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Trimming the fat boosts blood recovery after marrow transplant

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Seeking ways to improve blood recovery after chemotherapy or bone marrow transplant, researchers at Children's Hospital Boston have discovered that fat cells, which accumulate in bone marrow as people age, inhibit the marrow's ability to produce new blood cells. Their study, published by the journal *Nature*, suggests that blocking this fatty infiltration could help enhance patients' recovery after transplant.

Patients who have had radiation or chemotherapy show fatty infiltration in their marrow, and it's known that the more fat cells, the less blood-forming activity the marrow engages in. What hasn't been clear is whether the fat cells actually influence blood formation, or simply fill in empty space in the marrow.

Working with mice, researchers led by George Q. Daley, MD, PhD, director of the Stem Cell Transplantation Program at Children's, and Olaia Naveiras, MD, PhD, of the Division of Pediatric Hematology/Oncology at Children's and the Dana-Farber Cancer Institute, looked at marrow from different parts of the skeleton, which vary in fat composition. They found that the relatively fat-rich tail bones had only 25 percent as many blood-forming stem cells and up to three times fewer specialized blood progenitors than did the leaner thoracic vertebrae.

In cell culture, the mere presence of adipocytes (fat cells) was enough to reduce proliferation of blood-forming cells. The fat cells seemed to somehow slow the natural cell cycle of the blood stem cells and

progenitor cells.

"Our study contradicts the classical dogma that bone marrow adipocytes are merely space fillers," says Daley. "Rather, they make it harder to recover from chemotherapy or radiation because they actively suppress blood production. If we could prevent them from invading the bone marrow, patients might be able to recover faster from marrow and cord-blood transplants."

Mice that were treated with a compound that inhibits fat formation, or that were genetically incapable of forming fat cells, were quicker to build up their bone marrow after it was depleted by irradiation. In particular, they were quicker to build up the rapidly proliferating blood cell progenitors that are known in mice - as well as humans - to be the most important in surviving the immediate post-transplant period.

Several adipocyte inhibitors, such as PPAR-gamma inhibitors, are already being tested clinically against obesity, but might also serve as adjuvants to speed engraftment and recovery of the blood system after a bone marrow transplant, Daley says.

"We are now testing whether these anti-obesity drugs have a beneficial effect on blood formation in mice," says Naveiras. Meanwhile, further studies will address exactly how adipocytes inhibit blood formation at the molecular level.

Source: Children's Hospital Boston (news : web)