Food withdrawal results in stabilization of important tumor suppressor

December 21 2016

Tumor suppressors stop healthy cells from becoming cancerous. Researchers from Charité - Universitätsmedizin Berlin, the Medical University of Graz and the German Institute of Human Nutrition in Potsdam-Rehbruecke have found that p53, one of the most important tumor suppressors, accumulates in liver after food withdrawal. They also show that p53 in liver plays a crucial role in the body's metabolic adaptation to starvation. These findings may provide the foundation for the development of new treatment options for patients with metabolic or oncologic disorders. Results of this study have been published in *The FASEB Journal*.

Previously described as the 'guardian of the genome' and voted 'Molecule of the Year' in 1993, p53 is one of the most important proteins regulating cell growth and a major focus for oncology research. It is a protein that has the ability to interrupt the cell cycle and block the division of diseased cells. In order to better understand its physiological regulation, the researchers around Prof. Dr. Michael Schupp from Charité's Institute of Pharmacology studied the regulation and function of p53 in normal, healthy cells. After withholding food from mice for several hours, the researchers were able to show that p53 protein accumulates in the liver. In order to determine which type of liver cells cause this accumulation, the researchers repeated the experiment using cultured hepatocytes. They found that the starvation-induced accumulation of p53 was indeed detectable in hepatocytes, irrespective of whether these cells were of mouse or human origin.

"Our data also suggest that the accumulation of p53 is mediated by a cellular energy sensor, and that it is crucial for the metabolic changes associated with starvation," explains Prof. Michael Schupp. The researchers were able to show that mice with an acute inactivation of the p53 gene in liver had difficulties in adapting their metabolisms to starvation. "Food intake seems crucial in determining the protein levels of p53 in liver, and p53 also plays an important role in normal liver metabolism," says Prof. Schupp. The researchers are planning to study whether their observations are limited to liver cells, or whether this p53 accumulation also occurs in other tissues and organs. Prof. Schupp concludes: "It would be interesting to conduct further experiments to test whether the starvation-induced accumulation of p53 has an effect on the development of specific forms of cancer, or whether certain ways of timing meals might affect p53 protein levels in such a way as to promote cancer development."

More information: A. Prokesch et al, Liver p53 is stabilized upon starvation and required for amino acid catabolism and gluconeogenesis, *The FASEB Journal* (2016). DOI: 10.1096/fj.201600845R

Provided by Charité - Universitätsmedizin Berlin