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 γ irradiation from a ^{137}Cs source. Twenty-four hours later, the animals were given a tail vein injection of phosphate-buffered saline (PBS), Ad5CMVntlacZ-transduced mMSCs, or Ad5CMVECSOD-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 ntlacZ 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 O_2^- in the irradiated tissues such as bone marrow and gastrointestinal tract by ECSOD secreted from Ad5CMVECSOD-transduced MSCs.

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Contribution: A.S.A.-M., A.J.S., D.W.P., and R.H.C. designed the research; T.A.G. and R.V.H. helped perform experiments; and W.D. designed the research and performed experiments. All authors analyzed results and wrote the paper.

**A.S.A.-M. and A.J.S. contributed equally to this work.*

Conflict-of-interest disclosure: A patent application related to the methodology described in the present work has been filed by W.D., A.S.A.-M., D.W.P., R.H.C., and A.J.S., all of whom are employees of Spectrum Health; the patent belongs to Spectrum Health. The authors declare no other competing financial interests.

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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 al[1] 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 improved survival times (log-rank test, $P = .05$). We found that SSX2IP expression did not predict the survival of AML patients who had 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 al[5]) we found a significant correlation with SURVIVIN (Pearson correlation, $P = 3.97 \times 10^{-5}$) and RHAMM (Pearson correlation, $P = 4.3 \times 10^{-5}$). Greiner et al[1] 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 al[1]). 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,

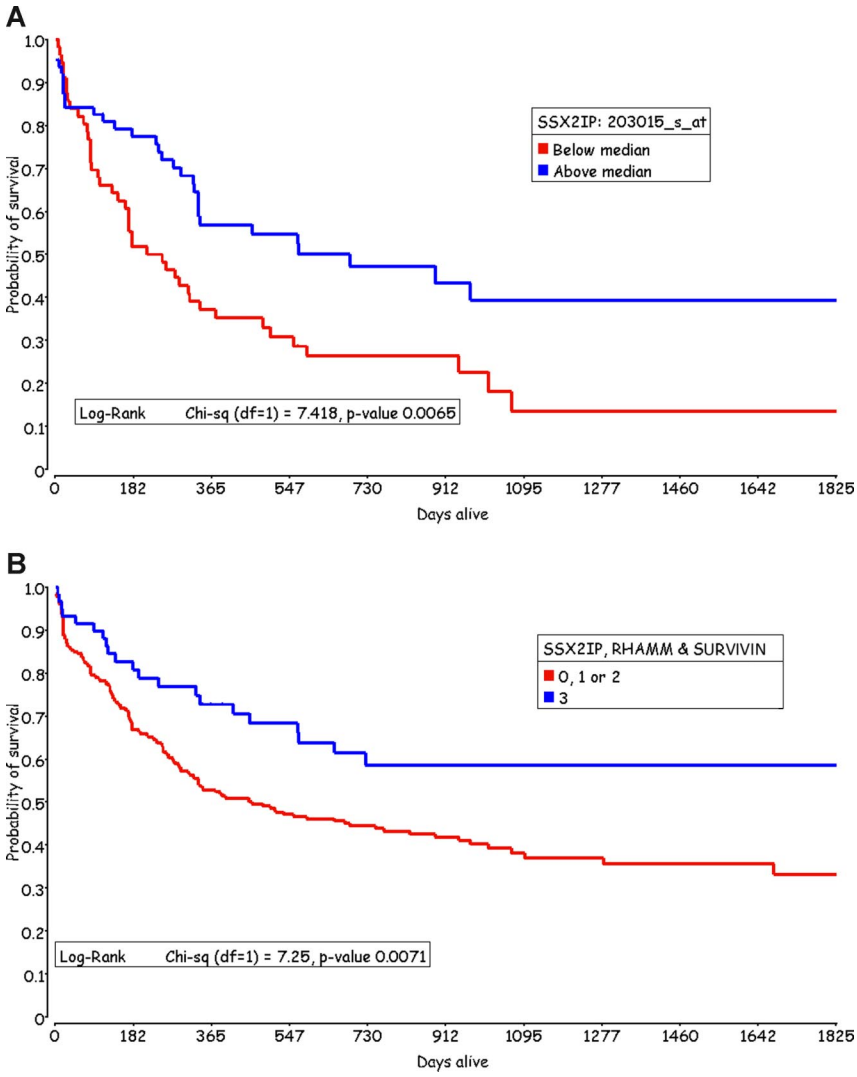

Figure 1. SSX2IP expression indicates survival rates in AML patients who lack cytogenetic abnormalities. (A) In patients with a normal karyotype, elevated SSX2IP was associated with significantly improved survival rates (log-rank test, $P = .007$). (B) The expression of all 3 (RHAMM, SURVIVIN, and SSX2IP) LAAs above the median was associated with significantly extended survival times in patients with a normal karyotype, compared with having elevated expression of 2 or fewer of these LAAs (0, 1, or 2; log-rank test, $P = .021$). The x-axis shows days alive over a 5-year follow-up period and the y-axis indicates probability of survival.

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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