

Novel export-inhibitor shows promise for treating chronic lymphocytic leukemia

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An experimental drug that works by blocking the export of key control molecules from the nucleus of cancer cells shows promise as a treatment for chronic lymphocytic leukemia (CLL) and other incurable B-cell malignancies, 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 agent, called KPT-SINE, belongs to a new class of drugs called selective inhibitors of nuclear export (SINE). The agent was developed by Karyopharm Therapeutics Inc. It is designed to kill [cancer cells](#) by restoring biochemical pathways that normally cause unhealthy cells to self-destruct through a process called programmed cell death, or apoptosis.

The agent targets a protein called CRM1, which, until now, has not been adequately explored in CLL, the researchers say. During disease progression, cancer cells use CRM1 to shunt certain apoptosis-related proteins out of the nucleus, thereby avoiding cell death.

"We believe that KPT-SINE and other nuclear-export inhibitors may represent a unique, entirely new therapeutic strategy for treating cancer by simultaneously restoring multiple normal cell death pathways," says OSUCCC – James research scientist Dr. Rosa Lapalombella who is a co-investigator on the study with Dr. John Byrd, director of the division of hematology and co-director of the OSUCCC – James CLL Experimental Therapeutics Laboratory at OSUCCC – James.

The researchers hypothesize that KPT-SINE will inhibit CRM1 and keep these regulatory proteins in the nucleus where they can initiate programmed cell death.

Lapalombella will discuss the role of CRM1 inhibition in the treatment of CLL on Monday, December 12, at 7:00 a.m. during the 53rd Annual Meeting of the American Society of Hematology in San Diego, CA.

The study, which used CLL cells from patients and a mouse model of CLL, provides essential proof-of-concept data to design and initiate phase I clinical testing of KPT-SINE in patients with these incurable diseases, Lapalombella notes.

"We are excited by our preliminary findings that KPT-SINE represents a promising targeted therapy for CLL patients," Byrd says. "We look forward to transitioning our research toward early clinical development in patients with CLL and related diseases, based upon the data generated by our team."

Provided by Ohio State University Medical Center

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