

EGZERSİZ VE İRİSİN

Yazar

Dr. Öğr. Üyesi Fırat AKCAN

Editör

Doç. Dr. Davut Sinan KAPLAN

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Doç. Dr. Davut Sinan KAPLAN

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Akademisyen Kitabevi A.Ş.

Halk Sokak 5 / A

Yenişehir / Ankara

Tel: 0312 431 16 33

siparis@akademisyen.com

www.akademisyen.com

TEŞEKKÜR

Tez çalışmama beni yönlendiren ve çalışmanın her aşamasında yardımlarını esirgemeyen tez danışmanım Sayın Dr. Öğr. Üyesi Davut Sinan KAPLAN ve yardımcı tez danışmanım Sayın Doç. Dr. Mustafa ÖZDAL'a, Fizyoloji Anabilimdalının değerli öğretim elemanlarına, başında bulunduğu birimin tüm imkanlarını seferber ederek teze çok büyük katkı sağlayan Beden Eğitimi ve Spor Anabilimdalı başkanı ve değerli büyüğüm Sayın Doç. Dr. Mürsel BİÇER'e, aynı şekilde biyokimya laboratuvarlarını bize açarak tezin bu hale gelmesine çok büyük katkı sağlayan Biyokimya Anabilim Dalı Başkanı Sayın Prof. Dr. Mehmet TARAKÇIOĞLU'na, Doç. Dr. Hülya ÇİÇEK hocama ve katkısı çok olan hemşerim ve değerli arkadaşım Ar. Gör. Hasan ULUSALA'ya, lisansüstü öğrenimim boyunca büyük fedakârlık ve sabır gösteren sevgili eşim Ceylan AKCAN'a, tezin yazım aşamasında sabır ve desteğini her an yanımda hissettiğim kıymetli meslektaşım ve değerli arkadaşım Dr. Öğr. Üyesi Fikret ALINCAK'a, hayatım boyunca yanımda olan ve zor anlarımda desteklerini hiç bir zaman eksik etmeyen annem ve babama, teşekkürlerimi borç bilirim. Tez çalışmam sırasında sahip oldukları sonsuz sevgi ve enerjiyle motivasyon kaynağım olan çocuklarım; Dicle, Barış ve Murat iyi ki varsınız. Tezime gönüllü olarak katılım gösteren arkadaşlara, kan örneklerinin toplanmasında ve egzersizlerin uygulanmasında emeği geçen, Arş. Gör. Sayın Zarife PANCAR'a, Arş. Gör. Mehmet VURAL'a, öğrencilerim; Esmâ Kevser

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KISALTMALAR ve SİMGELER LİSTESİ

ATP	: Adenozin Trifosfat
BAD	: Beyaz Adipoz Doku
BKİ	: Beden Kitle İndeksi
DM	: Diyabetes Mellitus
DSÖ	: Dünya Sağlık Örgütü
ELISA	: Enzyme-Linked ImmunoSorbent Assay
ENHO	: Energy homeostasis associated gene (Enerji homeostazi ilişkili gen)
eNOS	: Endotelial Nitrik Oksit Sentaz
FGF21	: Fibroblast büyüme faktörü 21
FNDC5	: Fibronektin tip III domaini içeren protein 5
Hb	: Hemoglobin
HDL	: Yüksek Dansiteli Lipoprotein
KAD	: Kahverengi Adipoz Doku
MI	: Miyokard Infarktüsü
HOMA	: Homeostasis model assessment
HRP	: Horseradish peroksidaz
IGF II	: Insulin-like growth factor 2
IL-6	: İnterlökin-6
SBKK	: Sağlıklı Beslenelim Kalbimizi Koruyalım
PGC 1- α	: Peroxisome proliferator-activated receptor gamma coactivator 1-alpha
PPAR α	: Peroxisome proliferator-activated receptors alpha
TK	: Total Kolesterol
TEKHARF	: Türk Erişkinlerinde Kalp Hastalıkları ve Risk Faktörleri
TG	: Trigliserid
TOAD	: Türkiye Obezite Araştırma Derneği
TURDEP	: Türkiye Diyabet Epidemiyoloji Çalışması
TOHTA	: Türkiye Obezite ve Hipertansiyon Araştırması
UCP 1	: Uncoupling protein 1



