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Gene-modified stem cells help protect bone marrow from toxic side effects of chemotherapy

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Although chemotherapy is used to kill cancer cells, it can also have a strong toxic effect on normal cells such as bone marrow and blood cells, often limiting the ability to use and manage the chemotherapy treatment. Researchers at Fred Hutchinson Cancer Research Center reported at today's annual meeting of the American Society of Gene and Cell Therapy in Seattle that one possible approach to reduce this toxic effect on bone marrow cells is to modify the cells with a gene that makes them resistant to chemotherapy.

Hans-Peter Kiem, M.D., a member of the Hutchinson Center's Clinical Research Division, and colleagues Jennifer Adair, Ph.D., a research associate in the Clinical Research Division, and Maciej Mrugala, M.D., Ph.D., M.P.H., a neuro-oncololgist at the Seattle Cancer Care Alliance and the University of Washington, presented data from a clinical trial in which bone marrow stem cells from patients with brain tumors were removed and modified with a retrovirus vector to introduce the chemotherapy-resistant gene. The cells were then re-infused into the patients. In the trial, which was designed to evaluate safety and feasibility, patients were safely administered gene-modified blood stem cells that persisted for more than one year and did not show any apparent harmful effects.

This approach was first attempted in patients with a terminal form of brain cancer called glioblastoma. Currently, median survival for

glioblastoma patients is just 12 to 15 months. The prognosis for glioblastoma patients is poor not only because no curative treatment is available but because doctors cannot effectively use the treatment that does exist. Glioblastoma cells make a large amount of a protein called MGMT that makes them resistant to chemotherapy, so doctors use a second drug, called benzylguanine, to knock down MGMT and make the tumor cells susceptible to the chemotherapy. However, this potent one-two punch is not limited to the brain tumor cells. Benzylguanine also disables MGMT in normal blood and bone marrow cells, leaving them also susceptible to the effects of chemotherapy. The effects on patients' blood and bone marrow can be pronounced and often limit the ability to effectively administer the chemotherapy.

"Our initial results are encouraging because our first patient is still alive and without evidence of disease progression almost two years after diagnosis," Kiem said.

The results of the trial suggest the administration of the modified cells represent a safe method for protecting marrow and blood cells from the harmful effects of chemotherapy in brain tumor patients. Future clinical trials will be done to determine whether this combination chemotherapy will also improve the survival of patients with glioblastoma.

Provided by Fred Hutchinson Cancer Research Center

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