Mechanisms of Diet-Induced Thermogenesis

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Brown adipose tissue (BAT) has been considered a vital organ in response to non-shivering adaptive thermogenesis, which could be activated during cold exposure through the sympathetic nervous system (SNS) or under postprandial conditions contributing to diet-induced thermogenesis (DIT). Humans prefer to live within their thermal comfort or neutral zone with minimal energy expenditure created by wearing clothing, making shelters, or using an air conditioner to regulate their ambient temperature; thereby, DIT would become an important mechanism to counter-regulate energy intake and lipid accumulation. In addition, there has been a long interest in the intriguing possibility that a defect in DIT predisposes one to obesity and other metabolic diseases.

diet-induced thermogenesis BAT regulatory mechanism obesity

1. Introduction

The thermogenic activity of Brown adipose tissue (BAT) is stimulated by cold and also by a meal that induced a parallel increase in heat production, which has been well-documented to resist obesity through facilitating adaptive thermogenesis and energy expenditure (EE) both in rodents and humans [1]. BAT possesses a higher capacity to metabolize glucose and fatty acids, promotes heat production and EE, and is characterized by multilocular small lipid droplets, high mitochondrial density, and the expression of key thermogenic protein-uncoupling protein 1 (UCP1). There is evidence supporting that BAT could significantly affect whole-body energy metabolism in rodents and humans [2][3]. Therefore, BAT activation has been considered a potential therapeutic target in the treatment of obesity and related diseases [4].

In humans and rodents, the resting metabolic rate (RMR) accounts for 60–70% of whole-body EE, which is required for the performance of cellular and organ functions [5][6]. RMR is majorly determined by fat-free mass in the body. In general, gender difference and aging are the two main physiological factors to affect RMR [7][8][9], which may be due to differences in fat-free mass, especially skeletal muscle [10]. DIT is the increase in EE associated with food intake [11] and accounts for 5–15% of total EE [12]. The magnitude of the thermic effect of food depends on diet composition and caloric intake. DIT represents about 10% of daily total EE in healthy subjects [11]. DIT also could be affected by oral stimuli (i.e., the duration of tasting food and chewing in the mouth) [13], and environmental factors [14].

2. Sympathetic Nervous System (SNS)–BAT Axis

CIT could be generated by activating SNS and inducing BAT thermogenesis through the β3-adrenergic receptor (ADRB3) in mice and β2-adrenergic receptor in humans [15]. Based on the principal role of the SNS-βAR axis for CIT, it is conceivable that this axis might also be a key mechanism in DIT. For instance, SNS activity in BAT calculated from tissue norepinephrine turnover rate is increased in mice with long-term cafeteria and high-calorie diet feeding [16][17]. In addition, studies [18] also showed that surgical denervation of BAT could significantly attenuate metabolic activation of BAT after intake of a liquid meal in rats. Accordingly, denervation of BAT also alleviates the increase in mitochondrial GDP binding, total UCP1 protein content, and mitochondrial content in rats on an energy-enriched diet [19]. These results support the content that BAT activation in DIT is, at least in part, mediated through SNS activation. Moreover, previous reports have further demonstrated that food palatability and oropharyngeal taste sensation are also substantially involved in diet-induced sympathetic activation and BAT thermogenesis [20][21][22].

3. Gut-Secreted Peptides and Hormones and Bile Acids

Since the release of gastrointestinal peptides is one of the acute physiological responses to eating, some of these peptides have been reported to act as mediators to regulate DIT. For instance, gut hormones could activate BAT through their effects on the efferent SNS tone, such as cholecystokinin (CCK) [23][24] and glucagon-like peptide (GLP-1) [25]. In addition, the study of Li et al. [26] revealed a novel endocrine gut–BAT–brain axis triggered by secretin that initiates the canonical secretin receptor (SCTR)–cAMP–PKA–lipolysis–UCP1 pathway in brown adipocytes from the intestine during a meal. Their observation supported that a postprandial increase in circulating secretin activates BAT thermogenesis by binding to SCTR in brown adipocytes. On the other hand, bile acids have been documented to activate BAT directly through Takeda G-protein receptor 5 (TGR5) in brown adipocytes [27]. Watanabe et al., [28] further demonstrated that bile acids activate TGR5 in mouse brown adipocytes and then, facilitate thermogenic activity through type 2 deiodinase (D2) activation. Accordingly, direct stimulatory effects of bile acids (chenodeoxycholic acid) on BAT activity have been evidenced in humans using brown adipocytes in vitro and using FDG-PET/CT scan in vivo [28][29]. TGR5 has also been demonstrated to participate in browning of white adipose tissue under cold exposure and prolonged HFD feeding [30]. Thereby, targeting TGR5–BAT axis with bile acids or drugs could be a promising target for combating obesity and related metabolic disorders in humans.

