Research Article

Effect of Resistance Training on Adipose Tissue and Serum METRNL Levels in Sucrose Solution Fed Rats

Hadiseh Abdi Ziari [1] and Alireza Safarzade [1, 2, *]

[1]Department of Exercise Physiology, Faculty of Sports Sciences, University of Mazandaran, Babolsar, Iran
[2]Athletic Performance and Health Research Center, University of Mazandaran, Babolsar, Iran

Corresponding author: Department of Exercise Physiology, Faculty of Sports Sciences, University of Mazandaran, Babolsar, Iran. Email: a.safarzade@umz.ac.ir

Abstract

Background: Meteorin-like protein (METRNL) is a novel adipomyokine that may improve glucose tolerance, and its circulating levels are affected by changes in body weight.

Objectives: This study aimed to evaluate the effects of eight weeks of resistance training (RT) and high sucrose consumption on serum and adipose tissue METRNL levels in male rats.

Methods: In this study, 32 Wistar male rats were divided into normal diet and high sucrose diet groups. After 4 weeks, each group was divided into control and training groups. The rats in the training group were subjected to the RT program (3 days/week, for 8 weeks). In addition to serum and adipose tissue levels of METRNL, we measured epididymal and mesenteric fat mass, serum glucose, insulin, and homeostatic model assessment of insulin resistance (HOMA-IR).

Results: High sucrose diet increased fat weights and serum levels of glucose, insulin, and IR index; nevertheless, it reduced the serum levels of METRNL. RT decreased serum insulin concentrations and HOMA-IR. The result of two-way ANOVA and the *t*-test showed that eight weeks of RT decreased serum levels of METRNL, insulin, and HOMA-IR in sugar solution-fed rats.

Conclusions: The results suggest that RT may be an effective intervention to reduce serum METRNL and HOMA-IR levels, which is associated with improving body composition.

Keywords: Insulin Resistance, Resistance Training, Adipokines, Adipose Tissue

1. Background

Insulin resistance (IR) as a risk factor for developing type 2 diabetes (T2D) performs a key role in hyperglycemia (1). IR is caused by the intersection of multiple factors, including diet and a sedentary lifestyle (2). It is also stated that high-sugar diets play an axial role in metabolic dysregulation, leading to diseases including IR (3). Improving IR remains an important area of research in treating T2D and metabolic syndrome due to the need for new insulin-sensitizing therapies (4).

Improving insulin sensitivity and glucose uptake by exercise training plays an axial role in reducing insulin resistance through various pathways (5). Emerging studies have shown that exercise training stimulates the secretion of proteins from various tissues into the bloodstream, contributing to the beneficial effects on metabolism (6).

Secreted proteins such as adipokines and myokines are closely associated with the development of IR and have

drug development potential in treating such diseases (7). METRNL is a recently identified secreted adipomyokine that express in various tissues, including skeletal muscle and adipose tissue, and afterward enters the bloodstream (8, 9). METRNL increases energy expenditure and improves insulin sensitivity by inducing the expression of genes related to brown fats thermogenesis in mice (8, 9). However, further research mechanisms are needed to elucidate the mechanism of METRNL in insulin resistance (10).

Some studies have shown that METRNL secretion increases in muscle and white adipose tissue (WAT) through resistance exercise, increasing energy expenditure and improving insulin sensitivity (11, 12). Resistance training improves insulin sensitivity by focusing on increasing muscle mass and reducing body fat (5). However, the effect of RT on serum and WAT concentrations of METRNL has not been quite elucidated.

2. Objectives

Due to the effect of RT on target tissues for METRNL secretion, this study aimed to investigate the effects of eight weeks of RT on adipose tissue and serum levels of METRNL in rats fed a sugar solution.

3. Methods

3.1. Animals

Ethical principles and animal care were based on the Guidelines for the Care and Use of Laboratory Animals approved by the Ethics Committee of the University of Mazandaran (code: IR.UMZ.REC.1400.027). In this study, 32 Wistar male rats, 6 - 8 weeks old, were maintained at a standard animal lab under controlled light/dark (12/12 hours) and temperature (22 ± 2°C) conditions. After a week of acclimatization to their living conditions and how to exercise, the animals were randomly separated into 2 groups, including a normal diet and high sugar diet (30% (w/v) sucrose solution in water in water in a separate bottle) [13]. After 4 weeks, each group was divided into control and resistance training groups.