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1. Mandıracıođlu A. Dünyada ve Türkiye'de yaşlıların demografik özellikleri. Ege Tıp Dergisi. 2010;49.
2. Yaturu S. Obesity and type 2 diabetes. Journal of Diabetes Mellitus. 2011;1(04):79.
3. Eaton SB, Eaton SB. Physical Inactivity, Obesity, and Type 2 Diabetes: An Evolutionary Perspective. Research quarterly for exercise and sport. 2017;88(1):1-8.
4. Nesti MS. Exercise for health: serious fun for the whole person. Journal of Sport and Health Science. 2016;5(2):135-8.
5. Hall JE. Guyton and Hall textbook of medical physiology e-Book: Elsevier Health Sciences; 2015.
6. Powers SK, Howley ET. Exercise physiology: Theory and application to fitness and performance: McGraw-Hill Humanities/Social Sciences/Languages; 2014.
7. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. A PGC1- α -dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012;481(7382):463.
8. De Matteis R, Lucertini F, Guescini M, Polidori E, Zeppa S, Stocchi V, et al. Exercise as a new physiological stimulus for brown adipose tissue activity. Nutrition, metabolism and cardiovascular diseases. 2013;23(6):582-90.
9. Qiao X, Nie Y, Ma Y, Chen Y, Cheng R, Yin W, et al. Irisin promotes osteoblast proliferation and differentiation via activating the MAP kinase signaling pathways. Scientific reports. 2016;6:18732.
10. Elbelt U, Hofmann T, Stengel A. Irisin: what promise does it hold? Current Opinion in Clinical Nutrition & Metabolic Care. 2013;16(5):541-7.
11. Spiegelman BM, Korsmeyer SJ, editors. Irisin and the therapeutic benefits of exercise. BMC Proceedings; 2012: BioMed Central.
12. Kim H-J, Lee H-J, So B, Son JS, Yoon D, Song W. Effect of aerobic training and resistance training on circulating irisin level and their association with change of body composition in overweight/obese adults: a pilot study. Physiological research. 2016;65(2):271.
13. Moghadamfar M, Gorgani-Firuzjaee S. Exercise hormone (Irisin). Paramedical Sciences and Military Health. 2016;11(3):52-7.
14. Tsuchiya Y, Ando D, Goto K, Kiuchi M, Yamakita M, Koyama K. High-intensity exercise causes greater irisin response compared with low-intensity

- exercise under similar energy consumption. *The Tohoku journal of experimental medicine*. 2014;233(2):135-40.
15. Akgün N. *Egzersiz fizyolojisi*. Gökçe Ofset Matbaacılık, Ankara. 1989.
 16. Gallego G, Özer Ö. Integrating replenishment decisions with advance demand information. *Management science*. 2001;47(10):1344-60.
 17. Wilmore JH, Knuttgen HG. Aerobic exercise and endurance: improving fitness for health benefits. *The Physician and sportsmedicine*. 2003;31(5):45-51.
 18. Lenze E, Wetherell J, Hickman SD, Sinacore D. Mindfulness training and exercise: benefits for brain, mind, and body. *The American Journal of Geriatric Psychiatry*. 2016;24(3):S21.
 19. Anderson L, Oldridge N, Thompson DR, Zwisler A-D, Rees K, Martin N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis. *Journal of the American College of Cardiology*. 2016;67(1):1-12.
 20. Friedenreich CM. Abstract SY22-01: The role of exercise in cancer progression and mortality: Observational and molecular epidemiologic evidence. *AACR*; 2016.
 21. Larsson A, Palstam A, Löfgren M, Ernberg M, Bjersing J, Bileviciute-Ljungar I, et al. Resistance exercise improves muscle strength, health status and pain intensity in fibromyalgia—a randomized controlled trial. *Arthritis research & therapy*. 2015;17(1):161.
 22. Santos L, Elliott-Sale KJ, Sale C. Exercise and bone health across the lifespan. *Biogerontology*. 2017;18(6):931-46.
 23. Kitzman DW, Brubaker P, Morgan T, Haykowsky M, Hundley G, Kraus WE, et al. Effect of caloric restriction or aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure with preserved ejection fraction: a randomized clinical trial. *Jama*. 2016;315(1):36-46.
 24. Hsu CL, Best JR, Davis JC, Nagamatsu LS, Wang S, Boyd LA, et al. Aerobic exercise promotes executive functions and impacts functional neural activity among older adults with vascular cognitive impairment. *Br J Sports Med*. 2017:bjsports-2016-096846.
 25. Rowell LB, O'Leary DS. Reflex control of the circulation during exercise: chemoreflexes and mechanoreflexes. *Journal of Applied Physiology*. 1990;69(2):407-18.
 26. Astrand P. JB Wolffe Memorial Lecture." Why exercise?": *Medicine and Science in Sports and Exercise*. 1992;24(2):153-62.
 27. Foss ML, Keteyian SJ, Fox EL. *Fox's physiological basis for exercise and sport*: WCB/McGraw-Hill Boston; 1998.
 28. McARDLE A, Jackson MJ. Exercise, oxidative stress and ageing. *The Journal of Anatomy*. 2000;197(4):539-41.
 29. Karamizrak SO, Ergen E, Töre I, Akgün N. Changes in serum creatine kinase, lactate dehydrogenase and aldolase activities following supramaximal