4. Insulin

It is well recognized that the role of insulin as a key hormone in the storage of ingested nutrients, and also possesses the capacity to modulate energy balance after a meal. A recent study has indicated that insulin is a crucial protein involved in the mitochondrial bioenergetic and thermogenic capacity of brown adipocytes [31]. In fact, BAT appears to be differently activated by insulin and cold. When activated by cold, it dissipates energy in a perfusion-dependent manner. Nevertheless, in response to insulin, BAT glucose uptake could have a 5-fold increase independently of its perfusion [32][33]. In addition, it is suggested that insulin may play an important role in the dietary induction of facilitative adaptive thermogenesis. For instance, the study conducted with ten healthy lean volunteers and a euglycemic clamp method in conjunction with respiratory exchange measurements, has shown

the progressive increase in RMR along with the increase in the glucose infusion rate without changes in insulin and norepinephrine concentrations. It is implicated that insulin-stimulated glucose uptake is crucial for the thermogenic response of insulin [34]. On the other hand, Lee et al. have demonstrated that the recruitment of human BAT is accompanied by augmented DIT and postprandial insulin sensitivity [35]. Thus, it appears that the interactions between insulin and thermogenesis seen in rats could also exist in humans after meals.

Insulin resistance is a well-characterized consequence of obesity. Cafeteria diet feeding was conducted with normal and diabetic animals to assess changes in insulin-mediated glucose metabolism and to investigate the effects of insulin resistance on the development of DIT [36]. The attenuated DIT shown in cafeteria-fed diabetic rats was restored by an intensive program of insulin administration [36]. In addition, insulin resistance could result in a defect in insulin-mediated thermogenic response which contributes to the pathogenesis of obesity in humans [35]. The study of Aherne and Hull [37] conducted with human autopsy demonstrated that for obese infants of diabetic mothers exhibited impaired BAT function, further suggesting that maternal insulin deficiency may affect the thermogenic function of BAT in the offspring. Nevertheless, a recent report from Loeliger, R.C. has shown that DIT was not associated with BAT activity. DIT after an oral glucose load was not associated with stimulated ^{18}F-FDG uptake into BAT, suggesting that DIT is independent of BAT activity caused by facilitating glucose uptake in humans [38]. The underlying mechanism of insulin on DIT is needed to be further clarified.

5. Liver-Derived Factors

Hepatic tissue has been documented to be involved to a significant extent in the thermogenesis process. The study was conducted with rats fed chow or a cafeteria diet of highly palatable human foods and measured the RMRs (VO_2) before and shortly after two-thirds hepatectomy or sham operation at thermoneutrality (28 °C), and again after administration of propranolol (5 mg/kg). The difference in RMR between the resting period and propranolol treated period was used to represent the DIT. Their result suggests that liver is the major (70–100%) effector of the DIT [39][40]. In addition, Wallace et al. have demonstrated for the first time that the enhancement of specific calorigenic metabolic processes such as mitochondrial glycerophosphate oxidase within the liver contributes significantly to the heat production of DIT in cafeteria-fed rats [41]. These observations implicate that hepatic tissue might substantially take part in DIT under postprandial conditions.