3.2. Training Protocol

Rats in the training groups performed RT with the use of a ladder for three days per week and lasted 8 weeks. The initial training session with a load equivalent to 50% of the rat's body weight was repeated twice for the training group, 5 times for each round. During 2 weeks, the number of training sets gradually increased to 4 and 5 repetitions per set. Also, by observing the principle of overload in the third week and the following weeks, it was equal to 75, 100, 125, 150, 175, and 200% of the weight of rats, respectively, and the workload was constant in the final weeks (two weeks). The rats were weighed weekly to determine the appropriate weight for the training load. There was a 1-minute break between each repetition and a 2-minute break between each turn [14]. Before and after each training session, the rats climbed the stairs 2–3 times without weights to warm up and cool down.

3.3. Sample Collection

After an 8-hour overnight fast, the animals were anesthetized with an intraperitoneal injection of a combination of ketamine (70 mg/kg) and xylazine (3 - 5 mg/kg) 72 hours after the last training session. Blood samples were taken from animal hearts and centrifuged at 3000 rpm for 15 minutes at 4°C to separate the serum. Epididymal white adipose tissue (eWAT) samples, after weighing, were homogenized in a buffer containing one

mL of PBS buffer and 100 mg of adipose tissue powdered, followed by 10-min centrifugation at 4000 rpm; its supernatant was collected to evaluate Metrnl values. Serum and tissue samples were transferred to the freezer at minus 20°C for further investigation.

3.4. Biochemical Measurements

Insulin and METRNL levels were analyzed using ELISA kits (METRNL ZellBio Germany, insulin Mercodia Sweden). Serum glucose was measured by colorimetric assay using a glucose oxidase assay kit (Pars Azmoun Company, Iran). HOMA-IR index became calculated as follow: HOMA-IR; (insulin (mU/L) × glucose (mmol/L) /22.5)

3.5. Statistical Methods

Data normality was checked using Kolmogorov–Smirnov test. A two-way ANOVA was used to determine the main effects of the diet (normal vs. high sucrose), training status (control vs. trained), and their interactions. T-test was used when the two-way ANOVA test detected a statistical difference. To explore relationships between variables, Pearson's correlation coefficient was used. The statistical analyses were conducted using SPSS version 23, and statistical significance was set at $P < 0.05$.

4. Results

There were no significant differences in final body weight and changes in body weight between the groups ($P > 0.05$; see Table 1). The rats fed with a sugar solution had higher weights of epididymal and mesenteric fat (both absolute and relative) compared to rats on a normal diet (Table 1). Eight weeks of RT did not significantly affect the weights of fat pads.

High sucrose diet significantly increased serum glucose ($P = 0.004$) levels (Figure 1). RT had no significant effect on serum glucose levels.

The interaction effects of two-way ANOVA were significant for insulin ($P = 0.013$) and HOMA-IR ($P = 0.026$). Therefore, we examined the effect of diet (by comparing normal control and high sucrose control groups) and training in different diet (normal or high sucrose) groups. The results of the *t*-test demonstrated that the insulin levels and HOMA-IR were significantly higher in the high sucrose control group compared with the normal control group ($P < 0.05$). Only in the high sucrose group RT significantly decreased serum insulin concentration and HOMA-IR compared with the high sucrose control group ($P < 0.05$; Figure 1).

The interaction effects of two-way ANOVA was significant for serum METRNL concentration ($P = 0.009$).

Table 1. Body Weight and Fat Weights in Experiential Groups [a]

Variables	Normal Diet		Sugar Solution		Two-way ANOVA		
	Control	RT	Control	RT	Sugar Diet	Training	Interaction
Weight changes, g	190 ± 27.3	193.2 ± 40.8	208.3 ± 50.2	213 ± 26.3	0.162	0.769	0.959
Epididymal fat weight, g	4.91 ± 1.09	4.77 ± 1.03	7.22 ± 2.87	7.53 ± 2.24	0.002	0.908	0.757
Epididymal fat/body weight, %	1.42 ± 0.27	1.36 ± 0.23	1.92 ± 0.60	2.05 ± 0.65	0.002	0.833	0.589
Mesenteric fat weight, g	2.54 ± 0.78	2.81 ± 0.90	5.26 ± 1.98	3.86 ± 1.09	< 0.001	0.221	0.074
Mesenteric fat/body weight, %	0.73 ± 0.20	0.79 ± 0.21	1.42 ± 0.45	1.50 ± 0.30	< 0.001	0.177	0.055

