

addition, SENP2 overexpression selectively enhanced the expression of the PPAR- γ target genes FABP3 (fatty-acid-binding protein 3) and CD36 (fatty acid translocase), in the presence and absence of rosiglitazone, but had no effect on ADRP (adipose differentiation-related protein) [Chung SS et al. *Biochem J* 2011].

Prof. Park emphasized the important role that GPx3 plays in regulating oxidative stress, and its potential as a therapeutic target for both insulin resistance and T2DM. In addition, he also noted the potential for SENP2 as a potential therapeutic target to deal with excess fatty acids in skeletal muscle.

Thermogenesis-Based Obesity Interventions

Written by Nicola Parry

Yangha Kim, PhD, Ewha Woman's University, Seoul, South Korea, reviewed the role of thermogenic agents in the management of cardiometabolic risk. The global obesity pandemic represents a major public health problem, in particular since overweight and obesity are well-known risk factors that predispose patients to cardiovascular disease (CVD) and type 2 diabetes [Seale P, Lazar MA. *Diabetes* 2009]. Indicators of abdominal adiposity, specifically waist circumference and waist-to-hip ratio have been shown to be associated with coronary heart disease (CHD) risk in middle-aged women [Rexrode KM et al. *JAMA* 1998].

The search for strategies to stimulate thermogenesis in obesity management represents a current focus of significant attention. Brown adipose tissue is important in thermogenesis and contributes to energy expenditure, and studies have shown its activity significantly affects body weight in mice [Seale P, Lazar MA. *Diabetes* 2009].

Cells in brown adipose tissue contain large numbers of mitochondria, the organelles where respiration and thermogenesis occur. Mitochondria also contain uncoupling proteins (UCPs) that function as transporters to control the coupling between cell respiration and phosphorylation of ADP. UCP1 is expressed predominantly in brown adipose tissue, UCP2 is expressed in various body tissues, and UCP3 is expressed in high levels mainly in skeletal muscle and brown adipose tissue. Although UCP2 and UCP3 do not play direct roles in thermogenesis, they can contribute when fully stimulated by certain environmental factors, and skeletal muscle plays an important role in energy expenditure by activation of uncoupling proteins. In one study, long-term high-fat feeding resulted in increased fat storage in mice lacking UCP3 [Costford SR. *Am J Physiol Endocrinol Metab* 2008], suggesting it protects against fat gain on high-fat diets. Skeletal muscle UCP3 gene expression was also increased by dietary fish oil and docosahexaenoic acid.

Research is ongoing to identify agents to exploit thermogenesis, specifically in the areas of increasing lipolysis, uncoupling protein expression, and body temperature:

- Various compounds have been shown to stimulate lipolysis, including green tea epigallocatechin-3-gallate [Lee MS et al. *Phytother Res* 2009], polyunsaturated acid (eicosapentaenoic acid; EPA) [Lee MS et al. *Genes Nutr* 2008], capsaicin [Lee MS et al. *Phytother Res* 2011], and L-carnitine [Lee MS et al. *J Med Food* 2006].
- Upregulation of UCP2 has also been described in studies in which rodents were fed capsaicin [Ann JY et al. *J Food Sci Nutr* 2011]. Prof. Kim reviewed recently published data from an *in vitro* study, demonstrating that EPA and DHA directly control UCP3 gene expression in muscle cells [Lee MS et al. *Nutrients* 2013].
- Increased body temperature, reduced body weight, and white adipose tissue weight were reported in high-fat diet-induced obese mice supplemented with epigallocatechin-3-gallate [Lee MS et al. *Ann Nutr Metab* 2009]. Increased energy expenditure has also been demonstrated in people following capsinoid ingestion.

It is suggested that these agents target the AMP-activated protein kinase pathway. This pathway is important in cellular energy homeostasis, in particular through inhibition of fat synthesis and promotion of thermogenesis [Lee MS et al. *Nutrients* 2013]. Manipulating these mechanisms may therefore provide novel ways to harness the body's thermogenic potential for the development of new therapies for millions of obese or diabetic patients.

Management of Cardiovascular Risk Factors in Asymptomatic Patients With Hypertension

Written by Brian Hoyle

Hyuk-Jae Chang, MD, PhD, Severance Cardiovascular Hospital, Seoul, South Korea, presented the results of the Cardiovascular Risk factors managEment in Asymptomatic hypertensIVE Subjects (CREATIVES) study. CREATIVES was a prospective, observational study conducted between January 2010 and May 2011.

National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) risk stratification that is based largely on the low-density lipoprotein cholesterol (LDL-C) level can overlook many patients with acute