radiation-injured tissues such as bone marrow and gut after intravenous administration.10 Therefore, the improvement in survival of irradiated mice might result from the scavenger of O2− in the irradiated tissues such as bone marrow and gastrointestinal tract by ECSOD secreted from Ad5CMVECOSD-transduced MSCs.

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To the editor

Elevated expression of the leukemia-associated antigen SSX2IP predicts survival in acute myeloid leukemia patients who lack detectable cytogenetic rearrangements

Greiner et al1 described a positive association between elevated leukemia-associated antigen (LAA) expression (RHAMM, G250/CA9, and PRAME) and survival in 116 acute myeloid leukemia (AML) patients by microarray. We have analyzed 312 presentation AML samples using 199 133A chips and 113 Plus2 chips and segregated AML patients based on above- and below-median levels of expression of the LAA synovial sarcoma X breakpoint 2–interacting protein (SSX2IP).2−4 Analysis of Kaplan-Meier curves showed an association between elevated SSX2IP expression and survival in 116 acute myeloid leukemia patients who lack detectable cytogenetic abnormalities; however, it was significantly associated with improved survival rates in patients with no detectable cytogenetic rearrangements (log-rank test, n = 180; P = .007; Figure 1A). We also found a correlation between elevated SSX2IP expression and other clinical parameters that are considered to be good prognostic markers: days in remission (log-rank test, P = .03), age at diagnosis (< 60 years; t test, P = .003), and FLT3 WT (t test, P = .004).

When we examined SSX2IP together with the expression of other LAAs known to be associated with improved survival (reviewed in Greiner et al3) we found a significant correlation with SURVIVIN (Pearson correlation, P = 3.97 × 10−5) and RHAMM (Pearson correlation, P = 4.3 × 10−5). Greiner et al3 suggested that the expression of distinct LAAs on leukemic blasts may lead to the eradication of residual disease after intensive chemotherapy. RHAMM and SURVIVIN, like SSX2IP, have increased expression in proliferating cells,6,7 while RHAMM and SSX2IP are both expressed on the surface of malignant cells.7 There appears to be a small but growing group of LAAs that are coexpressed in AML patients and are associated with improved survival (our results here and Greiner et al3). We examined whether having 1 or more of SSX2IP, SURVIVIN, or RHAMM affected survival in patients with a normal karyotype and found that having expression of none, 1. Fliedner TM. Nuclear terrorism: the role of hematology in coping with its health consequences. Curr Opin Hematol. 2006;13:436-444.
1, 2, or all 3 of these LAAs was a significant prognostic indicator (log-rank test, \( P = .021 \), respectively; Figure 1B). With regard to the presence of cytogenetic abnormalities, these appear to supersede the influence of elevated LAA expression on prognosis.

In summary, we have found that SSX2IP expression at disease presentation predicts good survival in AML patients with no detectable cytogenetic rearrangements. This may, in part, explain why patients with low LAA expression (often the elderly) fail to elicit effective immune responses and tend to have poorer survival. A new phase in cancer-targeted therapy will be particularly difficult, but especially needed, for AML patients whose tumors lack cytogenetic abnormalities and detectable immunogenic LAA expression and whose survival rates are notably reduced.

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References


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