- exercise in athletes. *The Journal of sports medicine and physical fitness*. 1994;34(2):141-6.
30. Cooper CB, Sowash J, Taylor M, Storer TW. Office-Based Cardiopulmonary Exercise Testing Empowers Medical Decision Making. *Chest*. 2003;124(4):164S.
 31. Zimmerman BJ, Granger DN. Reperfusion injury. *The surgical clinics of North America*. 1992;72(1):65-83.
 32. Åstrand P, Rodahl K, Dahl H, Strömme S. Evaluation of physical performance on the basis of tests. *Textbook of work physiology: physiological bases of exercise*. 1986;4:273-98.
 33. Foss M, Keteyian S. Exercise, body composition, and weight control. *Physiological Basis for Exercise and Sport*. 1998:422-46.
 34. Morton J, MacLaren D, Cable N, Campbell I, Evans L, Bongers T, et al. Elevated core and muscle temperature to levels comparable to exercise do not increase heat shock protein content of skeletal muscle of physically active men. *Acta physiologica*. 2007;190(4):319-27.
 35. Newham D. The consequences of eccentric contractions and their relationship to delayed onset muscle pain. *European journal of applied physiology and occupational physiology*. 1988;57(3):353-9.
 36. Proske U, Morgan D. Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. *The Journal of physiology*. 2001;537(2):333-45.
 37. Myers J, Ashley E. Dangerous curves: a perspective on exercise, lactate, and the anaerobic threshold. *Chest*. 1997;111(3):787-95.
 38. Mitat K. Egzersizin Endokrin Sistem Üzerine Etkileri ve Hormonal Regülasyonlar. *Türkiye Klinikleri J Physiother Rehabil-Special Topics*. 2016;2(1):48-56.
 39. Günay M, Cicioğlu İ, Kara E. Egzersize metabolik ve ısı adaptasyonu. *Gazi Kitapevi*, Ankara. 2006.
 40. Tekin A, Saraymen R, Gouml K, Eliouml M. The effect of acute exercises on blood hematological parameters in handball players. *African Journal of Microbiology Research*. 2012;6(9):2027-32.
 41. Cormack SJ, Newton RU, McGuigan MR. Neuromuscular and endocrine responses of elite players to an Australian rules football match. *International journal of sports physiology and performance*. 2008;3(3):359-74.
 42. Elloumi M, Maso F, Michaux O, Robert A, Lac G. Behaviour of saliva cortisol [C], testosterone [T] and the T/C ratio during a rugby match and during the post-competition recovery days. *European journal of applied physiology*. 2003;90(1-2):23-8.
 43. Ahtiainen JP, Pakarinen A, Kraemer WJ, Hakkinen K. Acute hormonal responses to heavy resistance exercise in strength athletes versus nonathletes. *Canadian Journal of Applied Physiology*. 2004;29(5):527-43.
 44. Ahtiainen JP, Pakarinen A, Alen M, Kraemer WJ, Häkkinen K. Short vs. long rest period between the sets in hypertrophic resistance training: inf-

