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PHF20-mediated SREBP regulation is required for the enhancement of lipogenesis and hepatic steatosis in PHF20 transgenic mice

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The importance of PHD finger protein 20 (PHF20) in the cellular process is recently emerging as a regulator for the p53 and NF- κ B signaling. In this study, we have provided the clear evidence that PHF20 exhibit the novel function in hepatic steatosis by regulating lipogenic genes. Transgenic (TG) mice with PHF20 expression are glucose intolerant; however the insulin sensitivity of peripheral tissue in PHF20 TG mice appeared to be unaffected. Interestingly, the total contents of insulin amount in pancreatic islets and the glucose stimulated-insulin secretion of isolated islet were reduced in PHF20 TG mice compared to wild type mice, indicating that the phenotypic characteristics of PHF20 mice with glucose-intolerance is due to the lack of insulin production/secretion in pancreatic beta-cells in PHF20 TG mice. Administration of PHF20 TG mice with high fat diet for 8 weeks leads to increase the body weight compared to control mice. By screening the profile array of transcription factor activation with PHF20, SREBP1 was found to be activated by PHF20 overexpression in HeLa cells. Chromatin-immunoprecipitation analysis revealed that PHF20 directly bind the promoter of SREBP1. Furthermore analysis of quantitative PCR with liver tissues from PHF20 TG mice showed the up-regulation of SREBP1 target genes. Taken together, PHF20 appears to be positive regulator for lipogenesis and PHF20-mediated SREBP1 up-regulation is responsible for the accumulation of hepatic lipid, leading to weight gain phenotype. Thus, this study provided the new concept for glucose metabolism and novel pharmacological target in obesity.

Biography

Jisoo Park has completed her Master's degree from Sookmyung Women's University and has experience of cellular signaling in the terminal differentiation of keratinocyte. She has then moved to University of Cincinnati, Ohio, USA and worked as a Research Associate in the lab of Prof. George Thomas to learn the cellular signaling of mTOR/S6K1 pathway in the field of energy metabolism by using animal models. She returned back to Korea to obtained PhD in the field of Energy Metabolism at the Department of Pharmacology, College of Medicine, Chungnam National University. She is currently investigating the putative roles of PHF20 in the regulation of glucose metabolism. She has published 9 papers in reputed journals including *Metabolism*, *Cellular Signaling* and *Head & Neck*.

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