[a] The values are expressed as mean ± SD (n = 8 rats per group). Weight change = final weight - initial weight. fat to body weight ratio = (fat weight / final weight) × 100.
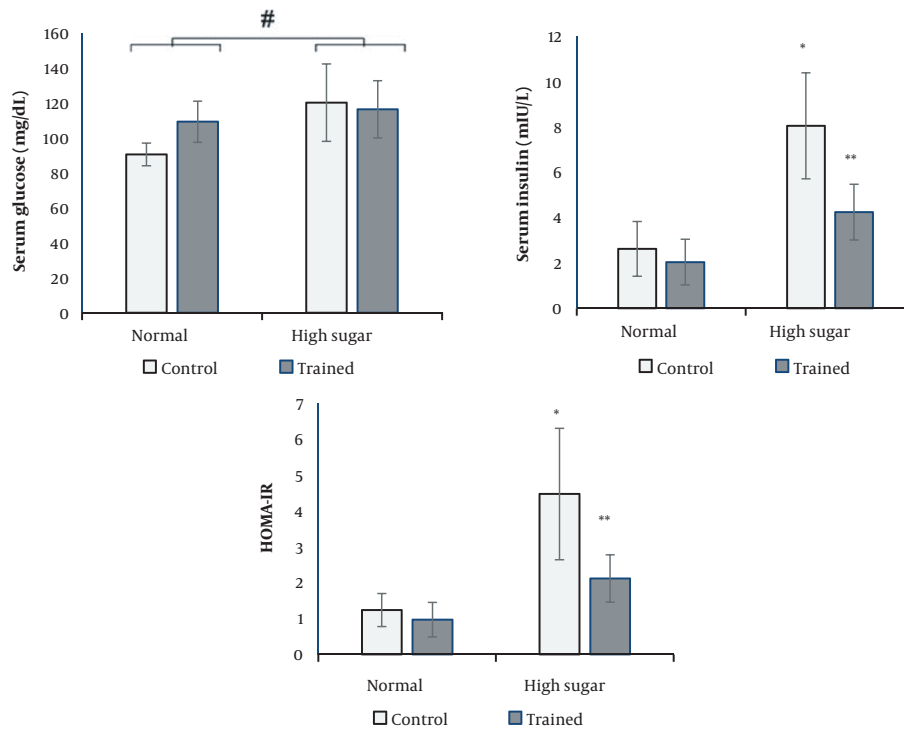

Figure 1. Serum metabolic parameters at the end of the experiment. HOMA-IR, homeostasis model assessment of insulin resistance. * vs. normal control diet; ** vs. high sugar control diet; # vs. high sugar diet.

Only in the high sucrose group RT significantly decreased serum METRNL levels compared with the high sucrose control group (P = 0.002; Figure 2). Neither RT nor diet had a significant effect on adipose tissue METRNL levels (Figure 2).

We examined the simple correlation between mesenteric and epididymal fat weights and other metabolic or tissue and serum METRNL levels (Table 2). A positive correlation was observed between mesenteric fat weight and glucose levels (r = 0.611, P < 0.001), insulin (r = 0.621, P < 0.001), and HOMA-IR (r = 0.745, P < 0.001). Furthermore, positive correlations were found between

epididymal fat mass and glucose levels (r = 0.522, P = 0.004), insulin (r = 0.560, P = 0.002), and HOMA-IR (r = 0.690, P < 0.001). There was no correlation between mesenteric and epididymal fat weight and tissue or serum METRNL levels.