6. Leptin

The adipocyte-derived leptin is a key factor in the regulation of energy balance [42], which is significantly increased in the obese state [43]. In fact, leptin has been reported to activate BAT sympathetic activity [44] and heat production [45][46][47]. In addition, a recent report has shown that refeeding increased plasma leptin concentrations in 48-h-fasted lean rats and leptin could mediate the increases in body temperature through hypothalamus-adrenal medulla-adipose tissue crosstalk after a meal [48]. Accordingly, chronic leptin treatment could stimulate BAT-mediated thermogenesis in leptin-deficient *ob/ob* mice by enhancing sympathetic innervation and activation [49]. Furthermore, BAT-ectomized rats reduced the thermogenic effect of food by 60% [48], suggesting that BAT appears

to be a crucial mediator of leptin-induced thermogenesis. However, some earlier studies have found that female leptin-deficient *ob/ob* mice fed a palatable cafeteria diet still result in increased leptin-independent SNS activity and thermogenesis in BAT [50]. Some other reports also pointed out that leptin do not possess thermogenic function [51] [52] and act as the mediator of DIT. These controversial observations might attribute to the differences in gender, methods, and experimental condition, which are needed to be further elucidated.

In contrast to leptin, adiponectin exhibits several characteristics of inhibiting energy expenditure. For instance, adiponectin inhibits UCP1 expression by reducing ADRB3 expression in brown adipocytes, along with reducing BAT thermogenesis in mice [53]. Previous report showed that neither fasting nor refeeding changed adiponectin serum levels in both young and old male rats [54]. The involvement of adiponectin in DIT process remains ambiguous.

7. Muscle

Sarcolipin (SLN) is a regulator of the Sarco/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) pump in muscle has been proposed to play an important role in DIT [55][56][57][58] and EE [59]. For instance, SLN regulates muscle-based non-shivering thermogenesis and is up-regulated with HFD. In addition, SLN KO mice are prone to develop diet-induced obesity and glucose intolerance. On the other hand, mice with SLN gene deletion gained comparable weight as UCP1-deficient mice on HFD, implicating that loss of muscle-based thermogenesis has similar consequences on weight gain as loss of UCP1-mediated thermogenesis [57]. Moreover, the body weight of mice with SLN overexpression is significantly lower than that of littermate control and they were resistant to HFD-induced obesity [58]. These mechanistic experiments indicated that SLN as an uncoupler of SERCA pump might create both energy demand and increase energy expenditure and are essential for counter-regulation of diet-induced energy intake.

8. Thyroid Hormones

Thyroid hormones, thyroxine (T4) and triiodothyronine (T3), have been well-documented to be a crucial determinant of energy expenditure and basal metabolic rate and also involved in the regulation of thermogenic responses to cold and diet [60]. Both cold-challenged and cafeteria-fed rats exhibited increases in circulating thyroid hormone levels [61]. In rats, overnutrition induced by a cafeteria diet is accompanied by a large increase in EE along with plasma T3 concentration [62]. T3 also acts as the main regulator of producing DIT in birds [63]. Accordingly, long-term over-feeding in men also exhibited accelerated metabolic rate and an increase in circulating T3 level [64]. Taken together, these observations implicate that thyroid hormone, especially T3, might substantially contribute to the generation of DIT under postprandial condition.

