Adipocytokines and obesity-related diseases

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To elucidate the biological characteristics of adipose tissue, we analyzed the gene expression profile in visceral and subcutaneous fat. Unexpectedly, adipose tissues, especially visceral fat expressed a variety of genes for secretory proteins. About 30% of the whole genes expressed in visceral adipose tissue are genes encoding secretory proteins and most of them are various biologically active molecules which we call adipocytokines. We found plasminogen activator inhibitor type1(PAI-1) and heparin binding EGF-like growth factor and production of these atherogenic adipocytokines was shown to increase with the accumulation of visceral fat, which may be one of mechanism of vascular disease in visceral obesity.

We found a unique novel collagen-like protein, adiponectin encoded by the most abundant expressed gene in adipose tissue, named apM1(adipose most abundant gene transcript-1). Plasma levels of adiponectin ranged from 0.3~3mg/dl and decreased in patients with visceral obesity, type 2 diabetes and coronary artery disease. Screening of mutation in adiponectin gene revealed that patients carrying missense mutation showed markedly decreased plasma levels of adiponectin and had CAD. These data suggest that hypoadiponectinemia can be considered an important risk factor of CAD. Cell biological studies revealed that adiponectin has a potent inhibitory effect on the expression of adhesion molecules in endothelial cells and a inhibitory effect on the expression in macrophages.

In order to confirm these antidiabetic and antiatherogenic functions of adiponectin, we developed adiponectin knockout (KO) mice. Adiponectin KO mice showed severe insulin resistance with impaired glucose metabolism, when a high fat/ high sucrose diet was loaded. KO mice also developed intimal thickening when endothelial injury was given.

In conclusion dysregulation of adipocytokine might have major roles in the development of obesity-related diseases.