5. Discussion

The main results of this study were that the animals that consumed a continuous 30% sugar solution showed an increase in mesenteric and epididymal fat weights, as well as elevated levels of serum glucose, insulin, and IR
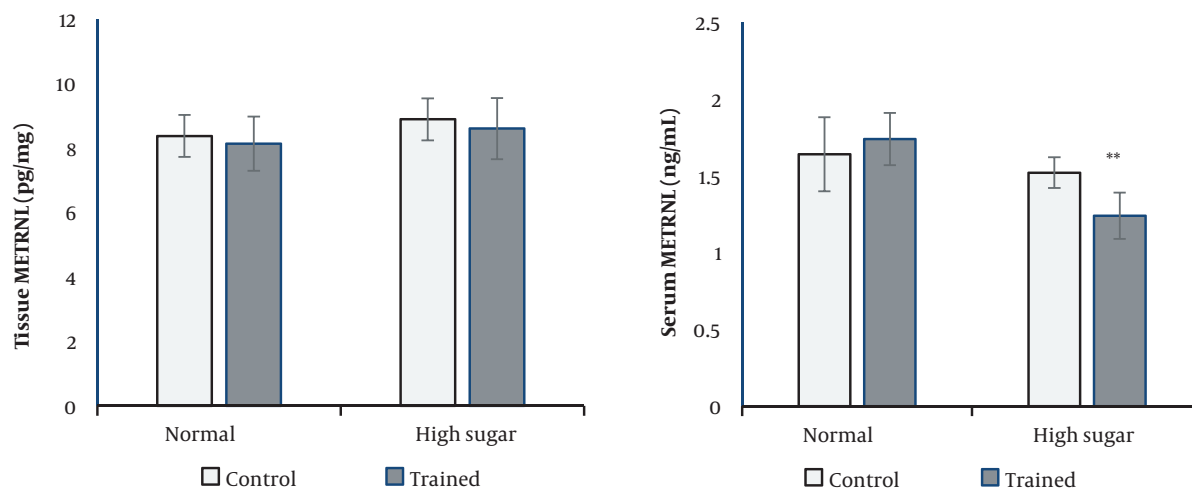
Figure 2. Serum and adipose tissue METRNL levels at the end of the experiment. ** vs. control high sugar diet.

Table 2. Simple Pearson Correlation Between Mesenteric and Epididymal Fat Weights (g) with Other Variables

Variables	Mesenteric Fat Weight, g		Epididymal Fat Weight, g	
	r	P-Value	r	P-Value
Glucose, mg/dL	0.611	< 0.001	0.522	0.004
Insulin, mIU/L	0.621	< 0.001	0.560	0.002
HOMA-IR	0.745	< 0.001	0.690	< 0.001
Tissue METRNL, pg/mg	0.132	0.50	0.136	0.499
Serum METRNL, ng/mL	-0.328	0.95	-0.305	0.129

Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance.

index. At the same time, there was a decrease in the serum levels of METRNL. On the other hand, eight weeks of RT improved sugar solution-induced metabolic disturbances such as serum insulin levels, IR index, and lower serum METRNL levels.

The findings of this study revealed that serum levels of METRNL partially decreased due to continuous consumption of sugar solution. Since serum insulin levels and IR index increased after consumption of sugar solution in the present study, accumulation of adipogenic compounds can also be a factor in decreasing serum METRNL. A study showed that elevated METRNL serum levels may increase the risk of T2D due to developmental IR (10). The results of the present study are in line with the results of Loffler et al. (15), Lee et al. (16), and El-Ashmawy et al. (17). They concluded that accumulation of adipogenic compounds, such as insulin, inhibits the expression of METRNL.

It has been shown that 8 weeks of RT did not lead

to a significant change in serum METRNL levels. The results of Rao et al. (11) and Eaton et al.'s (12) showed that muscle damage caused by exercise is an effective factor in increasing the secretion of METRNL because the hormone METRNL invokes immune cells involved in tissue repair (18, 19). METRNL secretion is primarily performed by macrophages as a response to local injury (18). Based on the findings, METRNL responds to acute metabolic challenges such as a single bout of resistance exercise and acute cold pressure; further research is needed on the compatibility of this hormone with regular RT.

The results of the present study demonstrated that a combination of sugar-soluble feeding and RT led to a further decrease in serum METRNL levels. While most studies suggest that RT increases METRNL levels in the body, there are several possible mechanisms that could explain the synergistic effect of combining RT and sugar-soluble feeding in decreasing serum METRNL levels. Elevated serum METRNL levels have been associated

with chronic inflammation that may have a potential therapeutic role in inflammation (20). In our study, the maximum carrying capacity increased after the second week of RT until the end of the program. Studies show that RT reduces inflammatory cytokines by increasing strength and muscle mass (21). RT and sugar-soluble feeding can affect hormonal responses, which play a role in insulin sensitivity (2, 22). RT has been shown to decrease inflammation markers (23), while consuming sugar-soluble foods after exercise may further reduce inflammation by increasing the availability of nutrients for muscle repair and recovery (24). The synergistic effect of combining RT and sugar-soluble feeding in reducing serum METRNL levels may involve multiple mechanisms that act together to improve insulin sensitivity.