References

1. Okamatsu-Ogura, Y.; Kuroda, M.; Tsutsumi, R.; Tsubota, A.; Saito, M.; Kimura, K.; Sakaue, H. UCP1-dependent and UCP1-independent metabolic changes induced by acute cold exposure in brown adipose tissue of mice. Metabolism 2020, 113, 154396.
2. Yang, L.; Zhao, D.; Yin, R.; Ma, Y.; Zhang, N. Combined effects of voluntary running and liraglutide on glucose homeostasis, fatty acid composition of brown adipose tissue phospholipids, and white adipose tissue browning in db/db mice. Chin. J. Physiol. 2022, 65, 117.
3. Saito, M.; Matsushita, M.; Yoneshiro, T.; Okamatsu-Ogura, Y. Brown Adipose Tissue, Diet-Induced Thermogenesis, and Thermogenic Food Ingredients: From Mice to Men. Front. Endocrinol. 2020, 11, 222.
4. Cheng, L.; Wang, J.; Dai, H.; Duan, Y.; An, Y.; Shi, L.; Lv, Y.; Li, H.; Wang, C.; Ma, Q.; et al. Brown and beige adipose tissue: A novel therapeutic strategy for obesity and type 2 diabetes mellitus. Adipocyte 2021, 10, 48–65.
5. Speakman, J.R. Measuring energy metabolism in the mouse-theoretical, practical, and analytical considerations. Front. Physiol. 2013, 4, 34.
6. Reed, G.W.; Hill, J.O. Measuring the thermic effect of food. Am. J. Clin. Nutr. 1996, 63, 164–169.
7. Byrne, N.M.; Hills, A.P.; Hunter, G.R.; Weinsier, R.L.; Schutz, Y. Metabolic equivalent: One size does not fit all. J. Appl. Physiol. 2005, 99, 1112–1119.
8. Dionne, I.; Després, J.; Bouchard, C.; Tremblay, A. Gender difference in the effect of body composition on energy metabolism. Int. J. Obes. 1999, 23, 312–319.
9. Bosy-Westphal, A.; Wolf, A.; Bührens, F.; Hitze, B.; Czech, N.; Mönig, H.; Selberg, O.; Settler, U.; Pfeuffer, M.; Schrezenmeir, J.; et al. Familial influences and obesity-associated metabolic risk factors contribute to the variation in resting energy expenditure: The Kiel Obesity Prevention Study. Am. J. Clin. Nutr. 2008, 87, 1695–1701.
10. Muller, M.J.; Bosy-Westphal, A.; Kutzner, D.; Heller, M. Metabolically active components of fat-free mass and resting energy expenditure in humans: Recent lessons from imaging technologies. Obes. Rev. 2002, 3, 113–122.
11. Rothwell, N.J.; Stock, M.J.; Stribling, D. Diet-induced thermogenesis. Pharmacol. Ther. 1982, 17, 251–268.
12. Okla, M.; Kim, J.; Koehler, K.; Chung, S. Dietary Factors Promoting Brown and Beige Fat Development and Thermogenesis. Adv. Nutr. Int. Rev. J. 2017, 8, 473–483.
13. Hamada, Y.; Hayashi, N. Chewing increases postprandial diet-induced thermogenesis. Sci. Rep. 2021, 11, 23714.
14. Wang, B.; Tsakiridis, E.E.; Zhang, S.; Llanos, A.; Desjardins, E.M.; Yabut, J.M.; Green, A.E.; Day, E.A.; Smith, B.K.; Lally, J.S.V.; et al. The pesticide chlorpyrifos promotes obesity by inhibiting diet-

induced thermogenesis in brown adipose tissue. Nat. Commun. 2021, 12, 1–12.