- fluence on muscle strength, size, and hormonal adaptations in trained men. *Journal of Strength and Conditioning Research*. 2005;19(3):572.
45. Hakkinen K, Pakarinen A. Acute hormonal responses to two different fatiguing heavy-resistance protocols in male athletes. *Journal of Applied Physiology*. 1993;74(2):882-7.
 46. Kasımay Ö, Metin G. Kronik Hastalıklarda Egzersiz. *Klinik Gelişim Dergisi*. 2009;7(1):44-9.
 47. Black LE, Swan PD, Alvar BA. Effects of intensity and volume on insulin sensitivity during acute bouts of resistance training. *The Journal of Strength & Conditioning Research*. 2010;24(4):1109-16.
 48. Cook KS, Min HY, Johnson D, Chaplinsky RJ, Flier JS, Hunt CR, et al. Adipsin: a circulating serine protease homolog secreted by adipose tissue and sciatic nerve. *Science*. 1987;237(4813):402-5.
 49. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature*. 1994;372(6505):425.
 50. Goldstein M. Humoral nature of the hypoglycemic factor of muscular work. *Am Diabetes Assoc*; 1961.
 51. Scherer PE. Adipose tissue: from lipid storage compartment to endocrine organ. *Diabetes*. 2006;55(6):1537-45.
 52. Pedersen BK, Febbraio MA. Muscles, exercise and obesity: skeletal muscle as a secretory organ. *Nature Reviews Endocrinology*. 2012;8(8):457.
 53. Organization WH. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation presented at the World Health Organization, June 3-5, 1997, Geneva, Switzerland. Geneva, Switzerland: WHO. 1997.
 54. Organization WH. Obesity 2018, Haziran 30. Available from: <http://www.who.int/topics/obesity/en/>.
 55. Index BM. Body Mass Index (BMI). Retrieved from <http://www.cdc.gov/healthyweight/assessing/bmi/> (accessed 1 January 2016); 2015.
 56. Onat A, Keleş İ, Sansoy V, Ceyhan K, Uysal Ö, Çetinkaya A, et al. Yetişkinlerimizin 10-yıllık takibinde obezite göstergeleri artışta: Beden kitle indeksi erkeklerde koroner olayların bağımsız öngördürücüsü. *Türk kardioloji derneği arşivi*. 2001;29(7):430-6.
 57. Simsek F, Ulukol B, Berberoglu M, Gülnar S, Adryaman P, Öcal G. Ankarada bir ilköğretim okulu ve lisede obezite sıklığı. *Ankara Üniversitesi Tıp Fakültesi Mecmuası*. 2005;58:163-6.
 58. Levin B. Synergy of nature and nurture in the development of childhood obesity. *International Journal of Obesity*. 2009;33(S1):S53.
 59. Bal Ö, Özgür G, Gümüş AB. Obez bireylerin stresle başa çıkma yöntemleri. 2006.
 60. Livingstone B. Epidemiology of childhood obesity in Europe. *European journal of pediatrics*. 2000;159(1):S14-S34.
 61. Canetti L, Bachar E, Berry EM. Food and emotion. *Behavioural processes*. 2002;60(2):157-64.