There was no change in the METRNL levels of epididymal white adipose tissue (eWAT) in our study, in line with the results seen in the study of Rao et al. (11). A study of thermogenic stimulus regulation showed that acute cold pressure could significantly increase the expression of the METRNL gene in eWAT fat, while RT may not affect it (11).

The findings of the present study showed that fat pad weights increased due to continuous consumption of sugar solution. It seems that visceral white adipose tissue depots such as mesenteric uptake the Glucose for use in triacylglycerides (TAG) production (25, 26). It is well established, along with obesity, that the WAT presents an increase in inflammatory markers and infiltration of immune cells (27). The results of the present study are in line with some studies. They concluded that IR has a close correlation with visceral fat obesity (28).

5.1. Conclusions

RT appears to reduce the serum METRNL levels of sugar-fed rats. It can be attributed to the decreased adipose tissue inflammation, which in turn can be improved IR.

Footnotes

Authors' Contribution: Study concept and design: Alireza Safarzade; Analysis and interpretation of data: Hadiseh Abdi Ziari; Drafting of the manuscript: Hadiseh Abdi Ziari; Critical revision of the manuscript for important intellectual content: Alireza Safarzade, and Hadiseh Abdi Ziari; Statistical analysis: Hadiseh Abdi Ziari.

Conflict of Interests: The authors declare no conflict of interest.

Ethical Approval: This study is approved under the ethical approval code of IR.UMZ.REC.1400.027.

References

1. Lima J, Moreira NCS, Sakamoto-Hojo ET. Mechanisms underlying the pathophysiology of type 2 diabetes: From risk factors to oxidative stress, metabolic dysfunction, and hyperglycemia. *Mutat Res Genet Toxicol Environ Mutagen.* 2022;**874-875**:503437. [PubMed ID: 35151421]. https://doi.org/10.1016/j.mrgentox.2021.503437.

2. Banaszak M, Gorna I, Przyslawski J. Non-Pharmacological Treatments for Insulin Resistance: Effective Intervention of Plant-Based Diets-A Critical Review. *Nutrients.* 2022;**14**(7). [PubMed ID: 35406013]. [PubMed Central ID: PMC9002735]. https://doi.org/10.3390/nu14071400.

3. Li Y, Chang P, Sankaran S, Jang H, Nie Y, Zeng A, et al. Optical Metabolic Imaging Uncovers Sex-and Diet-dependent Lipid Changes in Aging Drosophila Brain. *bioRxiv.* 2022. https://doi.org/10.1101/2022.10.01.510416.

4. Menezes R, Matafome P, Freitas M, Garcia-Conesa MT. Updated Information of the Effects of (Poly)phenols against Type-2 Diabetes Mellitus in Humans: Reinforcing the Recommendations for Future Research. *Nutrients.* 2022;**14**(17). [PubMed ID: 36079821]. [PubMed Central ID: PMC9460145]. https://doi.org/10.3390/nu14173563.

5. Bronczek GA, Soares GM, de Barros JF, Vettorazzi JF, Kurauti MA, Marconato-Junior E, et al. Resistance exercise training improves glucose homeostasis by enhancing insulin secretion in C57BL/6 mice. *Sci Rep.* 2021;**11**(1):8574. [PubMed ID: 33883630]. [PubMed Central ID: PMC8060292]. https://doi.org/10.1038/s41598-021-88105-x.

6. Sabaratnam R, Wojtaszewski JFP, Hojlund K. Factors mediating exercise-induced organ crosstalk. *Acta Physiol (Oxf).* 2022;**234**(2). e13766. [PubMed ID: 34981891]. https://doi.org/10.1111/apha.13766.

7. Shen S, Liao Q, Chen X, Peng C, Lin L. The role of irisin in metabolic flexibility: Beyond adipose tissue browning. *Drug Discov Today.* 2022;**27**(8):2261–7. [PubMed ID: 35364272]. https://doi.org/10.1016/j.drudis.2022.03.019.

