In this Issue of *Adipocyte*

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**Ethanol-Induced Injury**

pp. 225–31
Several studies have shown that adipose tissue may play a role in alcoholic liver disease (ALD) via the secretion of adipokines or adipocytokines. Ethanol has also been shown to contribute to alcohol-induced injury of adipose tissue by altering metabolic and immune activities. This review by Kema, Mojerla, Kahn, and Mandal discusses literature surrounding the effect of ethanol on adipose tissue and the progression of ALD. Understanding the role that ethanol induced adipose tissue injury plays with regards to ALD progression may open doors to future therapeutic targets.

**Adipogenesis Control**

pp. 239–47
Adipose tissue is central in the control of metabolic homeostasis and energy balance, and as such, studies surrounding the control of adipogenesis are of prime interest. This review by Toneatto, Charo, Galigniana, and Piwien-Pilipuk examines the recent findings surrounding the roles of heat shock protein (Hsp) 90 and high molecular weight immunophillin FKBP51 in adipocyte differentiation. Studies have shown that both Hsp 90 and FKBP51 may have a role in the regulation of the key transcription factor PPARγ, linking them to adipogenesis control.

**Mysteries of Early Adipogenesis**

pp. 248–55
The transcription factor KLF4 is vital for adipose differentiation, however it is not the only factor in play during adipogenesis. In this research paper, Cervantes-Camacho et al. present findings that show GSK3β activity is in fact required in order for KLF4 as well as KLF5 to be expressed during adipogenesis. In addition, through their research they found evidence supporting the notion that during early adipogenesis, an unknown protein is required for the transient expression of KLF4, KFL5 and C/EBPβ. These pathways warrant further research, as the early

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**Statins and Increased Risk for Diabetes**

pp. 232–8
While statins are proven and widely prescribed in the fight against high cholesterol and cardiovascular disease risk, recent findings have shown a possible link between statins and an increased risk of diabetes. Here, Henriksbo and Schertzor present a summary of statin-induced insulin resistance, inflammation and cell immunity, highlighting the role of the NLRP3 inflammasome. Evidence might suggest that the cardiovascular benefits of statins and the possible related insulin resistance occur on separate pathways, and more research into this topic may serve to improve the drug class as a whole (Fig. 1).

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Figure 1. Possible mechanisms linking statin-induced NLRP3 inflammasome activation and insulin resistance. Henriksbo et al., p. 234.
stages of adipogenesis appears more complex than previously thought (Fig. 2).

**Fat size and Insulin Sensitivity**

pp. 256–63

There is a correlation between obesity and insulin resistance, and the size and distribution of adipose cells seems to be insulin-sensitivity dependent. A change in energy intake or diet can also result in changes in fat mass. Authors Li, Gaillard, McLaughlin, Sørensen, and Periwal look deeper into the relationship of adipose tissue dynamics and diet compositions through the comparison of gender and insulin sensitivity-dependent differences. Their findings suggest that changes in energy intake and diet may have a greater effect on adipose cell-size in individuals who are insulin resistant when compared to those who are insulin sensitive.

**The Elastin Net and MMP-12**

pp. 264–72

The expansive network of proteins known as the extracellular matrix (ECM) is important for proper metabolic regulation and adipose tissue function. This research paper by authors Martinez-Santiago et al. looks into the diet induced obesity response of elastin, a fairly unexplored adipose tissue ECM component. In the visceral fat elastin forms a mesh-like net which becomes denser during weight gain, while in the subcutaneous fat it is organized in a linear fashion. Although metalloelastase, MMP-12 producing macrophages were closely associated with adipose elastin fibers, studies with Mmp12 null mice indicate that MMP-12 does not regulate the elastin network nor does it play a role in ATM recruitment and overall metabolism (Fig. 3).

**The Diabetic Toll on Adipose Cell Size**

pp. 273–9

The risk of insulin resistance may increase due to regional deposition of adipose tissue and adipocyte morphology, and authors Fang, Guo, Zhou, Stahl, and Grams studied the possible association between subjects metabolic profile and anthropomorphic data with type 2 diabetes. Through the observation of clinical data, adipocyte cell diameters were measured from the subcutaneous fat, omentum, and mesentery of 30 morbidly obese subjects. While a bimodal
Adipocyte size distribution was observed for all three adipose depots, it was the smaller adipocytes that showed an association with type 2 diabetes, fasting glucose and HbA1c.

Reference Genes for Brown Adipose qPCR Analysis

Recently, a focus in the research community on human brown adipose tissue has resulted in a need for reference genes which are required to correct for variations during quantitative PCR studies. These genes tend to have a uniform expression even under different conditions and can be used to account for variations in experimentation environment. Authors Taube et al. sought to do just that in this research paper through the use of microarray data in order to find reference gene candidates. Their findings show that PSMB2, GNB2 and GNB1 may be suitable reference genes for the study of human BAT via qPCR analysis.

The Vital Role of ClipR-59

The membrane associated protein, ClipR-59, has a modulation effect on adipocyte glucose transport through the regulation of Akt membrane compartmentalization. It is speculated that ClipR-59 has a role in body glucose homeostasis regulation as well. In this research paper, authors Du and Yingmin explored the effects of forcing ClipR-59 expression in adipose tissue and how this might change body glucose homeostasis. Through the generation of adipose specific ClipR-59 transgenic mice, the authors found these mice to have a higher glucose tolerance, enhanced insulin sensitivity, and a lower blood glucose level. Additionally these mice exhibited a reduced fat mass, which supports the idea that ClipR-59 is indeed an important regulator of body glucose homeostasis as well as adipocyte function (Fig. 4).

The Lineages of 3T3-L1 Adipocytes

Differentiated 3T3-L1 adipocytes are used extensively as an in vitro model for white adipocyte study, and although white and brown adipocytes are usually derived from different cell lineages there have been cases of beige adipocyte identification. Morrison and McGee show in this brief report that 3T3-L1 adipocytes actually display the features of multiple adipocyte lineages. Here, 3T3-L1 adipocytes with typical white adipocyte profiles increased brown adipocyte gene expression and oxygen consumption when...
exposed to catecholamines. While attempts to differentiate beige adipocytes did not induce a beige adipocyte phenotype in 3T3-L1 fibroblasts, the findings here on multiple lineages are important when studying data derived from 3T3-L1 adipocytes.

**A BAT Culture System**

pp. 303–10

Due to the prevalence of obesity and metabolic disorders associated with it, the study of brown fat and brown adipocyte differentiation has been gaining more and more attention. A lack of a human primary brown adipocyte cell culture system as well as of a well-characterized human model has slowed discoveries in the field, and in this brief report authors Seiler et al. describe the first primary brown adipocyte cell culture system from human fetal interscapular brown adipose tissue (BAT). Through culturing pre-adipocytes taken from this fetal tissue, it was found that they demonstrated an increase in classical brown fat marker expression. The cell culture system described here may be valuable to the brown adipocyte research community, as well as important in the fight against obesity.

*Figure 4. The impact of ClipR-59 expression on adipose growth. Du et al. p. 289.*