Study identifies drug resistance of CLL in bone marrow and lymph nodes

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In research to be presented at the American Society of Hematology (ASH) annual meeting, investigators at Dana-Farber Cancer Institute in Boston offer a new explanation of why chronic lymphocytic leukemia (CLL) tends to recur in the lymph nodes and bone marrow after being cleared from the bloodstream by chemotherapy. Their findings will be reported during in an oral session on Monday, Dec. 6.

To uncover the reasons for CLL's resilience in the marrow and lymph nodes, the researchers employed a technique called BH3 profiling, which had been devised by senior author Anthony Letai, MD, PhD, and his Dana-Farber colleagues in 2005. The technique makes it possible to identify cancer cells that are less likely to undergo mitochondrial apoptosis (a form of programmed cell death involving cell structures called mitochondria) because of alterations in the Bcl-2 family of proteins. These abnormalities can make such cells less susceptible to both standard chemotherapy and novel, targeted agents.

In the current study, Letai and his associates found that when CLL cells from patients were grown with non-cancerous support cells from the bone marrow and lymph nodes, the CLL cells were more resistant to apoptosis – and hence harder to kill with treatment – than were CLL cells from the bloodstream. Using BH3 profiling, they discovered that although circulating CLL cells were likely to die by mitochondrial apoptosis in response to treatment, CLL cells grown among non-cancerous cells were much less likely to die this way. The presence of these normal cells, known as stroma, apparently helped the CLL cells

survive, despite receiving treatment that would otherwise have resulted in their death.

"We hope that by clearly identifying the ability of stromal cells to reduce the CLL cells' capability to undergo apoptosis, we can exploit strategies to selectively target the 'help' that stromal cells give to CLL cells," says Letai.

Provided by Dana-Farber Cancer Institute