8. Jung TW, Lee SH, Kim HC, Bang JS, Abd El-Aty AM, Hacimuftuoglu A, et al. METRNL attenuates lipid-induced inflammation and insulin resistance via AMPK or PPARdelta-dependent pathways in skeletal muscle of mice. *Exp Mol Med.* 2018;**50**(9):1–11. [PubMed ID: 30213948]. [PubMed Central ID: PMC6137187]. https://doi.org/10.1038/s12276-018-0147-5.

9. Lee JO, Byun WS, Kang MJ, Han JA, Moon J, Shin MJ, et al. The myokine meteorin-like (metrnl) improves glucose tolerance in both skeletal muscle cells and mice by targeting AMPKalpha2. *FEBS J.* 2020;**287**(10):2087–104. [PubMed ID: 32196931]. [PubMed Central ID: PMC7383816]. https://doi.org/10.1111/febs.15301.

10. Wang K, Li F, Wang C, Deng Y, Cao Z, Cui Y, et al. Serum Levels of Meteorin-Like (Metrnl) Are Increased in Patients with Newly Diagnosed Type 2 Diabetes Mellitus and Are Associated with Insulin Resistance. *Med Sci Monit.* 2019;**25**:2337–43. [PubMed ID: 30928991]. [PubMed Central ID: PMC6454984]. https://doi.org/10.12659/MSM.915331.

11. Rao RR, Long JZ, White JP, Svensson KJ, Lou J, Lokurkar I, et al. Meteorin-like is a hormone that regulates immune-adipose interactions to increase beige fat thermogenesis. *Cell.* 2014;**157**(6):1279–91. [PubMed ID: 24906147]. [PubMed Central ID: PMC4131287]. https://doi.org/10.1016/j.cell.2014.03.065.

12. Eaton M, Granata C, Barry J, Safdar A, Bishop D, Little JP. Impact of a single bout of high-intensity interval exercise and short-term interval training on interleukin-6, FNDC5, and METRNL mRNA expression in human skeletal muscle. *J Sport Health Sci.* 2018;**7**(2):191–6. [PubMed ID: 30356443]. [PubMed Central ID: PMC6180539]. https://doi.org/10.1016/j.jshs.2017.01.003.

13. Diepenbroek C, Eggels L, Ackermans MT, Fliers E, Kalsbeek A, Serlie MJ, et al. Differential effects of hypercaloric choice diets on insulin sensitivity in rats. *J Endocrinol*. 2017;**232**(1):49–57. [PubMed ID: 27754934]. https://doi.org/10.1530/JOE-16-0265.

14. Aram Y, Jun-Young H, Soon-Mi C, Dong-Woo H, Ki-Jeong K, Suk-Ho L. Comparison of Multiple Sets and Progressive Single Set of Resistance Training on Muscle Mass and Strength in Rat. *Exercise Science*. 2015;**24**(3):267–74. https://doi.org/10.15857/ksep.2015.24.3.267.

15. Loffler D, Landgraf K, Rockstroh D, Schwartze JT, Dunzendorfer H, Kiess W, et al. METRNL decreases during adipogenesis and inhibits adipocyte differentiation leading to adipocyte hypertrophy in humans. *Int J Obes (Lond)*. 2017;**41**(1):112–9. [PubMed ID: 27748745]. https://doi.org/10.1038/ijo.2016.180.

16. Lee JH, Kang YE, Kim JM, Choung S, Joung KH, Kim HJ, et al. Serum Meteorin-like protein levels decreased in patients newly diagnosed with type 2 diabetes. *Diabetes Res Clin Pract*. 2018;**135**:7–10. [PubMed ID: 29097285]. https://doi.org/10.1016/j.diabres.2017.10.005.

17. El-Ashmawy HM, Selim FO, Hosny TAM, Almassry HN. Association of low serum Meteorin like (Metrnl) concentrations with worsening of glucose tolerance, impaired endothelial function and atherosclerosis. *Diabetes Res Clin Pract*. 2019;**150**:57–63. [PubMed ID: 30825562]. https://doi.org/10.1016/j.diabres.2019.02.026.

