Adiponectin and its receptors - New insights in the pathogenesis of metabolic syndrome -

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We identified adiponectin as therapeutic target adipokine for metabolic syndrome by using combination of genome-wide scanning and DNA chips. Genetic studies on SNP of adiponectin gene as well as functional analyses including generation of transgenic or knockout mice suggest that reduced adiponectin levels play a causal role in the development of metabolic syndrome. Moreover, human adiponectin mutations analyses led to identification of high molecular weight (HMW) adiponectin as most active form. We then developed an ELISA system and showed that measurement of HMW is useful for prediction of metabolic syndrome. Recently, it has been shown that adiponectin regulates energy expenditure and food intake also centrally. We also identified adiponectin receptors (AdipoR1 and R2) by expression cloning and found that AdipoRs were also decreased in obesity. Overexpression by adenoviruses suggest that strategies to increase AdipoRs should serve as treatment strategies for metabolic syndrome. Moreover, network analyses revealed that AdipoR1 may be tightly linked to activation of AMP kinase pathway, whereas AdipoR2 may be tightly linked to activation of PPARalpha pathway. Simultaneous disruption revealed that AdipoR1 and R2 serve as the predominant receptors for adiponectin in vivo and play important roles in the regulation of glucose and lipid metabolism, inflammation and oxidative stress in vivo. Finally, we showed that PPARgammą agonist up-regulated total and HMW adiponectin, whereas PPARalphą agonist up-regulated AdipoRs. Moreover, osmotin, present in fruits and vegetables, activated AMPK via AdipoRs in myocytes.