15. Blondin, D.P.; Nielsen, S.; Kuipers, E.N.; Severinsen, M.C.; Jensen, V.H.; Miard, S.; Jespersen, N.Z.; Kooijman, S.; Boon, M.R.; Fortin, M.; et al. Human Brown Adipocyte Thermogenesis Is Driven by β2-AR Stimulation. Cell Metab. 2020, 32, 287–300.e7.
16. Young, J.B.; Saville, E.; Rothwell, N.J.; Stock, M.J.; Landsberg, L. Effect of Diet and Cold Exposure on Norepinephrine Turnover in Brown Adipose Tissue of the Rat. J. Clin. Investig. 1982, 69, 1061–1071.
17. Yoshida, T.; Fisler, J.S.; Fukushima, M.; Bray, G.A.; Schemmel, R.A. Diet, lighting, and food intake affect norepinephrine turnover in dietary obesity. Am. J. Physiol. Content 1987, 252, R402–R408.
18. Saito, M.; Minokoshi, Y.; Shimazu, T. Metabolic and sympathetic nerve activities of brown adipose tissue in tube-fed rats. Am. J. Physiol. Metab. 1989, 257, E374–E378.
19. Rothwell, N.J.; Stock, M.J. Effects of denervating brown adipose tissue on the responses to cold, hyperphagia and noradrenaline treatment in the rat. J. Physiol. 1984, 355, 457–463.
20. Leblanc, J.; Cabanac, M.; Samson, P. Reduced postprandial heat production with gavage as compared with meal feeding in human subjects. Am. J. Physiol. Metab. 1984, 246, E95–E101.
21. Leblanc, J.; Brondel, L. Role of palatability on meal-induced thermogenesis in human subjects. Am. J. Physiol. Metab. 1985, 248, E333–E336.
22. Diamond, P.; Brondel, L.; Leblanc, J. Palatability and postprandial thermogenesis in dogs. Am. J. Physiol. Metab. 1985, 248, E75–E79.
23. Blouet, C.; Schwartz, G.J. Duodenal Lipid Sensing Activates Vagal Afferents to Regulate Non-Shivering Brown Fat Thermogenesis in Rats. PLoS ONE 2012, 7, e51898.
24. Yamazaki, T.; Morimoto-Kobayashi, Y.; Koizumi, K.; Takahashi, C.; Nakajima, S.; Kitao, S.; Taniguchi, Y.; Katayama, M.; Ogawa, Y. Secretion of a gastrointestinal hormone, cholecystokinin, by hop-derived bitter components activates sympathetic nerves in brown adipose tissue. J. Nutr. Biochem. 2018, 64, 80–87.
25. Beiroa, D.; Imbernon, M.; Gallego, R.; Senra, A.; Herranz, D.; Villarroya, F.; Serrano, M.; Fernø, J.; Salvador, J.; Escalada, J.; et al. GLP-1 Agonism Stimulates Brown Adipose Tissue Thermogenesis and Browning Through Hypothalamic AMPK. Diabetes 2014, 63, 3346–3358.
26. Li, Y.; Schnabl, K.; Gabler, S.-M.; Willershäuser, M.; Reber, J.; Karlas, A.; Laurila, S.; Lahesmaa, M.; Din, M.U.; Bast-Habersbrunner, A.; et al. Secretin-Activated Brown Fat Mediates Prandial Thermogenesis to Induce Satiation. Cell 2018, 175, 1561–1574.e12.
27. Vítek, L.; Haluzik, M. The role of bile acids in metabolic regulation. J. Endocrinol. 2016, 228, R85–R96.

28. Watanabe, M.; Houten, S.; Mataki, C.; Christoffolete, M.; Kim, B.W.; Sato, H.; Messaddeq, N.; Harney, J.W.; Ezaki, O.; Kodama, T.; et al. Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation. Nature 2006, 439, 484–489.
29. Broeders, E.P.; Nascimento, E.B.; Havekes, B.; Brans, B.; Roumans, K.H.; Tailleux, A.; Schaart, G.; Kouach, M.; Charton, J.; Deprez, B.; et al. The Bile Acid Chenodeoxycholic Acid Increases Human Brown Adipose Tissue Activity. Cell Metab. 2015, 22, 418–426.
30. Velazquez-Villegas, L.A.; Perino, A.; Lemos, V.; Zietak, M.; Nomura, M.; Pols, T.W.H.; Schoonjans, K. TGR5 signalling promotes mitochondrial fission and beige remodelling of white adipose tissue. Nat. Commun. 2018, 9, 245.
31. Golic, I.; Kalezic, A.; Jankovic, A.; Jonic, S.; Korac, B.; Korac, A. Insulin Modulates the Bioenergetic and Thermogenic Capacity of Rat Brown Adipocytes In Vivo by Modulating Mitochondrial Mosaicism. Int. J. Mol. Sci. 2020, 21, 9204.
32. Orava, J.; Nuutila, P.; Lidell, M.E.; Oikonen, V.; Noponen, T.; Viljanen, T.; Scheinin, M.; Taittonen, M.; Niemi, T.; Enerbäck, S.; et al. Different Metabolic Responses of Human Brown Adipose Tissue to Activation by Cold and Insulin. Cell Metab. 2011, 14, 272–279.
33. Stanford, K.I.; Middelbeek, R.J.; Townsend, K.L.; An, D.; Nygaard, E.B.; Hitchcox, K.M.; Markan, K.R.; Nakano, K.; Hirshman, M.F.; Tseng, Y.-H.; et al. Brown adipose tissue regulates glucose homeostasis and insulin sensitivity. J. Clin. Investig. 2013, 123, 215–223.
34. Ravussin, E.; Bogardus, C. Thermogenic response to insulin and glucose infusions in man: A model to evaluate the different components of the thermic effect of carbohydrate. Life Sci. 1982, 31, 2011–2018.
35. Lee, P.; Smith, S.; Linderman, J.; Courville, A.B.; Brychta, R.J.; Dieckmann, W.; Werner, C.D.; Chen, K.Y.; Celi, F.S. Temperature-Acclimated Brown Adipose Tissue Modulates Insulin Sensitivity in Humans. Diabetes 2014, 63, 3686–3698.
36. Rothwell, N.J.; Stock, M.J. A role for insulin in the diet-induced thermogenesis of cafeteria-fed rats. Metab.-Clin. Exp. 1981, 30, 673–678.
37. Aherne, W.; Hull, D. Brown adipose tissue and heat production in the newborn infant. J. Pathol. Bacteriol. 1966, 91, 223–234.
38. Loeliger, R.C.; Maushart, C.I.; Gashi, G.; Senn, J.R.; Felder, M.; Becker, A.S.; Müller, J.; Balaz, M.; Wolfrum, C.; Burger, I.A.; et al. Relation of diet-induced thermogenesis to brown adipose tissue activity in healthy men. Am. J. Physiol. Metab. 2021, 320, E93–E101.
39. Ma, S.W.; Nadeau, B.E.; Foster, D.O. Evidence for liver as the major site of the diet-induced thermogenesis of rats fed a “cafeteria” diet. Can. J. Physiol. Pharmacol. 1987, 65, 1802–1804.

