Targeting stem cells suggests way to cure leukemia, mice study shows

17:28:34 EDT Sep 24, 2006

Canadian Press: SHERYL UBELACKER

TORONTO (CP) - Canadian scientists are investigating a novel way of treating a deadly form of leukemia: By targeting the stem cells that allow the cancer to return after chemotherapy has resulted in apparent remission.

Using an experimental drug, researchers at Princess Margaret Hospital in Toronto were able to cure some mice transplanted with the human form of acute myeloid leukemia (AML). The discovery offers promise that the drug could have the same effect in humans with the disease.

The drug, developed by scientists in France, interferes with a protein on the stem cells, which give rise to the cancerous cells that cause leukemia - a disease of the blood and bone marrow.

For leukemia stem cells to survive, they must be able to migrate to specific spots in the bone marrow, called niches. Blocking a protein on their surface, known as CD44, stops the cancerous stem cells from travelling to and tucking into their home base.

"The principles that anti-cancer therapies have been developed on over the last five decades is based on the notion that cancer is cells that grow too much," said principal investigator Dr. John Dick, a senior scientist at Princess Margaret's Ontario Cancer Institute. "And most of chemotherapy is targeting cells that grow too much."

But because stem cells are slow-growing, standard chemotherapy drugs are ineffectual against them, Dick explained.

"They can be swimming in a sea of chemotherapy and they aren't targeted with those drugs. So the question is how are we going to target those cells that don't grow very much?"

Dick and his team used specially bred laboratory mice and injected them with leukemia cells from human patients. They then injected the animals with the drug, known as a monoclonal antibody.

All of the mice had a reduction in leukemia cells, and some were completely cured.

"By adding the monoclonal antibody, it seems that the stem cells aren't able to traffic, able to migrate, into the bone marrow of these animals," he said. "They seem to have to traffic at least back to the bone marrow, and if they can't do that ... they can't maintain their stem cell potential anymore."

Stem cells are the body's tiny blueprints: they produce, or differentiate into, all the various cells in the body. But when stem cells for the blood become cancerous, for instance, they produce abnormal red and white cells that lead to leukemia. Of the billions of blood cells circulating in the body, maybe one in a million is a stem cell.

Dick likens stem cells to a plant's root, and the cancerous cells they spawn to the leaves and flowers above ground.

"If you think of the tumours being like the dandelion in your backyard, you can go out there and keep clipping the leaves off the dandelion, but it's always going to keep regrowing."

"But (it's not) until you cut the root that the leaves will wither away. It seems that what we're doing here is we're starting to tap that root in a fairly precise way," said Dick, whose study was published online Sunday in the journal Nature Medicine.

Dr. Donna Hogge, a leukemia specialist and researcher at the B.C. Cancer Research Centre, said there are many types of acute myeloid leukemia, and the disease is most common in people over 60.

"One of the frustrations of treating AML is that it is quite routine to get a remission of the leukemia,

where we give the patients chemotherapy and the leukemia appears to disappear from the blood and bone marrow," Hogge said from Vancouver. "Patients feel well and look well, only to have - a year or two later - the leukemia come back again."

That has led scientists to look for new ways to treat leukemia, including Dick's method of targeting CD44 on stem cells, said Hogge, who was not involved in the research.

While calling the approach "exciting," she cautioned that only some of the mice were cured, suggesting that different types of AML may require different drugs.

Her other caveat: "It's a long way from human leukemia engrafted in mice to actually treating a patient in the clinic. So this is a model system that's showing some very interesting results, but the prediction is it would be quite a number of years before you would be able to work your way up to treating patients with this kind of a strategy."

Dick estimates that it would take at least five to 10 years of further research before the CD44-targeting drug could even be tested in humans.

Dr. Alan Bernstein, president of the Canadian Institutes of Health Research, said the study results suggest "a whole new strategy for trying to treat cancers."

The finding may have applications for other cancers, since stem cells that underlie human breast cancer also carry the CD44 protein, Bernstein noted.

"This has been looking at human cells going into mice, but I think we have reason to think that this is as good a model as it gets before you actually do the human clinical trials."