**Metabolic Syndrome : Definition and Pathophysiology**

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Metabolic syndrome is characterized by a constellation of diabetes, hyperlipidemia and hypertension, and represents a major cause of cardiovascular disease. Insulin resistance and visceral fat accumulation are thought to play causal roles in the development of metabolic syndrome. In fact, both insulin receptor substrate (IRS)-1 knockout and IRS-2 knockout mice show features of metabolic syndrome. Metabolic syndrome in humans is caused by insulin resistance linked to obesity and visceral fat accumulation. Adiponectin is a fat-specific hormone which sensitizes the body to insulin. Targeted disruption of adiponectin show features of metabolic syndrome such as insulin resistance, glucose intolerance, hypertriglyceridemia, and hypertension. Obesity is associated with down-regulation of adiponectin, which is causally involved in obesity-linked insulin resistance and metabolic syndrome. Adiponectin activates AMPkinase and PPAR $\alpha$ pathway via adiponectin receptors (AdipoR1 and AdipoR2), thereby stimulating β-oxidation of lipids, reducing tissue triglyceride content and ameliorating insulin resistance in liver and skeletal muscle. AdipoR1 knockout, AdipoR2 knockout, and AdipoR1/R2 double knockout mice show insulin resistance and impaired glucose tolerance and analyses of these mice have revealed that AdipoR1 and AdipoR2 mediate the major part, if not all the part, of adiponectin binding and adiponectin-induced biological effects. Obesity is associated with down-regulation of adiponectin receptors and adiponectin resistance. PPAR $\gamma$ agonists upregulate the reduced adiponectin levels in obesity, whereas PPAR $\alpha$ agonists upregulate the reduced adiponectin receptors in obesity. In an attempt to identify agonists toward adiponectin receptors, we have recently identified osmotin, a plant defense protein, can bind and activate mammalian adiponectin receptors. In this symposium, I will talk about recent data on molecular mechanisms and treatment strategies of insulin resistance, metabolic syndrome and cardiovascular diseases with an emphasis on the adiponectin pathway.

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