40. Ma, S.W.; Foster, D.O. Brown adipose tissue, liver, and diet-induced thermogenesis in cafeteria diet-fed rats. Can. J. Physiol. Pharmacol. 1989, 67, 376–381.
41. Berry, M.; Clark, D.; Grivell, A.; Wallace, P. The contribution of hepatic metabolism to diet-induced thermogenesis. Metabolism 1985, 34, 141–147.
42. Schnabl, K.; Li, Y.; Klingenspor, M. The gut hormone secretin triggers a gut–brown fat–brain axis in the control of food intake. Exp. Physiol. 2020, 105, 1206–1213.
43. Friedman, J. The long road to leptin. J. Clin. Investig. 2016, 126, 4727–4734.
44. Collins, S.; Kuhn, C.M.; Petro, A.E.; Swick, A.G.; Chrunyk, B.A.; Surwit, R.S. Role of leptin in fat regulation. Nature 1996, 380, 677.
45. Commins, S.P.; Marsh, D.J.; Thomas, S.A.; Watson, P.M.; Padgett, M.A.; Palmiter, R.; Gettys, T.W. Norepinephrine is required for leptin effects on gene expression in brown and white adipose tissue. Endocrinology 1999, 140, 4772–4778.
46. Commins, S.P.; Watson, P.M.; Padgett, M.A.; Dudley, A.; Argyropoulos, G.; Gettys, T.W. Induction of uncoupling protein expression in brown and white adipose tissue by leptin. Endocrinology 1999, 140, 292–300.
47. Scarpace, P.J.; Matheny, M.; Pollock, B.H.; Tumer, N. Leptin increases uncoupling protein expression and energy expenditure. Am. J. Physiol. Metab. 1997, 273, E226–E230.
48. Perry, R.J.; Lyu, K.; Rabin-Court, A.; Dong, J.; Li, X.; Yang, Y.; Qing, H.; Wang, A.; Yang, X.; Shulman, G.I. Leptin mediates postprandial increases in body temperature through hypothalamus–adrenal medulla–adipose tissue crosstalk. J. Clin. Investig. 2020, 130, 2001–2016.
49. Wang, P.; Loh, K.H.; Wu, M.; Morgan, D.A.; Schneeberger, M.; Yu, X.; Chi, J.; Kosse, C.; Kim, D.; Rahmouni, K.; et al. A leptin–BDNF pathway regulating sympathetic innervation of adipose tissue. Nature 2020, 583, 839–844.
50. Himms-Hagen, J.; Hogan, S.; Zaror-Behrens, G. Increased brown adipose tissue thermogenesis in obese (ob/ob) mice fed a palatable diet. Am. J. Physiol. Metab. 1986, 250, E274–E281.
51. Fischer, A.W.; Cannon, B.; Nedergaard, J. Leptin-deficient mice are not hypothermic, they are anapyrexic. Mol. Metab. 2016, 6, 173.
52. Fischer, A.W.; Hoefig, C.S.; Abreu-Vieira, G.; de Jong, J.M.; Petrovic, N.; Mittag, J.; Cannon, B.; Nedergaard, J. Leptin Raises Defended Body Temperature without Activating Thermogenesis. Cell Rep. 2016, 14, 1621–1631.
53. Qiao, L.; Yoo, H.S.; Bosco, C.; Lee, B.; Feng, G.-S.; Schaack, J.; Chi, N.-W.; Shao, J. Adiponectin reduces thermogenesis by inhibiting brown adipose tissue activation in mice. Diabetologia 2014, 57, 1027–1036.

