

The protein modifier SUMO helps set apart females and males

September 2 2009

One way in which men and women differ is in their expression of liver proteins that control a large number of whole-body processes such as energy generation and lipid and steroid hormone production and turnover. Now, Walter Wahli and colleagues, at the University of Lausanne, Switzerland, have identified a new mechanism underlying this differential expression of proteins in male and female mice.

The protein PPAR-alpha is able to enter the nucleus, where it acts to control the expression of a large number of genes. In the study, PPAR-alpha was found to repress the expression of many liver genes responsible for making proteins involved in immunity and steroid production and turnover only in female mice.

One of the genes most strongly repressed in female mice by PPAR-alpha was Cyp7b1, which generates a protein involved in drug breakdown and the generation of cholesterol, steroids, and other fats. Detailed analysis revealed the mechanism by which PPAR-alpha repressed Cyp7b1 expression, it was modified by a process known as sumoylation. Importantly, this only occurred in female mice.

As PPAR-alpha-mediated repression protected female mice from estrogen-induced intrahepatic cholestasis, the most common liver disease during pregnancy, the authors suggest that PPAR-alpha agonists might provide a new approach to prevent this disease.

More information: Sumoylated PPAR-alpha mediates sex-specific gene



repression and protects the liver from estrogen-induced toxicity in mice, <u>Journal of Clinical Investigation</u>, <u>www.the-jci.org/article.php?id=39019</u>

Source: Journal of Clinical Investigation

Citation: The protein modifier SUMO helps set apart females and males (2009, September 2) retrieved 9 May 2024 from

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