Protein may represent a switch to turn off B cell lymphoma

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Researchers studying the molecular signals that drive a specific type of lymphoma have discovered a key biological pathway leading to this type of cancer. Cancerous cells have been described as being "addicted" to certain oncogenes (cancer-causing genes), and the new research may lay the groundwork for breaking that addiction and effectively treating aggressive types of B cell lymphoma.

B cell lymphomas, which occur both in children and adults, are cancers that attack B cells in the immune system.

"Our research suggests ways to devise more specific therapies to selectively kill tumor cells in a subset of lymphomas," said study leader Andrei Thomas-Tikhonenko, Ph.D., an oncology researcher at The Children's Hospital of Philadelphia.

The study, conducted in animal cells and human cell cultures, appeared May 1 in The Journal of Clinical Investigation.

An oncogene is a type of gene that normally produces a protein active in cell growth or regulation. However, when the gene is mutated or otherwise overproduced, it can cause cancer. One family of oncogenes is called MYC, and the current study focused on how the MYC oncogene drives B cell lymphoma. MYC codes for Myc, a type of protein called a transcription factor. At high levels, Myc causes the uncontrolled cell growth that is a hallmark of cancer.

The researchers focused on the crucial role of the cell surface receptor CD19, a protein residing on the surface of all B cells that normally recognizes foreign invaders. "We found that CD19 is absolutely required to stabilize the Myc protein," said Thomas-Tikhonenko. "When Myc is stable and present in high levels, it fuels cancer." Patients with high levels of the Myc protein are more likely to die of lymphoma.

Patients with high levels of Myc also had high levels of CD19, and the current study describes a previously unknown molecular pathway that depends on CD19. It also implicates CD19 as a molecular on-off switch on that pathway. Usually, said Thomas-Tikhonenko, when you inhibit one pathway, another pathway compensates to produce the same end result. But in this case, there is no such redundant pathway: "Without CD19, there is no Myc," he added, "so controlling that on-off switch could represent a powerful tool against lymphoma."

The findings are particularly relevant, said Thomas-Tikhonenko, to current oncology clinical trials that are testing antibodies that act broadly against the CD19 receptor. Such antibodies kill all B cells, and thus weaken the immune system. His study suggests that understanding the CD19 pathway could enable researchers to design a more specific therapy that selectively kills tumor cells while sparing healthy B cells.

Further studies in his lab, he added, will further investigate these molecular pathways and how to translate this knowledge into future anti-cancer treatments.

More information: "CD19 is a major B cell receptor-independent activator of MYC-driven B-lymphomagenesis," *The Journal of Clinical Investigation*, published online May 1, 2012, doi:10.1172/JCI45851

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