In this issue of *Adipocyte*

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Landes Bioscience; Austin, TX

**Breaking It Down: The Story of Two TAG Hydrolysis Proteins**  
*pp. 123–31*

Neutral lipid storage disease (NLSD) is a rare, autosomal recessive metabolic disorder that results in an accumulation of triacylglycerols (TAGs) in organs and tissues throughout the body. Those with this condition suffer many symptoms, including metabolic disorders. Known mutations leading to NLSD, along with findings from mouse models, point to two key proteins that are involved in the catabolism of TAG, CGI-58 and ATGL. In this mini-review, Lord and Brown describe and suggest roles for these two proteins and also summarize other recent findings and insights surrounding TAG signaling and metabolism.

**The Effects of Hypoxia on Adipocytes**  
*pp. 132–41*

Low levels of oxygen, often caused by obesity, can disrupt the normal functioning of adipocytes in humans and mice. In this research paper, Famulla et al. differentiated human adipocytes at three different oxygen levels and looked at the expression of different proteins. The authors find that oxygen levels have a distinct effect on adipogenesis, altering the secretion of multiple proteins involved in adipocyte functionality.

**Haptoglobin Affects Adipocyte Function**  
*pp. 142–52*

When adipose tissue collects, and collects, to the point of obesity, an inflammatory response is elicited that leads to many metabolic disorders. Haptoglobin (Hp) is released under these conditions making it a good indicator of adiposity and inflammation. In this research paper, Gamucci et al. follow up on their recent findings that Hp knockout mice fed a high fat diet are partly protected from both insulin resistance and fatty liver. Using histology and gene expression data, the group compares Hp−− mice fed a high fat and a standard diet. Their results provide new insight into Hp function in adipose tissue.

**It’s Not Just What You Eat, but Also Where It Ends Up**  
*pp. 153–6*

The location where fat is deposited has a big effect on how lipolysis, the breakdown of lipids, occurs. In this brief report, Wueest, Schoenle and Konrad expand upon their recent study looking at insulin’s anti-lipolytic effects on murine perigonadal and mesenteric adipocytes. Differences were found based not only on where the depots were located but also on whether the mice were fed a normal or high fat diet. The authors look further into these diet, depot and function dependent differences of insulin sensitivity of adipocytes by including inguinal adipocytes to the study.

**Putting Obesity on ICE(R)**  
*pp. 157–60*

Obesity leads to an increase in the amount of free fatty acids (FFAs) lingering around in the blood. This can bring on a host of problems leading to metabolic disorders, such as defective insulin-mediated glucose uptake. Thankfully, an adipokine exists, adiponectin (ADIPOQ) that can decrease the amount of roaming FFAs and increase insulin sensitivity. Unfortunately, obesity hampers the production of ADIPOQ, leaving the amount of FFAs in the blood unchecked. In this commentary, Brajkovic et al. discuss other proteins involved in the cascade leading to reduced ADIPOQ and defective insulin-mediated glucose uptake. The authors focus on their findings involving ICER, an inducible cAMP early repressor, and its role in insulin signaling. Focusing on ICER may improve future therapies that combat insulin resistance and its cohort, type 2 diabetes.

**Help for Non-Healing Wounds in Type 2 Diabetes?**  
*pp. 161–3*

Wound healing is a chronic problem for those with diabetes. Even with a strict diet and monitored insulin levels, wound healing remains an issue. Over time, a loss of tissue repair mechanism can lead to amputation. In this commentary, Bitar reviews a recent report on a newly identified defect in the GSK-3β-Fyn-Nrf2 signaling pathway found in fibroblasts or wounds of type 2 diabetes. The discovery of this defect may lead to new therapies for non-healing chronic wounds.

**Myokine’s Contribution to Whole-Body Metabolism**  
*pp. 164–7*

Looking good in a swimsuit may be the sole reason some of us head to the gym; however, exercise does a lot more than allow us to squeeze into that bikini. Peptides released during exercise are able to target distant organs, thus mediating long-term metabolic changes. In this commentary, Pedersen and Hojman look at a newly defined myokine, CXCL-1, and find that overexpression of this skeletal muscle peptide is able to increase fatty acid oxidation and reduce diet-induced fat stockpiling in adipose tissue. Both effects
contribute to whole-body metabolism. This finding demonstrates the importance that myokines hold in preventing metabolic related diseases.

**A New Future for Leptin in Adipocytes**

In the not too distant past, leptin was thought to be the magic bullet for successful weight loss. Disappointingly, human studies with leptin did not pan out. With such great interest in leptin, surprisingly little is actually known about the transcriptional pathways that regulate adipocyte-specific expression of leptin. In this commentary, Wrann and Rosen report on recent studies that use cell culture and mouse models to unravel the mystery of the transcriptional regulation of leptin gene expression.

**The Omega-3 Contradiction**

One easy way to combat obesity is to increase consumption of omega-3 fatty acids. Well, this is the case if you happen to be a rodent. Unfortunately for humans, evidence for this effect is lacking, but not from want of trying. In this commentary, Madsen and Kristiansen discuss how other dietary influences in the human diet may be negating the antiobesity effect seen in rodents, such as a background diet of high glycemic index carbohydrates. They also review other possible dietary influences, such as linoleic acid and persistent organic pollutants, which may negatively influence human trials.

**Increasing Baseline Energy Expenditure Does Not Come for Free**

As the prevalence of obesity rises, new ways to tackle it are always welcome. Generally, obesity is caused by an imbalance between energy intake and energy expenditure. What if energy expenditure could be boosted at baseline levels? In this commentary, Simonds, Cowley and Enriori demonstrate that this actually does happen, via a leptin-mediated increase in thermogenesis. The authors discuss, in depth, the pathway leptin takes to increase sympathetic nerve activity, thus increasing thermogenesis, but in doing so, they also discover a dark side. The increase in thermogenesis and energy expenditure may come at a cost; an increase in hypertension and possibly cardiovascular disease.

**Angiopoietin-Like 4 and Fatty-Acid Homeostasis**

Fasting, running a marathon or being a couch potato all require a change in what fuel substrates the body uses for energy expenditure. Not being able to switch energy substrates seamlessly can create problems, problems that are too readily seen in the obese or insulin resistant. In this commentary, Koliwad, Gray and Wang discuss angiopoietin-like 4 (Angptl4), a protein involved in modulating triacylglycerol homeostasis. The group focuses on a new Angptl-4 dependent lipolytic regulatory mechanism and explores any possible physiological and therapeutic implications it may have.