Chapter

Introductory Chapter: Adipose Tissue

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1. Introduction

Adipose tissue is a kind of connective tissue. It is a highly specialized tissue that plays a significant role in humans and animals. Adipocytes, cells of adipose tissue, store lipids and triacylglycerol as well as synthesize fatty acids. It also protects against mechanical injury as well as against cold. Adipose tissue is also involved in process of thermogenesis. Adipose tissue is also a metabolic active organ. Adipose tissue, beside adipocytes, contains also the stromal vascular fraction (SVF) of cells including fibroblasts, vascular endothelial cells, and immune cells, for example, macrophages.

2. Types of adipose tissue

Based on colors, adipose tissue is classified as white adipose tissue (WAT) and brown adipose tissue (BAT). These two types of adipocytes arise from separate progenitor cell lines. They show distinct morphology, structure, localization in the body, and function [1, 2].

White adipocytes are globular cells. Their size varies between 25 and 200 μm and depends on the size of the single lipid droplet accumulated within them [3, 4]. They contain large, single lipid droplet, more than 90% of the cell volume. Therefore, the amount of cytoplasm is small, and the nucleus is decentralized [5] and has a low density of mitochondria [3, 4]. Their main function is to store lipids, as energetic molecules to provide energy to the cells between the meals. White adipose tissue secretes also several molecules, such as retinol, steroid, hormones, prostaglandins, and adipokines that are pro- and anti-inflammatory cytokines. These molecules influence human and animal physiology and pathology.

White adipose tissue may be differentiated based on the anatomical locations or depots: subcutaneous (under the skin in the hypodermis region) and visceral. Increased visceral fat increases the risk of metabolic and cardiovascular diseases [6, 7]. Subcutaneous fat may protect against metabolic derangements [8]. Two subcutaneous fat regions in humans are recognized: upper and lower body fat. Accumulation of fat in lower regions (around the gluteal and femoral, the so-called gluteofemoral regions) improves glucose tolerance [9], negatively correlates with insulin resistance [8], and is associated with reduced aortic calcification [10]. Visceral adipose tissue is generally regarded as intra-abdominal adipose tissue. Visceral fat surrounds the internal organs. The major visceral depots are the omental, retroperitoneal, perineal, mesenteric, and pericardial depots [11, 12]. The mesenteric and omental adipose tissues drain directly into the portal circulation. These adipocytes release free fatty acids and pro-inflammatory cytokines to the liver. This process causes the development of hepatic steatosis and insulin resistance

[13, 14]. Pericardial fat increases the risk of metabolic disorders and low-grade inflammation, involved in type 2 diabetes and cardiac complication. It may cause also increased diastolic pressure and fasting insulin levels [15, 16] and arterial calcium accumulation [17] and severity of coronary disease [18]. Increased perirenal and pararenal depots are associated with glomerulopathy [19], chronic kidney diseases in patients with type 2 diabetes [20], and hypertension [21, 22]. Increased thickness of mesenteric fat is correlated with increased risk of cardiovascular diseases [23], Crohn's disease [24], hepatic insulin resistance, and hepatosteatosis [25]. These observations suggest that increased visceral fat deposition is associated with diseases and metabolic derangements, whereas subcutaneous fat deposition is not so dangerous.

Brown adipose tissues have polygonal shape, and their diameter is variable. They are smaller in comparison to WAT (15–60 μm) [26]. They also contain lipid droplets, but as multiple, small vacuoles of varied size. These cells contain a large amount of cytoplasm and centralized nucleus [5]. The most characteristic organelles presented in brown adipocytes are the mitochondria [27, 28]. BAT is found in fetuses and newborn, whereas in adult humans is practically absent. It is present at discrete sites such as in the upper trunk [29].

Recently, the third type of adipose tissue has been described. It is termed "brown-in-white," "brite," or "beige" [26, 30]. Beige adipose tissue histologically is very similar to BAT. The development of beige AT is due to the browning of WAT. It is an adaptive response to stimulation, for example, cold exposure, exercise, natriuretic peptides, thyroid hormones, bile acids, and so on [31–33]. Beige AT exhibits several intermediate features between BAT and WAT. For example, its adipocytes have a predominant lipid vacuole in the cytoplasm and numerous mitochondria [27, 34]. They express genes involved in the process of thermogenesis [30, 32, 33]. On the other hand, adipocytes of beige AT express characteristic and distinct gene markers. These gene markers are specific for beige adipocytes and distinguish them from adipocytes of BAT and WAT [26, 30, 35, 36].

3. Adipose tissue as an endocrine organ

As mentioned earlier, adipose tissue is also an endocrine organ. It secretes several hormones that regulate the homeostasis. The first molecule with hormonal activity secreted by adipocytes was leptin. It is a satiety hormone that suppresses food intake and increases energy expenditure. The levels of leptin are positively correlated with the amount of body fat [37]. Subcutaneous white adipose tissue secretes greater amounts of leptin than visceral WAT [38, 39]. Adiponectin, another hormone secreted by adipose tissue, is secreted primarily by subcutaneous rather than visceral fat. It shows anti-inflammatory and insulin-sensitizing roles [40]. In obese humans and patients with insulin resistance, the level of adiponectin is low [41, 42]. Resistin, a peptide hormone, impairs glucose and insulin metabolism and is implicated in insulin resistance [43, 44]. Visfatin is a hormone implicated in the utilization of glucose, predominantly synthesized and secreted in visceral fat [45]; however, it is predominantly secreted from macrophages rather than adipocytes. It has endocrine, paracrine, and autocrine functions and can bind to insulin receptor. There are also other hormones synthesized and secreted by adipose tissue such as acylation-stimulating protein (ASP) which is concerned with fat storage.

Adipose tissue secretes also growth factors, such as fibroblast growth factors (FGFs), insulin-like growth factor-1 (IGF-1), hepatocyte growth factor (HGF), nerve growth factor (NGF), vascular endothelial growth factor (VEGF), and transforming growth factor (TGF). These growth factors stimulate several

processes such as adipogenesis [46], glucose metabolism [47], angiogenesis [48, 49], and thermogenesis [50]. On the other hand, some of these growth factors may be a pro-inflammatory adipokines. Adipose tissue secretes also other inflammatory cytokines such as interleukin-6, interleukin-8, interferon-γ, plasminogen activation inhibitor-1 as well as anti-inflammatory adipokines, such as adiponectin [51]. There are also many other molecules secreted by adipose tissue, such as retinol-binding protein 4 (RBP4), vaspin, omentin, chemerin, serum amyloid A (SAA), angiotensinogen, macrophage migration inhibitory factor (MIF), lipoprotein lipase, cholesterol ester transfer protein (CETP), prostaglandins, estrogens, glucocorticoids, and so on. All of these molecules influence human and animal processes. They have positive, as well as negative, effects on human health. Adipose tissue may be involved in the development of many diseases, such as type 2 diabetes mellitus [52, 53], metabolic syndrome [54], and several cancers (breast [55], cervical [56], endometrial [57], kidney [58], and gastrointestinal [59, 60]). Disturbances in functions of adipose tissue may cause also psychiatric diseases and disorders, such as depression [61], dementia [62], insomnia [63], and many others.

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