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Molecular mechanism of intracellular lipid accumulation: Suppressive effect of Pycnogenol^{R} in liver cells

Shoichiro Ikuyama, Bin Fan, Jian-Qiu Gu, Kumiko Mukae, Hideyuki Watanabe

Department of Metabolism, Hematology and Rheumatic Diseases (DMHRDs), Kyushu University Beppu Hospital, Beppu 874-0838, Japan

Corresponding Author: Shoichiro Ikuyama, Department of Metabolism, Hematology and Rheumatic Diseases (DMHRDs), Kyushu University Beppu Hospital, Beppu 874-0838, Japan

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ABSTRACT:

Cells are physiologically ready to accumulate lipids such as triacylglycerides in the cytoplasm. Five classes of perilipin (PLIN) family proteins are known to be involved in the process of intracellular lipid accumulation. PLIN2 is expressed ubiquitously including adipocytes, hepatocytes and macrophages. Over-expression of PLIN2 is demonstrated in the lesions of fatty liver diseases and atherosclerosis. Suppression of PLIN2 expression prevents from developing these pathological conditions in animal models, suggesting that PLIN2 could be a therapeutic target molecule for excessive intracellular lipid accumulation which leads to various metabolic derangements. The PLIN2 gene promoter has two important *cis*-acting elements in close proximity:AP-1 element which mediates inflammatory signals and PPRE which mediates free fatty acid effect. In NMuLi mouse liver cells, FFA such as oleic acid requires both functional AP-1 and PPRE simultaneously to stimulate the promoter activity, indicating the presence of intimate interaction of inflammatory and metabolic signals on this gene. Pycnogenol^{R}, French maritime pine bark extracts, suppressed the oleic acid-induced PLIN2 expression and lipid accumulation in NMuLi cells. We found that Pycnogenol^{R} did not suppress the PLIN2 promoter activity or AP-1 binding to DNA. Instead, Pycnogenol^{R} facilitates the PLIN2 mRNA degradation, leading to suppression of lipid accumulation. This effect seems to be independent of antioxidant effect of Pycnogenol^{R}. We raise the idea that PLIN2 is a putative target molecule for prevention of pathological condition induced by

excessive lipid accumulation, and this class of natural compounds could be putative therapeutic modalities.

Key words: Pycnogenol^{R}, lipid droplet, perilipin, fatty liver disease