The Role of Adipose Dysfunction in Heart Failure and Obesity.

Ippei Shimizu
Department of Cardiovascular Biology and Medicine
Division of Molecular Aging and Cell Biology
Niigata University Graduate School of Medical and Dental Sciences, Japan

The dramatic increase in obese population and the accompanying diabetic conditions puts a large part of the population at an increased risk of developing a variety of cardiovascular diseases. Systemic insulin resistance (hyperinsulinemia) develops in obesity/ diabetes and heart failure and promotes pathologies in these age related disorders. It is widely accepted that chronic inflammation in the visceral fat is causal for the development of systemic insulin resistance and we have recently demonstrated the pathological role of systemic metabolic dysfunction in obesity and heart failure (*Nature* 2007, *Nat Med* 2009, *J Clin Invest* 2010, *Cell Metab* 2012, 2013, 2014).

Brown adipose tissue (BAT) is abundant in newborn humans and small rodents. Accumulating evidence has shown that human adults also possess active brown adipose tissue and it is reported to decrease with obesity and aging. Recently we found that obesity causes capillary rarefaction and hypoxia in BAT leading to BAT “whitening” that is associated with diminished β-adrenergic signaling, the accumulation of large lipid droplets and mitochondrial dysfunction and loss. These changes in the BAT microenvironment impair thermogenic responses and contribute to dysfunctional glucose metabolism (*J Clin Invest* 2014). Interestingly, low body temperature is reported to predict poor prognosis of heart failure in patients. Our recent study has indicated that maintenance of BAT homeostasis is important for the suppression of pathologies in heart failure. We also found a previously unknown mechanism that induces BAT dysfunction upon metabolic stress. Here I would like to delineate the role of adipose dysfunction in age related diseases, especially focusing on the role of WAT and BAT dysfunction in obesity, diabetes and heart failure.