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Stem cells make bone marrow cancer resistant to treatment

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Scientists at the Johns Hopkins Kimmel Cancer Center say they have evidence that cancer stem cells for multiple myeloma share many properties with normal stem cells and have multiple ways of resisting chemotherapy and other treatments.

A report on the evidence, published in the Jan. 1 issue of the journal Cancer Research, may explain why the disease is so persistent, the Johns Hopkins scientists say, and pave the way for treatments that overcome the cells' drug resistance. Multiple myeloma affects bone marrow and bone tissue.

"Cancer stem cells that have distinct biology and drug sensitivity as compared with the bulk of a cancer may explain why multiple myeloma, like many other cancers, so often relapses even after chemotherapy puts patients into remission," says Richard J. Jones, M.D., professor and director of bone marrow transplant at Hopkins' Kimmel Cancer Center and one of the scientists who authored the new report.

The existence of cancer stem cells - a topic of some controversy in cancer biology - is seen by some scientists as a useful explanation for the long history of difficulty in overcoming some cancers' persistence.

The Hopkins investigators previously had uncovered a rare stem cell in myeloma, accounting for less than one percent of all the cancer's cells. Working with cell samples from myeloma patients, the team found that this stem cell originates from immune system B-cells and is capable of

giving rise to the malignant bone marrow cells characteristic of the disease.

In the current study, the scientists isolated stem cells from the blood of four patients with multiple myeloma and transplanted them into mice. All of the animals developed hind-limb paralysis and showed signs of cancer in the bone marrow. By contrast, plasma cells that were transplanted from multiple myeloma patients to mice did not engraft. The Hopkins scientists say that recreating the disease in mice provides more evidence that these cells act as cancer stem cells.

The Johns Hopkins scientists also compared the response of these special stem cells with the bulk of multiple myeloma plasma cells, to four different chemotherapy medications commonly used to treat patients with the disease: dexamethasone, lenadilomide, bortezomib and 4-hydroxycyclophosphamide. While all four agents significantly inhibited the growth of the plasma cells, none inhibited the stem cells.

To their surprise, the research team noted that the multiple myeloma stem cells resemble other types of adult stem cells and exhibit similar properties that may make them resistant to chemotherapy. They found that the stem cells contain high levels of enzymes that neutralize toxins, like cancer drugs, and expel them through miniature pumps on their cell surface. The investigators believe that these drug-fighting enzymes and pumps - also plentiful in normal stem cells - may help cancer stem cells resist treatment.

“Nature made normal stem cells very hearty for a reason, namely to survive and help repair damaged tissues and organs after injury or illness,” says William Matsui, M.D., an assistant professor of oncology at Hopkins and the study’s lead investigator. “To us, it makes sense that the same processes that protect normal stem cells also exist in cancer stem cells to make them resistant to chemotherapy. We need to develop new

ways to target the specific biology of cancer stem cells to prevent the continued production of mature tumor cells and disease relapse."

"Standard cancer therapy is like mowing the weed - it gets rid of the disease transiently but the dandelion always grows back. We need to get rid of the root to cure disease, and therefore need a different type of therapy - mowing won't work," says Jones.

Matsui says the work also may make it possible to track the rare myeloma stem cells as a marker of how well a patient is doing during treatment.

Multiple myeloma is the second most common blood cancer and strikes more than 14,000 Americans each year. Close to 11,000 will die from the disease.

Source: Johns Hopkins Medical Institutions