In this issue of Adipocyte

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The Future Is Brite
pp 4–9

In mammals, brown and white fat (characterized by their brown or white adipocytes) are the two major adipose tissue types that exist. While white fat is mainly used for energy storage, brown fat is used to generate energy in the form of heat in order to regulate body temperature. The term “brite adipocyte” has come to describe adipocytes within white adipose tissue that exhibit brown adipocyte characteristics, and has been found in response to stimuli such as colder temperatures. This mini review by Rosenwald and Wolfrum traces the current research and understanding of brite adipocytes including possible ways that it may be formed. The authors look to the future of brite adipose research as well, which may hold new ways to increase energy expenditure within the body (Fig. 1).

Stress and Inflammation of the Heart—a Potential Link to Adiponectin
pp 10–8

Clinical evidence suggests strong links between diabetes and cardiovascular disease with ER/SR stress and cardiac muscle tissue inflammation. And while adiponectin synthesized in adipose tissue has been found to have anti-diabetic, anti-atherogenic, and cardioprotective properties, diabetic patients have been shown to have lower levels of adiponectin when compared with their healthy counterparts. Authors Boddu et al. ask the question, is there an association between adiponectin and ER/SR stress? Using wild-type and adiponectin knockout mice that were placed on a regular or high fat diet, the authors of this research paper attempt to understand the role of ER/SR stress with regards to adiponectin regulation. They show that adiponectin confers cardioprotective effects by lowering ER/SR stress and inflammation.

Metabolic Consequences of Adipocyte-Specific Knockout of PKC-λ
pp 19–29

Knockout (KO) of atypical protein kinase C-λ (PKC-λ) in the muscle has been shown to produce insulin resistance by affecting insulin-stimulated glucose transport in the muscles. Liver-specific deletion of PKC-λ, however, produces insulin-hypersensitivity. Authors Sajan et al. generated mice where atypical PKC-λ was deleted in adipocytes (AλKO) in order to determine if aPKC is required for insulin-stimulated glucose transport in adipocytes as well as other metabolic processes with regards to adipocytes while also attempting to discover the potential consequences of loss of aPKC in these cells. In this research paper, the authors show evidence supporting the claim that in mice, PKC-λ is needed for insulin-stimulated glucose transport as well as ERK signaling in adipocytes. The impairments

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of these events in AΔKO mice produced a phenotype with reduced adiposity and enhanced insulin suppression of hepatic gluconeogenesis.

**Energy Balance and Ovine G6PDH**

pp 30–8

The rate-limiting enzyme of the pentose phosphate pathway, glucose 6-phosphate dehydrogenase (G6PDH), is a generator of the cellular reductant NADPH, which is used in de novo fatty acid synthesis. This enzyme is genetically diverse, with many different G6PDH variants in existence. In this research paper by Triantaphyllopoulos et al., the authors build on previous research regarding two differently expressed ovine G6PDH transcripts (oG6PDa and oG6PDDb) which may show a new role in lipid metabolism in sheep. Their research attempts to clarify and explain the two ovine G6PHD protein isoforms and their roles in energy balance as well as potential physiological effects of oG6PHDa/b proteins.

**Inflammatory Mediators during Diabetes Progression**

pp 39–45

While the human body requires a certain level of inflammation for immunity enhancement, chronic inflammation can lead to multiple metabolic disorders such as obesity, cardiovascular disease, and type 2 diabetes. As the number of diabetic and obese people continue to rise in developing countries such as India, this timely research paper by Upadhyaya et al. attempts to discover potential associations of the inflammatory markers adiponectin and IL-6 in healthy, prediabetic, and diabetic people in India. Their results show significant reductions in adiponectin and increase in IL-6 in prediabetic and hyperglycemic populations. Significant changes in these inflammatory markers were observed during the progression from healthy to a diabetic condition.

**Fibroblast Growth Factor and Nutritionally Induced Obesity**

pp 46–9

While fibroblast growth factor (FGF) and the FGF receptor (FGFR) system play a role in angiogenesis, its effect on adipose tissue-related angiogenesis is relatively unknown. In this brief report by Scroyen, Vranckx, and Lijnen, the authors investigate the possible effect of SSR (an inhibitor of multiple FGFRs) on adipose tissue with regards to angiogenesis and fat development in the presence of nutritionally induced obesity. However, this SSR treatment did not seem to have an effect on adipose tissue growth or angiogenesis.

**Silence of the (MMP-9) Genes**

pp 50–3

It is well known that white adipose tissue can be drastically affected by nutritional status, and certain metalloproteinases (MMPs) play key roles in this process. Previous studies have implicated that the MMP gelatinase B (MMP-9) might have an important role in adipose tissue growth via its effects on adipogenesis. In this brief report by Bauters, Van Hul, and Lijnen, the authors use gene silencing of MMP-9 in 3T3-F442A preadipocytes to determine its effects on adipogenesis, and concludes that MMP-9 does not contribute the differentiation of preadipocytes into mature adipocytes.

