

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Introductory Chapter: Adipose Tissue

*Leszek Szablewski*

## 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  $\mu\text{m}$  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  $\mu\text{m}$ ) [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- $\gamma$ , 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.

IntechOpen

### **Author details**

Leszek Szablewski  
Medical University of Warsaw, Warsaw, Poland

\*Address all correspondence to: [leszek.szablewski@wum.edu.pl](mailto:leszek.szablewski@wum.edu.pl)

### **IntechOpen**

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

## References

- [1] Scheja L, Heeren J. Metabolic interplay between white, beige, brown adipocytes and the liver. *Journal of Hepatology*. 2016;**64**:1176-1186
- [2] Gaggini M, Carli F, Gastaldelli A. The color of fat and its central role in the development and progression of metabolic diseases. *Hormone Molecular Biology and Clinical Investigation*. 2017;**31**:1-14
- [3] Schosserer M, Grillari J, Wolfrum C, Scheidler M. Age-induced changes in white, brite, and brown adipose depots: A mini-review. *Gerontology*. 2018;**64**:229-236
- [4] Mathew H, Castracane VD, Mantzoros C. Adipose tissue and reproductive health. *Metabolism*. 2018;**86**:18-32
- [5] Cinti S. The role of brown adipose tissue in human obesity. *Nutrition, Metabolism, and Cardiovascular Diseases*. 2006;**16**:569-574
- [6] Gastaldelli A, Miyazaki Y, Pettiti M, Matsuda M, Mahankali S, Santini E, et al. Metabolic effects of visceral fat accumulation in type 2 diabetes. *The Journal of Clinical Endocrinology and Metabolism*. 2002;**87**:5098-5103
- [7] Kissebah AH, Vydellingum N, Murray R, Evans DJ, Hartz AJ, Kalkhoff RK, et al. Relation of body fat distribution to metabolic complications of obesity. *The Journal of Clinical Endocrinology and Metabolism*. 1982;**54**:254-260
- [8] Zhang M, Hu T, Zhang S, Zhou L. Associations of different adipose tissue depots with insulin resistance: A systemic review and meta-analysis of observational studies. *Scientific Reports*. 2015;**5**:18495
- [9] Snijder MB, Dekker JM, Visser M, Yudkin JS, Stehouwer CD, Bouter LM, et al. Larger thigh and hip circumferences are associated with better glucose tolerance: The hoorn study. *Obesity Research*. 2003;**11**:104-111
- [10] Tanko LB, Bagger YZ, Alexandersen P, Larsen PJ, Christiansen C. Peripheral adiposity exhibits an independent dominant antiatherogenic effect in elderly women. *Circulation*. 2003;**107**:1626-1631
- [11] Cinti S. The adipose organ at a glance. *Disease Models & Mechanisms*. 2012;**5**:588-594
- [12] Chusyd DE, Wang D, Huffman DM, Nagy TR. Relationships between rodent white adipose fat pads and human white adipose fat depots. *Frontiers in Nutrition*. 2016;**63**:10
- [13] Tchkonina T, Thomou T, Zhu Y, Karagiannides I, Pothoulakis C, Jensen MD, et al. Mechanisms and metabolic implications of regional differences among fat depots. *Cell Metabolism*. 2013;**17**:644-656
- [14] Sackmann-Sala L, Berryman DE, Munn RD, Lubbers ER, Kopchick JJ. Heterogeneity among white adipose tissue depots in male C57BL/6J mice. *Obesity (Silver Spring)*. 2012;**20**:101-111
- [15] Fernández Muñoz MJ, Basurto Acevedo L, Córdova Pérez N, Vázquez Martínez AL, Tepach Gutiérrez N, Vega García S, et al. Epicardial adipose tissue is associated with visceral fat, metabolic syndrome, and insulin resistance in menopausal women. *Revista Española de Cardiología (English Edition)*. 2014;**67**:436-441
- [16] Iacobellis G, Ribaldo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters

