Researchers identify factor boosting leukemia's aggressiveness

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Chronic lymphocytic leukemia (CLL) cells survive and thrive not just by their own innate wiles, but by also acquiring aid and support from host cells in their surrounding environment. In a paper published online this week in The *Proceedings of National Academy of Sciences*, an international team of researchers led by cancer specialists at the University of California San Diego School of Medicine and the Moores UCSD Cancer Center identify a particular relationship that can promote notably aggressive leukemias and lymphomas.

"The microenvironment is the term used to describe the cells that cluster around CLL cells in the lymph nodes, spleen and bone marrow. These cells secrete factors that can protect CLL cells from dying," said Thomas J. Kipps, MD, PhD, Evelyn and Edwin Tasch Chair in Cancer Research, Professor of Medicine, Deputy Director of Research Operations at the Rebecca and John Moores UCSD Cancer Center and senior co-author of the paper with Michael Karin, PhD, Distinguished Professor of Pharmacology in UCSD's Laboratory of Gene Regulation and Signal Transduction.

Kipps, Karin and colleagues from Iowa, The Netherlands and Taiwan looked specifically at a protein called B-cell activating factor or BAFF, which is produced in high levels by "nurselike cells" in the CLL microenvironment. Nurselike cells are a subset of blood cells in CLL patients that help cancer cells avoid apoptosis or natural cell death. Kipps and colleagues first described this relationship in 2000.

The researchers found that BAFF interacts with a gene linked to leukemogenesis - the development of leukemia - called c-MYC. Normal MYC genes help regulate cell proliferation, but when upregulated or increased by mutations, c-MYC can promote more aggressive leukemias and lymphomas. To what degree this relationship influences CLL - the most common form of adult leukemia - remains unknown, though Kipps said the findings suggest therapeutic promise.

"We found that BAFF can upregulate expression of c-MYC in CLL cells and that patients who have CLL cells with high levels of c-MYC have aggressive disease," said Kipps. "These findings may lead to improvements in our ability to treat patients with CLL, either by blocking the effect of BAFF on CLL cells or inhibiting the signaling pathways triggered by BAFF that can lead to upregulation of MYC."

Provided by University of California -- San Diego