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Epidermal growth factor aids stem cell regeneration after radiation damage

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Epidermal growth factor has been found to speed the recovery of blood-making stem cells after exposure to radiation, according to Duke Medicine researchers. The finding could open new options for treating cancer patients and victims of dirty bombs or nuclear disasters.

Reported in the Feb. 3, 2013, issue of the journal *Nature Medicine*, the researchers explored what had first appeared to be an anomaly among certain genetically modified mice with an abundance of epidermal growth factor in their bone marrow. The mice were protected from radiation damage, and the researchers questioned how this occurred.

"Epidermal growth factor was not known to stimulate hematopoiesis, which is the formation of blood components derived from hematopoietic stem cells," said senior author John Chute, M.D., a professor of medicine and professor of pharmacology and cancer biology at Duke University. "However, our studies demonstrate that the epidermal growth promotes hematopoietic stem cell growth and regeneration after injury."

Hematopoietic stem cells, which constantly churn out new blood and immune cells, are highly sensitive to radiation damage. Protecting these cells or improving their regeneration after injury could benefit patients who are undergoing bone marrow transplantation, plus others who suffer radiation injury from accidental environmental exposures such as the Japanese nuclear disaster in 2011.

The Duke researchers launched their investigation using mice specially

bred with deletions of two genes that regulate the death of endothelial cells, which line the inner surface of blood vessels and are thought to regulate the fate of hematopoietic stem cells. Blood vessels and the hematopoietic system in these mice were less damaged when exposed to high doses of radiation, improving their survival.

An analysis of secretions from bone marrow endothelial cells of the protected mice showed that epidermal growth factor (EGF) was significantly elevated - up to 18-fold higher than what was found in the serum of control mice. The researchers then tested whether EGF could directly spur the growth of stem cells in irradiated bone marrow cultured in the lab. It did, with significant recovery of stem cells capable of repopulating transplanted mice.

Next, the Duke team tried the approach in mice using three different solutions of cells in animals undergoing bone marrow transplants. One group received regular bone marrow cells; a second group got bone marrow cells from donors that had been irradiated and treated with EGF; a third group got bone marrow cells from irradiated donors treated with saline.

The regular bone marrow cells proliferated well and had the highest rate of engraftment in the recipient mice. But mice that were transplanted with the cells from irradiated/EGF-treated donors had 20-fold higher engraftment rate than the third group.

Additional studies showed that EGF improved survival from a lethal radiation exposure, with 93 percent of mice surviving the radiation dose if they subsequently received treatment with EGF, compared to 53 percent surviving after treatment with a saline solution.

Chute said it appears that EGF works by repressing a protein called PUMA that normally triggers stem cell death following radiation

exposure.

"We are just beginning to understand the mechanisms through which EGF promotes stem cell regeneration after radiation injury," Chute said. "This study suggests that EGF might have potential to accelerate the recovery of the blood system in patients treated with chemotherapy or radiation."

Provided by Duke University Medical Center

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