Lipid involved with gene regulation uncovered

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(PhysOrg.com) -- Virginia Commonwealth University School of Medicine researchers have discovered a new role for the bioactive lipid messenger, sphingosine-1-phosphate, or S1P, that is abundant in our blood - a finding that could lead to a new generation of drugs to fight cancer and inflammatory disease.

In the Sept. 4 issue of the journal *Science*, a team led by Sarah Spiegel, Ph.D., professor and chair in the VCU Department of Biochemistry and Molecular Biology and co-leader of the VCU Massey Cancer Center's cancer cell biology program, reported that the cell nucleus, which contains the DNA that codes for all of our genes, also contains and produces S1P that is important for the regulation of certain genes. Researchers have known that the nucleus contains several kinds of lipids, but their functions have remained unknown until now. The team identified the mechanisms by which cancer cells produce S1P in the nucleus and uncovered its new function there to regulate gene expression .

Spiegel, who is internationally recognized for her pioneering work on new lipid mediators that regulate cell growth and cell death, and her colleagues first discovered the role of S1P in cell growth regulation nearly a decade ago.

In this study, the team demonstrated that S1P, produced by type 2 sphingosine kinase in the nucleus, regulates genes by acting like a widely used type of cancer chemotherapeutic drug known as histone deacetylase

inhibitors. Histone deacetylases are a family of enzymes that regulate expression of numerous genes that code for proteins involved in cancer and many other human diseases. Although several types of histone deacetylase inhibitors are now in clinical trials, the physiological regulators of these important enzymes were not known.

“Our work shows that S1P is a physiologically important regulator of histone deacetylases,” said lead author Spiegel.

“We believe that our studies will help in the development of a new class of histone deacetylase inhibitors that might be useful for treatment of cancer and inflammatory diseases,” she said.

According to Spiegel, previous investigations have shown that increased levels of type 1 sphingosine kinase, one of the two enzymes that produce S1P inside cells, but not in their nucleus, correlates with poor outcome in many types of human cancers. Spiegel and her team have previously developed a specific inhibitor of this type 1 sphingosine kinase and showed that it was effective in mice against growth of human leukemia and brain cancer tumors.

Provided by Virginia Commonwealth University (news : web)