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Tocopherol succinate-mobilized progenitors mitigate radiation injury and improve intestinal integrity after whole body irradiation

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The goal of this study was to elucidate the role of α-tocopherol succinate (TS)- and AMD3100-mobilized progenitors in mitigating the ionizing radiation-induced gastrointestinal (GI) syndrome in mice. We demonstrate the efficacy of a bridging therapy which will allow the lymphohematopoietic system of severely immunocompromised victims exposed to ionizing radiation to recover from high doses of radiation. CD2F1 mice were irradiated with a dose of radiation causing GI injury (11 Gy, cobalt-60 gamma-radiation) and then transfused intravenously (retro-orbital sinus) with whole blood or peripheral blood mononuclear cells (PBMC) from TS- and AMD3100-injected mice 2, 24, or 48 h post-irradiation and monitored for 30-day survival. Jejunum sections were analyzed for tissue area, surviving crypts, villi, mitotic figures, basal lamina enterocytes, and bacterial translocation. Our results demonstrate that infusion of whole blood or PBMC from TS- and AMD3100-injected mice significantly improved survival of mice receiving a high dose of radiation. Histopathology and immunostaining of jejunum from irradiated and TS- and AMD3100-mobilized PBMC-transfused mice reveal significant protection of GI tissue from radiation injury. We observed that the infusion of PBMC from TS- and AMD3100-injected mice significantly inhibited bacterial translocation to various organs compared to mice receiving cells from vehicle-mobilized cells. We demonstrate that TS and AMD3100 mobilize progenitors into peripheral circulation and that the infusion of mobilized progenitor-containing blood or PBMC acts as a bridging therapy for immune system recovery in mice exposed to potentially fatal doses of ionizing radiation. With further preclinical investigation in large animals, we may approach a simpler, improved protocol for the clinical management of individuals suffering from high ionizing radiation doses causing GI syndrome.

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