62. Fenster CP, Weinsier RL, Darley-USmar VM, Patel RP. Obesity, aerobic exercise, and vascular disease: the role of oxidant stress. *Obesity*. 2002;10(9):964-8.
63. Yanikkerem E, Mutlu S. Maternal Obezitenin Sonuçları ve Önleme Stratejileri. *TAF Preventive Medicine Bulletin*. 2012;11(3).
64. Baltacı D, Ünalacak M, Kara İH, Sarigüzel YC. Birinci Basamakta Obezite Tedavisi. *Türkiye Klinikleri J Fam Med-Special Topics*. 2015;6(3):96-102.
65. Association AD. Diagnosis and classification of diabetes mellitus. *Diabetes care*. 2010;33(Suppl 1):S62.
66. King H, Rewers M. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. *Diabetes care*. 1993;16(1):157-77.
67. Boyd CM, Darer J, Boulton C, Fried LP, Boulton L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *Jama*. 2005;294(6):716-24.
68. Tong Y, Lin Y, Zhang Y, Yang J, Zhang Y, Liu H, et al. Association between TCF7L2 gene polymorphisms and susceptibility to type 2 diabetes mellitus: a large Human Genome Epidemiology (HuGE) review and meta-analysis. *BMC medical genetics*. 2009;10(1):15.
69. Jansson SP, Andersson D, Svärdsudd K. Prevalence and incidence rate of diabetes mellitus in a Swedish community during 30 years of follow-up. *Diabetologia*. 2007;50(4):703-10.
70. Satman I, Yılmaz T, Sengül A, Salman S, Salman F, Uygur S, et al. Population-based study of diabetes and risk characteristics in Turkey: results of the Turkish diabetes epidemiology study (TURDEP). *Diabetes care*. 2002;25(9):1551-6.
71. Eray E, Balcı M. Tip 2 diyabet tedavisi. *Dahili Tıp Bilimleri Dergisi*. 2005;12(2):66-71.
72. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*. 2012;55(6):1577-96.
73. Alberti KGMM, Zimmet P, DeFronzo RA. *International textbook of diabetes mellitus*: J. Wiley; 1997.
74. İnci A, Aypak SÜ. İrisin ve Metabolik Etkileri. *Türkiye Klinikleri Journal of Endocrinology*. 2016;11(1):15-21.
75. Irving BA, Still CD, Argyropoulos G. Does IRISIN have a BRITE future as a therapeutic agent in humans? *Current obesity reports*. 2014;3(2):235-41.
76. Schumacher MA, Chinnam N, Ohashi T, Shah RS, Erickson HP. The Structure of Irisin Reveals a Novel Intersubunit β -Sheet Fibronectin Type III (FNIII) Dimer Implications for receptor activation. *Journal of Biological Chemistry*. 2013;288(47):33738-44.
77. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating con-

- centrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism-Clinical and experimental*. 2012;61(12):1725-38.
78. Roca-Rivada A, Castelao C, Senin LL, Landrove MO, Baltar J, Crujeiras AB, et al. FND5/irisin is not only a myokine but also an adipokine. *PloS one*. 2013;8(4):e60563.
 79. Kurdiova T, Balaz M, Vician M, Maderova D, Vlcek M, Valkovic L, et al. Effects of obesity, diabetes and exercise on Fndc5 gene expression and irisin release in human skeletal muscle and adipose tissue: in vivo and in vitro studies. *The Journal of physiology*. 2014;592(5):1091-107.
 80. Moreno-Navarrete JM, Ortega F, Serrano M, Guerra E, Pardo G, Tinahones F, et al. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. *The Journal of Clinical Endocrinology & Metabolism*. 2013;98(4):E769-E78.
 81. Aydin S, Kuloglu T, Aydin S, Kalayci M, Yilmaz M, Cakmak T, et al. A comprehensive immunohistochemical examination of the distribution of the fat-burning protein irisin in biological tissues. *Peptides*. 2014;61:130-6.
 82. Lv J, Pan Y, Li X, Cheng D, Ju H, Tian J, et al. Study on the distribution and elimination of the new hormone irisin in vivo: new discoveries regarding irisin. *Hormone and Metabolic Research*. 2015;47(08):591-5.
 83. Crujeiras A, Pardo M, Casanueva F. Irisin: 'fat' or artefact. *Clinical endocrinology*. 2015;82(4):467-74.
 84. Polyzos SA, Mantzoros CS. An update on the validity of irisin assays and the link between irisin and hepatic metabolism. *Metabolism-Clinical and Experimental*. 2015;64(9):937-42.
 85. Pilegaard H, Saltin B, Neufer PD. Exercise induces transient transcriptional activation of the PGC-1 α gene in human skeletal muscle. *The Journal of physiology*. 2003;546(3):851-8.
 86. Wu Z, Puigserver P, Andersson U, Zhang C, Adelmant G, Mootha V, et al. Mechanisms controlling mitochondrial biogenesis and respiration through the thermogenic coactivator PGC-1. *Cell*. 1999;98(1):115-24.
 87. Hofmann T, Elbelt U, Ahnis A, Kobelt P, Rose M, Stengel A. Irisin levels are not affected by physical activity in patients with anorexia nervosa. *Frontiers in endocrinology*. 2014;4:202.
 88. Besse-Patin A, Montastier E, Vinel C, Castan-Laurell I, Louche K, Dray C, et al. Effect of endurance training on skeletal muscle myokine expression in obese men: identification of apelin as a novel myokine. *International journal of obesity*. 2014;38(5):707.
 89. Hecksteden A, Wegmann M, Steffen A, Kraushaar J, Morsch A, Ruppenthal S, et al. Irisin and exercise training in humans—results from a randomized controlled training trial. *BMC medicine*. 2013;11(1):235.
 90. Raschke S, Elsen M, Gassenhuber H, Sommerfeld M, Schwahn U, Brockmann B, et al. Evidence against a beneficial effect of irisin in humans. *PloS one*. 2013;8(9):e73680.

