Researchers identify novel regulatory mechanism in inflammatory signaling of immune cells

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(PhysOrg.com) -- Using cancer cells that were originally isolated from an anaplastic large cell lymphoma patient, two researchers, including a faculty member of The University of Texas at Austin's College of Pharmacy, have identified a novel regulatory mechanism in inflammatory signaling of immune cells that may prove beneficial in treating cancer.

Their study is being published in the Jan. 9 issue of *Science* magazine.

Dr. Casey Wright, assistant professor of pharmacy, said researchers wanted to better understand how the membrane protein, CD30, contributes to lymphoma. CD30 is a cell surface receptor that communicates signals from the extracellular environment into the cell, resulting in a cellular response. It has been recognized since the early 1980s that CD30 is present in very high amounts in certain lymphomas and leukemias, much more than in normal cells.

"This makes CD30 an attractive therapeutic target," said Wright, who joined the pharmacology/toxicology pharmacy faculty in fall 2008. In the study, the researchers uncovered an unexpected partner protein that interacts with CD30. This protein, known as ARNT, is best characterized for its role in mediating the metabolism of environmental toxins and also for mounting the hypoxic response in cells exposed to low oxygen levels.

"Our research describes a novel role for ARNT, which had never been implicated in the signaling pathway of a membrane protein like CD30," said Wright, who conducted the study as a research fellow at the University of Michigan Medical School. His adviser at Michigan, Dr. Colin Duckett, is co-author of the article in *Science*.

In some lymphomas, like Hodgkin's lymphoma, the increased presence of CD30 results in a continual activation of five cellular proteins that are collectively referred to as nuclear factor-kappaB (NF- kB).

"NF-kB turns on genes whose products are involved in cellular proliferation and, thus, sustained NF-kB activity is thought to lead to cancer," Wright said.

The researchers also found that ARNT is a negative regulator of CD30 signaling in that it shuts down NF-kB at the DNA level.

"This is an important finding because how NF-kB is regulated at the level of DNA is less clear," Wright said. "The regulation of NF-kB by ARNT provides a link between human exposures to environmental toxins and the subsequent cancers of the immune system, like lymphoma, that often arise. While these findings are significant, this is only the beginning, and there is much more work to be done before we realize the full impact of our results."

Provided by University of Texas at Austin