Obesity reversal through carbon monoxide

pp. 1–10
Carbon monoxide releasing molecules (CO-RMs), or drugs that release carbon monoxide within the body, can influence and prevent obesity development with low level treatment. In this research paper by Hosick, AlAmodi, Hankins and Stec, the idea that CO-RM treatment can actually reverse obesity is explored. By treating dietary obese mice with CORM-A1, the authors observed decreases in body weight as well as lower fasting blood glucose, decreased hepatic steatosis, and improved insulin sensitivity. These results come through increases in metabolism brought on by the chronic CORM-A1 treatment (Fig. 1).

A tale of two rats

pp. 11–21
With instances of obesity reaching epidemic proportions, the amount of studies dedicated to it and associated metabolic complications have increased. And while numerous animal models have come about for use in these studies, two have become the standard. This research paper by Marques et al. pits the Wistar and Sprague-Dawley Rat models against each other for the first time in a direct comparison. Through several evaluations including blood biochemical analysis, glucose tolerance tests, and gut microbiota composition, the authors observed differences between the two models, concluding that while both are valid models of high fat diet-induced obesity, the Wistar Rat demonstrated more pronounced metabolic effects, possibly due to differences in gut microbial ecology (Fig. 2).

Aesthetic classifications

pp. 22–26
Although an entire industry has developed around the idea of reducing and removing unwanted adipose tissue accumulation, the terminology used differs greatly from that in the medical field due to, as author Pinto explains, a clash between marketing and science. This paper seeks to propose a way to classify and categorize various methods of local fat treatments in order to provide a level of consistency and reduce inaccuracies with regards to communication. The author focuses on several main criteria in order to make clear what each method actually entails, thus enhancing the general knowledge behind each procedure and making communication more consistent across the field.

Round ligament gene expression

pp. 27–34
This research paper by Mauriège et al. examines gene expression between round ligament (RL), omental and mesenteric adipose depots, testing the theory that RL adipose tissue may have certain characteristics that offset harmful effects of intraabdominal fat accumulation. Previous studies of severely obese women by the authors revealed higher fat cell size and Lipoprotein Lipase activity as well as higher insulin sensitivity on glucose transport and antilipolysis. Here, gene expression of different adipose depots in severely obese women was compared, with the results showing lower pro-inflammatory and pro-thrombotic profiles combined with higher lipogenic and adipogenic profiles in RL adipose tissue, supporting the author’s theory.

Figure 1. Body weights of treated mice over 30 week study. Hosick et al., p. 2.
CT-derived measurements to predict cardiometabolic risk

pp. 35–42
The Computed tomography (CT) scan has long been the preferred imaging technique in the measurement of abdominal body fat distribution. This paper by Côté et al. theorizes that increased cardiometabolic risk linked to visceral adipocyte hypertrophy can be explained through radiologic attenuation and visceral adipose tissue (VAT) area measurements via CT imaging. Through the measurements of fat cell weight of VAT and subcutaneous adipose tissue samples across numerous women, the authors found that both adipose tissue area and attenuation are related to adipocyte size. These CT-derived measurements can be used to predict cardiometabolic risk profiles associated with fat cell hypertrophy.

Angiotensin type 2 receptor-deficiency and adipocyte remodeling

pp. 43–52
The controversial role of the angiotensin type-2 receptor in adipose physiology is examined in this research paper by Noll et al., as the authors seek to shed light on whether a genetic deficiency in the receptor prevents or exaggerates changes in metabolic and adipose tissue morphometrics. By comparing wild type mice with angiotensin type 2 receptor-deficient mice both on and off a high fat/high fructose diet, the authors were able to study adipocyte size as well as post-prandial fatty acid uptake in various organ systems. In addition to lowering body weights and increased fasting blood glucose, due to their smaller adipocyte size, angiotensin type 2 receptor-deficient mice were found to have increased fatty acid uptake in ectopic non-adipose tissues. Additionally, early hypertrophic adipocyte remodeling induced by high-fat diets was all but erased in angiotensin type 2 receptor-deficient mice (Fig. 3).

Adipose-derived stromal/stem cells susceptible to infection

pp. 53–64
While human adipose-derived stromal/stem cells (ASCs) may have a promising future in regenerative therapies as well as treatments for autoimmune and inflammatory disorders, there is much to learn with regards to how susceptible they may be to infectious agents. Authors Zwezdaryk et al. tackle this topic here for the first time, showing that ASCs may be highly susceptible to infection via human cytomegalovirus (HCMV). The authors also

Figure 2. Fasting plasma insulin levels. Marques et al., p. 13.

Figure 3. Timeline used to observe intravenous uptake of [18F]-FTHA in mice (A) and an example of a coronal slice through the mPET image of FTHA uptake in a WT mouse on a normal diet obtained by this protocol (B). Noll et al., p. 50.
explain that HCMV can also inhibit basic functions of ASCs including differentiation. This suggests that while ASC therapy may still have potential, an active HCMV infection during therapy may lead to disappointing results (Fig. 4).

**Long term high glucose concentration may cause an adaptive response**

*pp. 65–80*

High glucose concentration exposure can impair the metabolic functions of adipocytes, and may eventually lead to a development of insulin resistance. An important player in the insulin transduction pathway, the mediator Caveolin-1 (Cav-1) experiences enhanced expression during adipocyte differentiation. Authors Palacios-Ortega et al. examine how Cav-1 expression and activation may be regulated while in the presence of high glucose concentration in this paper. Their findings show that high glucose exposure modifies DNA methylation in Cav-1 promoter, but the actual expression of Cav-1 was unaffected. Although Cav-1 and insulin receptor (IR) activation is lost in adipocytes exposed long-term to high glucose during adipogenesis, protein kinase B (AKT-2) phosphorylation and insulin-stimulated glucose uptake is maintained in these cells. In contrast, mature adipocytes exposed short-term to high glucose showed reduced Cav-1 and IR activation, as well as reduced AKT-2 phosphorylation and insulin-induced glucose transport.

**Three day fat delay**

*pp. 81–87*

The ability of adipose tissue to dynamically respond to dietary changes is a key part of mammalian metabolism, with adipose tissue serving as an energy buffer and storing excess calories in the body. Ailments such as dyslipidemia and lipotoxicity can occur when adipose tissue is not able to store this excess, thus contributing to insulin resistance and obesity. Authors Li, Periwal, Cushman, and Stenkula investigate whether there is a delay between the recruitment of new adipocytes and an increase in caloric intake. Through the use of dynamic modeling, the authors found a 3 day delay in adipocyte recruitment and the beginning of a high fat diet, furthering our understanding of cell recruitment and lipid turnover as well as how adipose cell function can change in response to energy intake.