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Scientists design new drug type to kill lymphoma cells

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A new type of drug designed to kill non-Hodgkin lymphoma tumor cells could lead to potential nontoxic therapies for cancer patients.

Three researchers who are recipients of a collaborative grant from the Samuel Waxman Cancer Research Foundation have developed a new type of drug designed to kill non-Hodgkin lymphoma tumor cells. The breakthrough could lead to potential non-toxic therapies for cancer patients. The Foundation-funded investigators include Ari Melnick, M.D., of Weill Cornell Medical College, Alexander MacKerell, Ph.D., of the University of Maryland and Gilbert Privé, Ph.D., of the University of Toronto. The researchers, who published their findings in the April issue of Cancer Cell, have identified a drug that targets an oncogene known as BCL6.

BCL6 functions as a master regulatory protein. "It's a protein that controls the production of thousands of other genes," said Dr. Melnick, an associate professor of medicine at Weill Cornell Medical College in New York City. "Because of that, it has a very profound impact on cells and is required for lymphoma cells to survive and multiply."

BCL6 causes the majority of diffuse large B cell lymphomas, the most common form of non-Hodgkin lymphoma. Currently, about 60 percent of diffuse large B cell lymphomas can be cured with chemo-immunotherapy, said Dr. Melnick. "The hope is that we can improve that to a higher percent, and in the long term reduce the need for chemotherapy," he added.

Traditional cancer drugs target enzymes, which have small pockets on their surfaces that can be blocked with molecules. Until now, pharmaceutical companies have been reluctant to create drugs that target a protein like BCL6 because they function through a different mechanism involving interactions with cofactor proteins involving extensive protein surfaces. "And because the real estate covered by these interactions is so large, the drug companies have viewed these as being not druggable targets," said Dr. Melnick.

He and his colleagues were able to identify a "hot spot" on BLC6 that they predicted would play a critical role in protein interactions. They showed that their BCL6 inhibitor drug was specific to BCL6, and did not block other master regulatory proteins. The drug had powerful lymphoma killing activity and yet was non-toxic to normal tissues. "This is the first time a drug of this nature has been designed and it shows that it's not actually impossible to target factors like BCL6," he said.

Emerging data from other investigators suggests that BCL6 is important in many other tumor types, including forms of leukemia.

"The Samuel Waxman Cancer Research Foundation has always supported the collaborative work of scientists, funding innovative cancer research grants," said Samuel Waxman, M.D., the scientific director of the Foundation. "The Foundation has supported the work of Alexander MacKerell, Ari Melnick and Gilbert Privé for a number of years because we believe their work highlights the critical and important mission of our organization—that collaboration can lead to potential effective cures."

Provided by Samuel Waxman Cancer Research Foundation