

Antibody found in lupus may protect against certain cancers

Yale UniversityYale University

Yale Cancer Center researchers report that an antibody associated with the autoimmune disease systemic lupus erythematosus may actually offer a treatment for certain cancers. The study appears online in the Oct. 24 issue of *Science Translational Medicine*.

In autoimmune diseases such as lupus, the immune system attacks and damages the body's own cells and tissue, rather than destroying foreign invaders. Antibodies targeting the host's DNA are found in lupus, and many of these antibodies are toxic. Some of these lupus antibodies penetrate living cells and nuclei.

One unusual cell-penetrating lupus autoantibody that is not harmful to normal cells or tissues was previously isolated from a mouse model of lupus by Richard H. Weisbart, M.D. of UCLA. The antibody, known as 3E10, is not only benign but has the capacity to penetrate both healthy and malignant cells and cell nuclei.

Knowing that capacity, Yale researchers were investigating whether 3E10 could be used as a drug-delivery vehicle. But they discovered to their surprise that the antibody already had the ability to sensitize cancer cells to radiation and chemotherapy and interfere with their ability to sustain themselves through DNA repair.

With the discovery of this cancer cell susceptibility, the researchers further found that 3E10, when used alone, could selectively kill cancer cells with DNA repair deficiencies such as those with mutations in the BRCA2 gene. BRCA2 is a tumor suppressor that, when damaged or deficient, can lead to malignancies such as breast, ovarian, pancreatic, and prostate cancers.

"Finding this characteristic of 3E10 opens up a new avenue for researching treatment of BRCA2-related cancers," said lead author Peter M. Glazer, M.D., professor and chairman of therapeutic radiology, professor of genetics, and a member of Yale Cancer Center. "It may also lead us to new therapies for other types of cancers such as brain gliomas."

This discovery may also lead to important new insights into lupus itself. "The most immediate relevance of our findings to human disease is the new recognition that lupus antibodies might be able to be harnessed as new therapies for cancer," said author James E. Hansen, M.D. assistant professor of therapeutic radiology and a member of Yale Cancer Center. "It also opens up new windows for exploration into the biology of lupus antibodies and may explain the unexpectedly low rates of breast, ovarian, and prostate cancer in lupus patients. It also may help explain why lupus patients appear to be very sensitive to DNA-damaging agents."

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