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Agent selectively targets malignant B cells in chronic leukemia, study shows

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A new experimental drug selectively kills the cancerous cells that cause chronic lymphocytic leukemia, according to a new study by researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

The study shows that the experimental agent PCI-32765 selectively kills the malignant B lymphocytes that cause chronic lymphocytic leukemia (CLL).

The researchers say the findings, published online in the journal *Blood*, are important because current CLL therapies kill T lymphocytes along with the cancerous B lymphocytes.

T lymphocytes and B lymphocytes make up the adaptive immune system. When CLL treatment destroys them both, patients become highly susceptible to life-threatening infections.

"A drug that kills malignant B lymphocytes and spares T lymphocytes could dramatically improve outcomes for CLL patients," says study leader Dr. John C. Byrd, director, division of hematology and professor of medicine, of medicinal chemistry and of veterinary biosciences at the OSUCCC – James.

"Our collective results indicate that PCI-32765 is an outstanding candidate for further development as a therapeutic for CLL," says study

co-director Dr. Amy J. Johnson, assistant professor of hematology and medicinal chemistry, and a CLL researcher with the OSUCCC-James.

The research by Byrd, Johnson and a group of colleagues used CLL cells from ten patients. It had several key findings related to PCI-32765:

- The agent specifically targets an important signaling molecule called Bruton's tyrosine kinase, which is overexpressed in CLL cells and absent in T cells.
- The agent inhibits the proliferation of CLL cells in laboratory culture and promotes their death by self-destruction (apoptosis).
- It blocks survival signals from cells in the surrounding microenvironment, including soluble factors such as IL-6, IL-4, and TNF-α, and stromal-cell contact.

Provided by Ohio State University Medical Center