

## New lymphoma therapy may be more effective with fewer side effects

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Diffuse large B-cell lymphoma (DLBCL) is a type of aggressive non-Hodgkin's lymphoma that accounts for approximately 40 percent of lymphomas among adults. If left untreated, it is fatal. The existing treatments have a cure rate that is slightly over 50 percent but destroy healthy cells along with the cancer cells.

Researchers at Weill Cornell Medical College have found a combination therapy that is more effective than traditional treatments and is able to kill the [cancer cells](#) without harm to surrounding tissues. In a paper published in the [Journal of Clinical Investigation](#) on Nov. 1, they report that by targeting a key lymphoma-causing factor called BCL6 with a specific inhibitor called RI-BPI in combination with either a histone deacetylases (HDAC) inhibitor or with a heat shock protein (Hsp90) inhibitor, they were able to suppress and in some cases eradicate human DLBCL in mice. The researchers said their findings provide the basis for rational, targeted combinational therapy for patients with DLBCL.

Dr. Ari Melnick, associate professor of medicine and director of the Raymond and Beverly Sackler Center for Biomedical and Physical Sciences at Weill Cornell Medical College, and his colleagues have been studying ways to kill lymphoma cancer [cells](#) more effectively and efficiently than standard treatments.

"Lymphomas are not easy to treat. The standard treatment using [monoclonal antibodies](#) and chemotherapy does not work for all patients and can cause undesirable side effects," says Dr. Melnick.

B cells are a type of white blood cell that produces antibodies to fight infections. BCL6 is a master regulatory factor that plays a critical role in keeping lymphoma cells alive. Dr. Melnick's study showed that therapeutic targeting of BCL6 with RI-BPI turned on another factor called EP300, a molecular switch that itself can turn on proteins that can restrain lymphoma cell growth and turn off other proteins that help [lymphoma](#) cells. The research team showed that turning on EP300 made lymphomas much more sensitive to the HDAC and Hsp90 inhibitors. Administering the drugs together is like "kicking both legs" of the [lymphoma cells](#), so they cannot regain their balance. Thus, the combined effect of the drugs is much greater than either drug alone and has very powerful anti-tumor effects. In contrast, normal cells and tissues are not damaged by this form of combination therapy, since they are not dependent on these two "legs."

Finally, the scientists also discovered that EP300 is sometimes mutated in lymphomas, which shows that this gene may normally protect B cells from becoming cancerous. Detection of these mutations in patients is important since such tumors may not be responsive to RI-BPI. Dr. Melnick says that there is much more work to be done but he hopes that his research will lead to a better understanding of the mechanisms of cancer at the cellular level and better treatments for lymphomas and other cancers.

Provided by New York- Presbyterian Hospital

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