18. Baht GS, Bareja A, Lee DE, Rao RR, Huang R, Huebner JL, et al. Meteorin-like facilitates skeletal muscle repair through a Stat3/IGF-1 mechanism. *Nat Metab*. 2020;**2**(3):278–89. [PubMed ID: 32694780]. [PubMed Central ID: PMC7504545]. https://doi.org/10.1038/s42255-020-0184-y.

19. Chazaud B. A macrophage-derived adipokine supports skeletal muscle regeneration. *Nat Metab*. 2020;**2**(3):213–4. [PubMed ID: 32694778]. https://doi.org/10.1038/s42255-020-0186-9.

20. Li Z, Gao Z, Sun T, Zhang S, Yang S, Zheng M, et al. Meteorin-like/Metrnl, a novel secreted protein implicated in inflammation, immunology, and metabolism: A comprehensive review of preclinical and clinical studies. *Front Immunol*. 2023;**14**:1098570. [PubMed ID: 36911663]. [PubMed Central ID: PMC9998503]. https://doi.org/10.3389/fimmu.2023.1098570.

21. Horii N, Hasegawa N, Fujie S, Uchida M, Iemitsu M. Resistance exercise-induced increase in muscle 5alpha-dihydrotestosterone contributes to the activation of muscle Akt/mTOR/p70S6K- and Akt/AS160/GLUT4-signaling pathways in type 2 diabetic rats. *FASEB J*. 2020;**34**(8):11047–57. [PubMed ID: 32627878]. https://doi.org/10.1096/fj.201903223RR.

22. Azamian Jazi A, Moradi Sarteshnizi E, Fathi M, Azamian Jazi Z. Elastic band resistance training increases adropin and ameliorates some cardiometabolic risk factors in elderly women: A quasi-experimental study. *BMC Sports Sci Med Rehabil*. 2022;**14**(1):178. [PubMed ID: 36207735]. [PubMed Central ID: PMC9542455]. https://doi.org/10.1186/s13102-022-00571-6.

23. Liu Y, Chu JMT, Ran Y, Zhang Y, Chang RCC, Wong GTC. Prehabilitative resistance exercise reduces neuroinflammation and improves mitochondrial health in aged mice with perioperative neurocognitive disorders. *J Neuroinflammation*. 2022;**19**(1):150. [PubMed ID: 35705955]. [PubMed Central ID: PMC9199135]. https://doi.org/10.1186/s12974-022-02483-1.

24. Cui P, Li M, Yu M, Liu Y, Ding Y, Liu W, et al. Advances in sports food: Sports nutrition, food manufacture, opportunities and challenges. *Food Res Int*. 2022;**157**:111258. [PubMed ID: 35761570]. https://doi.org/10.1016/j.foodres.2022.111258.

25. Lopez-Fontana CM, Pennacchio G, Zyla LE, Toneatto J, Bruna FA, Ortiz N, et al. Effects of hypothyroidism on the mesenteric and omental adipose tissue in rats. *Mol Cell Endocrinol*. 2019;**490**:88–99. [PubMed ID: 31004687]. https://doi.org/10.1016/j.mce.2019.04.011.

26. Wang X, Xu M, Li Y. Adipose Tissue Aging and Metabolic Disorder, and the Impact of Nutritional Interventions. *Nutrients*. 2022;**14**(15). [PubMed ID: 35956309]. [PubMed Central ID: PMC9370499]. https://doi.org/10.3390/nu14153134.

27. Moukarzel LA, Ferrando L, Stylianou A, Lobaugh S, Wu M, Nobre SP, et al. Impact of obesity and white adipose tissue inflammation on the omental microenvironment in endometrial cancer. *Cancer*. 2022;**128**(18):3297–309. [PubMed ID: 35793549]. [PubMed Central ID: PMC9976596]. https://doi.org/10.1002/cncr.34356.

28. Zang P, Yang CH, Liu J, Lei HY, Wang W, Guo QY, et al. Relationship Between Acyl and Desacyl Ghrelin Levels with Insulin Resistance and Body Fat Mass in Type 2 Diabetes Mellitus. *Diabetes Metab Syndr Obes*. 2022;**15**:2763–70. [PubMed ID: 36105430]. [PubMed Central ID: PMC9464628]. https://doi.org/10.2147/DMSO.S368770.