54. Kmiec, Z.; Pokrywka, L.; Kotlarz, G.; Kubasik, J.; Szutowicz, A.; Mysliwski, A. Effects of Fasting and Refeeding on Serum Leptin, Adiponectin and Free Fatty Acid Concentrations in Young and Old Male Rats. Gerontology 2005, 51, 357–362.
55. Rowland, L.A.; Maurya, S.K.; Bal, N.C.; Kozak, L.; Periasamy, M. Sarcolipin and uncoupling protein 1 play distinct roles in diet-induced thermogenesis and do not compensate for one another. Obesity 2016, 24, 1430–1433.
56. van den Berg, S.A.A.; Lichtenbelt, W.V.M.; van Dijk, K.W.; Schrauwen, P. Skeletal muscle mitochondrial uncoupling, adaptive thermogenesis and energy expenditure. Curr. Opin. Clin. Nutr. Metab. Care 2011, 14, 243–249.
57. Bal, N.C.; Maurya, S.K.; Sopariwala, D.H.; Sahoo, S.K.; Gupta, S.C.; Shaikh, S.A.; Pant, M.; Rowland, L.A.; Bombardier, E.; Goonasekera, S.A.; et al. Sarcolipin is a newly identified regulator of muscle-based thermogenesis in mammals. Nat. Med. 2012, 18, 1575–1579.
58. Maurya, S.; Bal, N.C.; Sopariwala, D.H.; Pant, M.; Rowland, L.A.; Shaikh, S.; Periasamy, M. Sarcolipin Is a Key Determinant of the Basal Metabolic Rate, and Its Overexpression Enhances Energy Expenditure and Resistance against Diet-induced Obesity. J. Biol. Chem. 2015, 290, 10840–10849.
59. Reis, M.; Farage, M.; De Meis, L. Thermogenesis and energy expenditure: Control of heat production by the Ca2+-ATPase of fast and slow muscle. Mol. Membr. Biol. 2002, 19, 301–310.
60. Yau, W.W.; Yen, P.M. Thermogenesis in Adipose Tissue Activated by Thyroid Hormone. Int. J. Mol. Sci. 2020, 21, 3020.
61. Obregon, M.-J. Adipose tissues and thyroid hormones. Front. Physiol. 2014, 5, 479.
62. Tulp, O.L.A.A.; Einstein, G.P. Treatment with α-Methylparatyrosine Inhibits Sympathetic but Not Thyroidal Responses to Diet-Induced Thermogenesis in Lean Cafeteria-Overfed Rats. Curr. Trends. Toxi Pharma. Res. 2022, 2, 1–6.
63. Gabarrou, J.-F.; Duchamp, C.; Williams, J.; Géraert, P.-A. A role for thyroid hormones in the regulation of diet-induced thermogenesis in birds. Br. J. Nutr. 1997, 78, 963–973.
64. Danforth, E.; Horton, E.S.; O'Connell, M.; Sims, E.A.; Burger, A.G.; Ingbar, S.H.; Braverman, L.; Vagenakis, A.G. Dietary-induced alterations in thyroid hormone metabolism during overnutrition. J. Clin. Investig. 1979, 64, 1336–1347.