- of metabolic syndrome: A new indicator of cardiovascular risk. *The Journal of Clinical Endocrinology and Metabolism*. 2003;**88**:5163-5168
- [17] Rosito GA, Massaro JM, Hoffmann U, Ruberg FL, Mahabadi AA, Vasan RS, et al. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors and vascular calcification in a community-based sample: The Framingham Heart Study. *Circulation*. 2008;**117**:605-613
- [18] Meenakshi K, Rajendran M, Srikumar S, Chidambaram S. Epicardial fat thickness: A surrogate marker of coronary artery disease—Assessment by echocardiography. *Indian Heart Journal*. 2016;**68**:336-341
- [19] Cignarelli M, Lamacchia O. Obesity and kidney disease. *Nutrition, Metabolism, and Cardiovascular Diseases*. 2007;**17**:757-762
- [20] Lamacchia O, Nicastro V, Camarchio D, Valente U, Grisorio R, Gesualdo L, et al. Para- and perirenal fat thickness is an independent predictor of chronic kidney disease, increased renal resistance index and hyperuricaemia in type-2 diabetic patients. *Nephrology, Dialysis, Transplantation*. 2011;**26**:892-898
- [21] Chughtai HL, Morgan TM, Rocco M, Stacey B, Brinkley TE, Ding J, et al. Renal sinus fat and poor blood pressure control in middle-aged and elderly individuals at risk for cardiovascular events. *Hypertension*. 2010;**56**:901-906
- [22] Ritz E, Koleganova N. Obesity and chronic kidney disease. *Seminars in Nephrology*. 2009;**29**:504-511
- [23] Liu KH, Chan YL, Chan WB, Kong WL, Kong MO, Chan JC. Sonographic measurement of mesenteric fat thickness is a good correlate with cardiovascular risk factors. Comparison with subcutaneous and preperitoneal fat thickness, magnetic resonance imaging and anthropometric indexes. *International Journal of Obesity and Related Metabolic Disorders*. 2003;**27**:1267-1273
- [24] Peyerin-Biroulet L, Gonzalez F, Dubuquoy L, Rousseaux C, Dubuquoy C, Decourcelle C, et al. Mesenteric fat as a source of C reactive protein and as a target for bacterial translocation in Crohn's disease. *Gut*. 2012;**61**:78-85
- [25] Wueest RR, Item F, Lucchini FC, Challa TD, Müller W, Blüher M, et al. Mesenteric fat lipolysis mediates obesity-associated hepatic steatosis and insulin resistance. *Diabetes*. 2016;**65**:140-148
- [26] Jeanson Y, Carrière A, Casteilla L. A new role for browning as a redox and stress adaptive mechanism? *Frontiers in Endocrinology (Lausanne)*. 2015;**6**:158
- [27] Cinti S. Transdifferentiation properties of adipocytes in the adipose organ. *American Journal of Physiology. Endocrinology and Metabolism*. 2009;**297**:E977-E986
- [28] Saelly CH, Geiger K, Drexel H. Brown versus white adipose tissue: A mini-review. *Gerontology*. 2012;**58**:15-23
- [29] Giralt M, Villarroya F. White, brown, beige/brite: Different adipose cells for different functions? *Endocrinology*. 2013;**154**:2992-3000
- [30] Vargas-Castillo A, Fuentes-Romero R, Rodriguez-Lopez LA, Torres N, Tovar AR. Understanding the biology of thermogenic fat: Is browning a new approach to the treatment of obesity? *Archives of Medical Research*. 2017;**48**:401-413
- [31] Azhar Y, Parmar A, Miller CN, Samuels JS, Ryalam S. Phytochemicals as novel agents for the induction of browning in white adipose tissue.

Nutrition & Metabolism (London). 2016;**13**:89

[32] Castro É, Silva TEO, Festuccia WT. Critical review of beige adipocyte thermogenic activation and contribution to whole-body energy expenditure. *Hormone Molecular Biology and Clinical Investigation*. 2017;**31**(2)

[33] Stanford KI, Goodyear LJ. Exercise regulation of adipose tissue. *Adipocytes*. 2016;**5**:153-162

[34] Aldiss P, Betts J, Sale C, Pope M, Symonds ME. Exercise-induced “browning” of adipose tissues. *Metabolism*. 2018;**81**:63-70

[35] Waldén TB, Hansen IR, Timmons JA, Cannon B, Nedergaard J. Recruited vs. nonrecruited molecular signatures of brown, “brite”, and white adipose tissues. *American Journal of Physiology. Endocrinology and Metabolism*. 2012;**302**:E19-E31

[36] Wu J, Boström P, Sparks LM, Ye L, Hoi JH, et al. Beige adipocytes are a distinct type of thermogenic fat cell in mouse and man. *Cell*. 2012;**150**:366-376

[37] Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. *European Cytokine Network*. 2006;**17**:4-12

[38] Atzmon G, Yang XM, Muzumdar R, Ma XH, Gabriely I, Barzilai N. Differential gene expression between visceral and subcutaneous fat depots. *Hormone and Metabolic Research*. 2002;**34**:622-628

[39] Montague CT, Prins JB, Sanders L, Zhang J, Sewter CP, Digby J, et al. Depot-related gene expression in human subcutaneous and omental adipocytes. *Diabetes*. 1998;**47**:1384-1391

[40] Fain JN, Madan AK, Hiler ML, Cheema P, Bahouth SW. Comparison of the release of adipokines by adipose tissue, adipose tissue matrix, and adipocytes from visceral and subcutaneous abdominal adipose tissues of obese humans. *Endocrinology*. 2004;**145**:2273-2282

