

A small subset of normal white blood cells gives rise to a rare leukemia, study shows

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New research has identified a small subset of normal white blood cells in the body that gives rise to a rare incurable form of leukemia.

The study, led by investigators at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James), shows that large granular lymphocyte [leukemia](#) can occur in a small subset of [white blood cells](#) called NKT [cells](#). NKT cells share features of immune cells called T lymphocytes and features of immune cells called natural killer (NK) cells.

The discovery, published online in the *Journal of Clinical Investigation*, arose from studies investigating why a mouse strain engineered to overexpress interleukin-15 often develops large granular lymphocyte leukemia, a disease more common in Asia than the United States, and it points to new ways to prevent the malignancy.

The researchers show that, in mice and in humans, the novel subset of NKT cells responsible for large granular lymphocyte leukemia are marked on their surface by a protein called NKp46. Only small numbers of these cells are present in mice and in humans. The study further shows that overexpression of interleukin-15 can drive these cells but not others to become leukemic.

"These novel NKT cells represent a small white-blood-cell population in normal mice or healthy humans, but they have the potential to develop

into large granular lymphocyte leukemia under certain circumstances, such as a high interleukin-15 environment," says first author Jianhua Yu, a research scientist with the OSUCCC – James.

"Our work suggests that targeting interleukin-15 signaling and NKp46 might offer a new way to prevent this leukemia as we learn more about who is susceptible," notes principal investigator Dr. Michael A. Caligiuri, director of Ohio State's Comprehensive Cancer Center and CEO of the James Cancer Hospital and Solove Research Institute. "In fact, we show that using an antibody to block interleukin-15 prevents large granular lymphocyte leukemia development in this mouse model."

Provided by Ohio State University Medical Center

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