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Memorial Sloan Kettering Cancer Center

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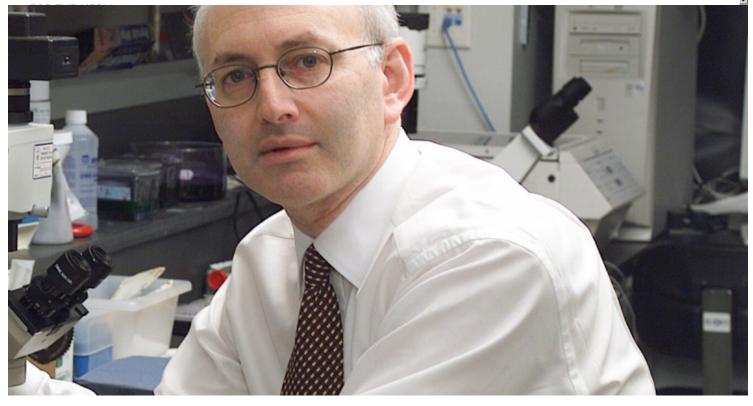
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The below press release is from Cancer Cell and is for a study published in the March issue of Cancer Cell.

Scientists have uncovered new information about what orchestrates the complex balance between blood stem cells and mature blood cells, a relationship that is often disrupted in leukemia. The results, published in the March issue of *Cancer Cell*, will lead to a better understanding of the behavior of leukemic cells and may have vital clinical applications for patients recovering from chemotherapy, radiation therapy, or bone marrow transplantation. [PubMed Abstract]

Recent studies have implicated reduced levels of a transcription factor called MEF with subtypes of leukemia. Drs. Stephen D. Nimer and Daniel Lacorazza from Memorial Sloan Kettering Cancer Center and colleagues examined the blood cells of mice that do not express MEF in their bone

marrow and found an increased population of hematopoietic (blood-forming) stem cells (HSCs). HSCs are immature cells in the bone marrow that have the capacity to differentiate into all types of mature blood cells. A delicate balance exists between self-renewal and differentiation of HSCs because the body must retain a sufficient population of HSCs while continually producing the multitude of new blood cells that are needed each day.

The researchers demonstrated that MEF regulates a little-understood state of quiescence that enables HSCs to exist in a kind of suspended animation until they are recruited to promote rapid repopulation of depleted blood cells, as would be needed following treatment with chemotherapy or radiation therapy. MEF-deficient mice accumulated quiescent HSCs with the capacity for repopulation and demonstrated enhanced resistance to the effects of chemotherapeutic drugs and radiation, which is also seen in wild-type mice transplanted with MEF-deficient HSCs. "This feature can also be helpful to maintain HSCs in an undifferentiated state during gene therapy protocols," explains Dr. Lacorazza, now a faculty member at Baylor College of Medicine.

These results suggest that MEF regulates HSCs' decision to remain quiescent or divide, and the researchers speculate that treatments to diminish MEF may improve recovery from chemotherapy and radiation. However, it is important to point out that while reduced expression of MEF might enhance recovery after myelosuppression, it is possible that certain leukemic stem cells may also be protected from these same treatments. "Myelotoxicity induced by chemotherapy or radiotherapy could be prevented by maintaining stem cells in a quiescent state during their administration to cancer patients. However, another implication of our work is that tumor stem cells are more quiescent than more differentiated tumor cells and could use similar mechanisms to resist the effects of chemotherapy or radiation," explains Dr. Nimer.

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