91. Aydin S, Kuloglu T, Aydin S, Eren MN, Celik A, Yilmaz M, et al. Cardiac, skeletal muscle and serum irisin responses to with or without water exercise in young and old male rats: cardiac muscle produces more irisin than skeletal muscle. *Peptides*. 2014;52:68-73.
92. Zhang Y, Li R, Meng Y, Li S, Donelan W, Zhao Y, et al. Irisin stimulates browning of white adipocytes through mitogen-activated protein kinase p38 MAP kinase and ERK MAP kinase signaling. *Diabetes*. 2014;63(2):514-25.
93. Dong J, Dong Y, Chen F, Mitch W, Zhang L. Inhibition of myostatin in mice improves insulin sensitivity via irisin-mediated cross talk between muscle and adipose tissues. *International journal of obesity*. 2016;40(3):434.
94. Shan T, Liang X, Bi P, Kuang S. Myostatin knockout drives browning of white adipose tissue through activating the AMPK-PGC1 α -Fndc5 pathway in muscle. *The FASEB Journal*. 2013;27(5):1981-9.
95. Palacios-González B, Vadillo-Ortega F, Polo-Oteyza E, Sánchez T, Ancira-Moreno M, Romero-Hidalgo S, et al. Irisin levels before and after physical activity among school-age children with different BMI: A direct relation with leptin. *Obesity*. 2015;23(4):729-32.
96. Rodríguez A, Becerril S, Méndez-Giménez L, Ramírez B, Sáinz N, Catalán V, et al. Leptin administration activates irisin-induced myogenesis via nitric oxide-dependent mechanisms, but reduces its effect on subcutaneous fat browning in mice. *International Journal of Obesity*. 2015;39(3):397.
97. Rachid TL, Penna-de-Carvalho A, Brighenti I, Aguila MB, Mandarim-de-Lacerda CA, Souza-Mello V. Fenofibrate (PPAR α agonist) induces beige cell formation in subcutaneous white adipose tissue from diet-induced male obese mice. *Molecular and Cellular Endocrinology*. 2015;402:86-94.
98. Li DJ, Huang F, Lu WJ, Jiang GJ, Deng YP, Shen FM. Metformin promotes irisin release from murine skeletal muscle independently of AMP-activated protein kinase activation. *Acta Physiologica*. 2015;213(3):711-21.
99. Yang Z, Chen X, Chen Y, Zhao Q. PGC-1 mediates the regulation of metformin in muscle irisin expression and function. *American journal of translational research*. 2015;7(10):1850.
100. Lee P, Linderman JD, Smith S, Brychta RJ, Wang J, Idelson C, et al. Irisin and FGF21 are cold-induced endocrine activators of brown fat function in humans. *Cell metabolism*. 2014;19(2):302-9.
101. Huh J, Dincer F, Mesfum E, Mantzoros C. Irisin stimulates muscle growth-related genes and regulates adipocyte differentiation and metabolism in humans. *International Journal of Obesity*. 2014;38(12).
102. Elsen M, Raschke S, Eckel J. Browning of white fat: does irisin play a role in humans? *Journal of Endocrinology*. 2014;222(1):R25-R38.
103. Xiong X-Q, Chen D, Sun H-J, Ding L, Wang J-J, Chen Q, et al. FNDC5 overexpression and irisin ameliorate glucose/lipid metabolic derangements and enhance lipolysis in obesity. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*. 2015;1852(9):1867-75.

104. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism*. 2012;61(12):1725-38.
105. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual: Human kinetics books Champaign; 1988.
106. Tamer K. Sporda fiziksel-fizyolojik performansın ölçülmesi ve değerlendirilmesi: Bağırğan Yayınevi; 2000.
107. Bernal W, Martin-Mateos R, Lipcsey M, Tallis C, Woodsford K, Mcphail MJ, et al. Aerobic capacity during cardiopulmonary exercise testing and survival with and without liver transplantation for patients with chronic liver disease. *Liver Transplantation*. 2014;20(1):54-62.
108. Kabak B. Elit sporcularda anaerobik egzersize miyokin cevabı: Selçuk Üniversitesi Sağlık Bilimleri Enstitüsü; 2016.
109. Tsuchiya Y, Ando D, Takamatsu K, Goto K. Resistance exercise induces a greater irisin response than endurance exercise. *Metabolism*. 2015;64(9):1042-50.
110. Löffler D, Müller U, Scheuermann K, Friebe D, Gesing J, Bielitz J, et al. Serum irisin levels are regulated by acute strenuous exercise. *The Journal of Clinical Endocrinology & Metabolism*. 2015;100(4):1289-99.
111. Qiu S, Bosnyák E, Treff G, Steinacker JM, Nieß AM, Krüger K, et al. Acute exercise-induced irisin release in healthy adults: Associations with training status and exercise mode. *European journal of sport science*. 2018:1-8.
112. Huh JY, Siopi A, Mougios V, Park KH, Mantzoros CS. Irisin in response to exercise in humans with and without metabolic syndrome. *The Journal of Clinical Endocrinology & Metabolism*. 2015;100(3):E453-E7.
113. Norheim F, Langleite TM, Hjorth M, Holen T, Kielland A, Stadheim HK, et al. The effects of acute and chronic exercise on PGC-1 α , irisin and browning of subcutaneous adipose tissue in humans. *The FEBS journal*. 2014;281(3):739-49.
114. Pekkala S, Wiklund PK, Hulmi JJ, Ahtiainen JP, Horttanainen M, Pöllänen E, et al. Are skeletal muscle FNDC5 gene expression and irisin release regulated by exercise and related to health? *The Journal of physiology*. 2013;591(21):5393-400.
115. Kraemer RR, Shockett PE, Webb ND, Shah U, Castracane VD. A Transient Elevated Irisin Blood Concentration in Response to Prolonged, Moderate Aerobic Exercise in Young Men and Women.: 1498 Board# 238 May 29, 9. *Medicine & Science in Sports & Exercise*. 2014;46(5S):404.
116. Huh JY, Mougios V, Kabasakalis A, Fatouros I, Siopi A, Douroudos II, et al. Exercise-induced irisin secretion is independent of age or fitness level and increased irisin may directly modulate muscle metabolism through AMPK activation. *The Journal of Clinical Endocrinology & Metabolism*. 2014;99(11):E2154-E61.

117. Huh JY, Mougios V, Skraparlis A, Kabasakalis A, Mantzoros CS. ELSEVIER: Irisin in response to acute and chronic whole-body vibration exercise in humans. . 2014;23:145-.
118. Nygaard H, Slettaløkken G, Vegge G, Hollan I, Whist JE, Strand T, et al. Irisin in blood increases transiently after single sessions of intense endurance exercise and heavy strength training. PloS one. 2015;10(3):e0121367.
119. Samy DM, Ismail CA, Nassra RA. Circulating irisin concentrations in rat models of thyroid dysfunction—effect of exercise. Metabolism. 2015;64(7):804-13.
120. Hazar S, Erol E, Gökdemir K. Kuvvet Antrenmanı Sonrası Oluşan Kas Ağrısının Kas Hasarıyla İlişkisi. Gazi Üniversitesi Beden Eğitimi ve Spor Bilimleri Dergisi. 2006;6(3):49-58.
121. Tanisawa K, Taniguchi H, Sun X, Ito T, Cao Z-B, Sakamoto S, et al. Common single nucleotide polymorphisms in the FNDC5 gene are associated with glucose metabolism but do not affect serum irisin levels in Japanese men with low fitness levels. Metabolism. 2014;63(4):574-83.
122. Kerstholt N, Ewert R, Nauck M, Spielhagen T, Bollmann T, Stubbe B, et al. Association of circulating irisin and cardiopulmonary exercise capacity in healthy volunteers: results of the Study of Health in Pomerania. BMC pulmonary medicine. 2015;15(1):41.