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WEIZMANN INSTITUTE SCIENTISTS DISCOVER:

A SURVIVAL MECHANISM FOR BLOOD CANCER CELLS

Chronic Lymphocytic Leukemia is a type of blood cancer in which specific white blood cells, called B lymphocytes or B cells, build up in the blood, bone marrow and lymph nodes. The lifespan of a normal B cell is limited by an internal self-destruct program but, in cancer cells, this mechanism breaks down. B cells that don't self-destruct can live on to multiply and eventually accumulate in dangerous amounts.

A team of scientists headed by Prof. Idit Shachar of the Weizmann Institute's Immunology Department and Dr. Michal Haran of the Hematology Institute of the Kaplan Medical Center recently discovered what makes these cancer cells stay alive. They then launched a targeted attack on the survival mechanism they discovered and succeeded to significantly raise cancer cell mortality rates. Their findings, which appeared recently in *Proceedings of the National Academy of Sciences* (PNAS), may lead to future treatments for this disease, as well as for other diseases in which B lymphocytes accumulate in the blood.

In previous research, Shachar had found that a specific receptor – a protein on the outer surface of healthy B cells – fulfills a crucial role in helping these cells to survive. She wondered if the same protein might also be a central player in the abnormally high survival rates of cancerous B cells.

Members of Shachar's research team, including Inbal Binsky, Diana Starlets, Yael Gore and Frida Lantner, together Kaplan Medical Center doctors Haran, Lev Shvidel, Prof. Alan Berrebi and Nurit Harpaz, scientists from Yale University and David Goldenberg of the Garden State Cancer Center in New Jersey, examined B cells taken from chronic lymphocytic leukemia patients. They discovered that, even in the earliest stages of the disease, these cells have an unusually high level of both the survival receptor and another protein that binds to the receptor. The scientists found that this protein, in binding to the receptor, initiates a series of events within the cell that leads to enhanced cell survival capabilities. For instance, in one of these events, a substance is produced that helps to regulate the cells' lifespan. This substance causes another protein to be produced, which then prevents the self-destruct program from being activated.

The team treated the chronic lymphocytic leukemia cells with an antibody that attached to the survival receptor, blocking its activity and causing the cancer cell death rate to soar.

The antibodies they used are produced by the firm Immunomedics, in New Jersey, and are currently entering clinical trials for the treatment of several different types of cancer. Following this research, which has revealed the mechanism for the antibody's actions, the company is planning trials for chronic lymphocytic leukemia, as well.



Shachar: "The abnormally elevated levels of this receptor seem to be important factors in the development of this disease, right from the beginning, and they are responsible for the longevity of these cancerous B cells. Blocking the receptor or other stages in the pathway they activate might be a winning tactic, in the future, in the war against cancers involving B cells."

Prof. Idit Shachar's research is supported by the Weizmann Institute of Science-Yale Exchange Program; the Abisch Frenkel Foundation for the Promotion of Life Sciences, Switzerland; and Mr. Joe Gurwin, New York, NY. Prof. Shachar is the incumbent of the Dr. Morton and Anne Kleiman Professorial Chair.

The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

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