**How Different is Human Brown Fat?**

pp 54–7

Although many studies focus on white, brown, and brite fat as classified in mice, this commentary by Scheele et al. discusses whether these fats as defined in mice can also be used to describe thermogenic adipocytes in humans. The authors focus on the human fat derived from the supraclavicular region, and show how the fat derived from this region in adult humans does in fact show characteristics of brown fat, as well as features often found in white and brite fat. This suggests that, while these adipocyte subtypes may work fine in mice, with regards to humans the classification and definitions may need to be changed.

**T-Bet-Deficient Mice Uncouple Adiposity from Insulin Resistance**

pp 58–62

This commentary by Stolarczyk et al. looks at a potential role for the immune cell transcription factor, T-bet (Tbx21), with regards to metabolic regulation. Originally seen as a main regulator of Th1 cell development, studies have recognized the role T-bet plays in the immune system as well as in the direction of T-cell homing to pro-inflammatory sites (Fig. 2). The interesting obese but insulin-sensitive phenotype of the T-bet-deficient mice was associated with reduced cytokine secretion, T-cell trafficking and immune cells in the adipose. The authors go on to discuss their findings that a deficiency of T-bet can enhance insulin sensitivity, an insight which may open the door to novel treatments of conditions that are closely
tied to insulin resistance, such as type 2 diabetes and obesity.

**Does Beige Fat Exist in Humans?**  
*pp 63–6*

The existence of metabolically active brown adipose tissue in humans has been widely accepted; and due to its ability to generate heat this brown fat is an attractive target for obesity and related metabolic disorders. However, studies in animals have found a second type of brown adipocyte (beige) that is found within white adipose tissue deposits, and this second type could prove to be another target for therapeutic intervention. This commentary by authors Lidell, Betz, and Enerbäck looks at recent studies in order to explore the questions regarding this second type of brown adipocyte and its potential existence in humans.

**A Potential New Pathway in Insulin Resistance**  
*pp 67–8*

The discovery of irisin as a peptidic hormone that can stimulate brown-fat development in white adipose tissues could have prolific benefits for numerous ailments including diabetes, obesity, and many pathological conditions. The recently discovered hormone betatrophin is connected to irisin via a new pathway, which Authors Sanchis-Gomar and Perez-Quilis say is clearly involved in insulin resistance. In this commentary, the authors hypothesize on how betatrophin and irisin may be linked, and how this discovery may impact the lives of future diabetic patients.

**The Prolific Profilin-1**  
*pp 69–74*

The small protein known as profilin-1 (PFN) is known to bind to numerous other groups of proteins which harbor poly-L-proline stretches, and through these bonds PFN is involved in signaling and regulation. Authors Pae and Romeo previously showed how PFN expression in white adipose tissue can be increased through a high fat diet, and that PFN heterozygote mice seemed to be protected from glucose intolerance and systematic inflammation brought on by this fatty diet. In this commentary, the authors discuss the interactions between PFN and its many diverse binding partners in order to further understand PFN’s effect on insulin sensitivity and metabolic inflammation.

**Letting Adipose Tissue Breathe**  
*pp 75–80*

The widespread existence of obesity has brought about an increase in white adipose tissue dysfunction, and although it has been proposed that adipose tissue hypoxia may be a key mechanism that triggers tissue dysfunction, in vivo data from humans is scarce. The oxygenation of human adipose tissue has been looked at; however these findings have been inconsistent. In this commentary, Hodson discusses their studies on elucidating a “metabolic signature” of hypoxia in human adipose tissues and explains the importance of using integrative physiological techniques in order to understand adipose tissue hypoxia in humans, as well as potential consequences of human adipose tissue hypoxia in vivo.

**Thrombospondin, Obesity, and Diabetes**  
*pp 81–4*

Thrombospondin (TSP)-1 is a matricellular protein that serves as an activator of transforming growth factor (TGF)-β as well as an angiostatic mediator. Due to its upregulation in the presence of diabetes and obesity, it is possible that TSP-1 may play a part in the genesis of organ dysfunction and metabolic dysregulation (Fig. 3). The studies presented by authors Kong et al. show a link between TSP-1 and inflammation, weight gain, and metabolic dysfunction in obesity models. The studies also show that in diabetic models, TSP-1 may be upregulated in tissue and organs such as the kidneys and vascular tissue where it may promote dysfunction as well. This commentary discusses the role of TSP-1 in metabolic disease, and shows how a better understanding of the actions that TSP-1 performs could lead to a number of ways to treat complications related to diabetes.