[41] Lafontan M, Girard J. Impact of visceral adipose tissue on liver metabolism. Part I: Heterogeneity of adipose tissue and functional properties of visceral adipose tissue. *Diabetes & Metabolism*. 2008;**34**(4 Pt 1):317-327

[42] Lihn AS, Bruun JM, He G, Pedersen SB, Jensen PF, Richelsen B. Lower expression of adiponectin mRNA in visceral adipose tissue in lean and obese subjects. *Molecular and Cellular Endocrinology*. 2004;**219**:9-15

[43] Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. *Nature*. 2001;**409**:307-312

[44] Muse ED, Obici S, Bhanot S, Monia BP, McKay RA, Rajala MW, et al. Role of resistin in diet-induced hepatic insulin resistance. *The Journal of Clinical Investigation*. 2004;**114**:232-239

[45] Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, et al. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin. *Science*. 2005;**307**:426-430

[46] Mejhert N, Galitzky J, Pettersson AT, Bambace C, Blomqvist L, Boulomié A, et al. Mapping of the fibroblast growth factors in human white adipose tissue. *The Journal of Clinical Endocrinology and Metabolism*. 2010;**95**:2451-2457

[47] Entingh A, Kahn R. Differential roles of the insulin and insulin-like growth factor-1 (EGF-1) receptors

in response to insulin and IGF-1. *The Journal of Biological Chemistry*. 2004;**279**:38016-38024

[48] Mick GJ, Wang X, McCormick K. White adipocyte vascular endothelial growth factor: Regulation by insulin. *Endocrinology*. 2002;**143**:948-953

[49] Bell LN, Ward JL, Degawa M, Bovenkerk J, Jones R, Cacucci B, et al. Adipose tissue production of hepatocyte growth factor contributes to elevated serum HGF in obesity. *American Journal of Physiology. Endocrinology and Metabolism*. 2006;**291**:E843-E848

[50] Nisoli E, Tonello C, Benarese M, Liberini P, Carruba MO. Expression of nerve growth factor in brown adipose tissue: Implications for thermogenesis and obesity. *Endocrinology*. 1996;**137**:495-503

[51] DeFuria J, Belkina AC, Jagannathan-Bogdan M, Snyder-Cappione J, Carr JD, Nersesova YR, et al. B cells promote inflammation in obesity and type 2 diabetes through regulation of T-cell function and an inflammatory cytokine profile. *Proceedings of the National Academy of Sciences of the United States of America*. 2013;**110**:5133-5138

[52] Fantuzzi G. Adipose tissue, adipokines, and inflammation. *Journal of Allergy and Clinical Immunology*. 2005;**115**:911-919

[53] Akash MSH, Rehman K, Liaqat A. Tumor necrosis factor- $\alpha$ : Role in development of insulin resistance and pathogenesis of type 2 diabetes mellitus. *Journal of Cellular Biochemistry*. 2018;**119**:105-110

[54] Mauvais-Jarvis F, Clegg DJ, Hevener AL. The role of estrogens in control of energy balance and glucose homeostasis. *Endocrine Reviews*. 2013;**34**:309-338

[55] White AJ, Nichols HB, Bradshaw PT, Sandler DP. Overall and central

adiposity and breast cancer risk in the sister study. *Cancer*. 2015;**121**:3700-3708

[56] Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: A meta-analysis. *European Journal of Cancer Prevention*. 2016;**25**:232-238

[57] Plaza-Parrochia F, Romero C, Valladares L, Vega M. Endometrium and steroids, a pathologic overview. *Steroids*. 2017;**126**:85-91

[58] Kovesdy CP, Furth SL, Zoccali C. Obesity and kidney disease: Hidden consequence of the epidemic. *Future Science Open Access*. 2017;**3**:Fso159

[59] Chen Y, Liu L, Wang X. Body mass index and risk of gastric cancer: A meta-analysis of a population with more than ten million from 24 prospective studies. *Cancer Epidemiology, Biomarkers and Prevention*. 2013;**22**:1395-1408

[60] Ning Y, Wang L, Giovannucci EL. A quantitative analysis of body mass index and colorectal cancer: Finding from 56 observational studies. *Obesity Reviews*. 2010;**11**:19-30

[61] Thormann J, Chittka T, Minkwitz J, Kluge M, Himmerich H. Obesity and depression: An overview on the complex interactions of two diseases. *Fortschritte der Neurologie-Psychiatrie*. 2013;**81**:145-153

[62] Yaffe K, Falvey C, Harris TB, Newman A, Satterfield S, Koster A, et al. Effect of socioeconomic disparities on incidence of dementia among biracial older adults: Prospective study. *British Medical Journal*. 2013;**347**:f7051

[63] Buysse DJ. Insomnia. *Journal of the American Medical Association*. 2013;**309**:706-716