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〈シンポジウム I〉
『次世代先端評価技術を駆使する』

栄養とエピジェネティクス
―エピゲノム変化と肥満インスリン抵抗性―

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Metabolic Syndrome and Epigenomic Regulations

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Abstract

All of our tissues contain the same 30,000 genes; however, in a given tissue and at a given stage, owing to an "epigenetic code," only a few of these genes are expressed, giving rise to the "phenotype." Disruption of the balance of epigenetic networks may cause several major diseases, including cancer, syndromes involving chromosomal instabilities, and mental retardation. However, the relevance of epigenetics to other physiopathological mechanisms in common diseases, such as metabolic syndrome, was less clear. Through genome wide identification of PPARγ targets by chromatin immunoprecipitation on Chip（ChIP-Chip）analysis, we identified several histone modification enzymes（HKMTs）and candidates' genes as new PPARγ targets. We show that these HKMTs function either anti-, or pro-adipogenic factor and coordinately regulated their gene expressions by PPARγ to promote adipogenesis. We therefore propose the novel action of PPARγ: controlling epigenomic status in fat cell differentiation. In addition, we demonstrate that JHDM2a, a demehtylase of H3K9me2, regulates metabolic genes related to energy homeostasis. Mice deficient in JHDM2a（*JHDM2a*−/−）develop adult onset obesity, hypertriglyceridemia, hypercholesterolemia, hyperinsulinemia, and hyperleptinemia, which are hallmarks of metabolic syndrome. Thus, H3K9 demethylase JHDM2a is a crucial regulator of genes involved in energy expenditure and fat storage, which suggests it is a previously unrecognized key regulator of obesity and metabolic syndrome.

Key words: obesity, metabolic syndrome, epigenome, PPARγ, adipocyte.