

Anti-inflammatory signal protein discovered

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(PhysOrg.com) -- Researchers at the Swedish medical university Karolinska Institutet have discovered a protein that is crucial in mediating the anti-inflammatory actions of nuclear lipid receptors. The findings, published in the research journal *Genes & Development*, link lipid metabolism and inflammation and open up new possibilities for developing treatments of metabolic diseases associated with inflammation, such as diabetes and atherosclerosis.

Nuclear receptors are regulatory proteins within the cell nucleus that can directly bind to a variety of hormones, metabolites and pharmaceuticals. Binding affects the activity of these proteins, causing them to switch genes on or off that in turn leads to increased or decreased production of the proteins that carry out diverse functions within the cell.

Numerous nuclear receptors are known as master regulators of <u>lipid</u> metabolism and homeostasis. Latest research indicates that these receptors also play important roles in the control of inflammation via mechanisms that remain to be clarified.

A team led by Professor Eckardt Treuter has now investigated the molecular mechanisms of how the nuclear lipid receptors LRH-1 and LXR inhibit inflammatory gene expression in liver during the so-called acute phase response. The study identified GPS2, a protein that directly interacts with receptors, as a central component of a sophisticated protein network - or 'genomic positioning system' - determining where and when these lipid receptors can function anti-inflammatory.



The identified pathway connects metabolism and inflammation and is therefore relevant for the understanding of metabolic diseases such as diabetes and atherosclerosis. The researchers suspect even broader roles of related pathways in different tissues linked to metabolic diseases and to cancers.

"We are now closer to understanding, at the molecular level, how dysregulation of individual components of these pathways causes alterations in gene expression that contribute to the development of metabolic diseases linked to inflammation. This knowledge may open up novel pharmacological interventions. For example, drugs that stabilize receptor interactions with GPS2 could possibly trigger the anti-inflammatory pathway", Eckardt Treuter says.

More information: GPS2-dependent corepressor/SUMO pathways govern anti-inflammatory actions of LRH-1 and LXRb in the hepatic acute phase response, *Genes & Development*, online February 16, 2010. genesdev.cshlp.org/content/24/4/381.abstract

Provided by Karolinska Institutet

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