

**Additional Table 1 Effects of physical exercise on the expression of growth factors and hormones**

Exerkine	Reference	Research subject	Tissue	Exercise paradigm	Regulatory effect
BDNF	Gómez-Pinilla et al., 2001	Sprague-Dawley rats	Muscle/spinal cord	Treadmill training	↑
	Berchtold et al., 2010	C57BL/6 mice	Hippocampus	Voluntary running	↑
	Erickson et al., 2011	Older adults	Serum	Aerobic exercise	↑
	Voss et al., 2013	Older adults	Serum	Aerobic walking	↑
	Wrann et al., 2013	C57BL/6 mice	Hippocampus	Endurance exercise	↑
	Hoffman et al., 2015	Post-traumatic stress disorder model rats	Hippocampus	Treadmill exercise	↑
	Saucedo Marquez et al., 2015	Healthy humans	Serum	Continuous exercise/high intensity interval training	↑ (High intensity interval training > continuous exercise)
	Müller et al., 2017	Older adults	Plasma	Dancing	↑
	Yu et al., 2017	Sprague-Dawley rats	Serum/soleus muscle	Downhill running	↑
	Wang et al., 2018	Myocardial infarction rats	Serum/heart	Treadmill training	↑
	Kujach et al., 2019	Young males	Serum	Sprint interval exercise	↑
	Rosa et al., 2019	Aβ1-40 induced depression model mice	Serum/hippocampus	Treadmill exercise	↑
	Lang et al., 2020	Type 2 diabetes mellitus mice	Hippocampus	Treadmill exercise	↑
	Tai et al., 2020	Sleep deprived mice	Hippocampus	Treadmill exercise	↑
NGF	Chae and Kim, 2009	D-galactose-induced aging Sprague-Dawley rats	Hippocampus	Treadmill exercise	↑
	O'Callaghan et al., 2009	Aged Wistar rats	Hippocampus	Treadmill exercise	↑
	Um et al., 2011	AD model mice (Tg-NSE/hPS2m)	Hippocampus	Treadmill exercise	↑
	Bonini et al., 2013	Athletes	Serum	Intense and prolonged exercise	↑
	Woo et al., 2013	Obesity-high fat diet model rats	Hippocampus	Treadmill exercise	↑
	Ando et al., 2016	Dogs	Serum	Exercise loads	↑
	Patel et al., 2016	Autoimmune encephalomyelitis rats	Soleus muscle	Forced exercise	↑
	Franzoni et al., 2017	Wistar rats	Hippocampus	Treadmill exercise	↑
	Okudan and Belviranlı, 2017	Social isolation model rats	Hippocampus	Voluntary running	↑
	Peake et al., 2017	Active men	Muscle	Unilateral lower-body resistance exercise	↑
Roh et al., 2017	Male college students	Serum	Low/medium/high intensity treadmill running	↑ (Medium and high intensity treadmill running > intensity treadmill running)	
Hall et al., 2018	Sprague-Dawley rats	Hippocampus	Voluntary running	↑	

VEGF	Paddock et al., 2018	Rats	DRG neurons	Treadmill/voluntary running	↑
	Leick et al., 2009	C57BL/6 mice	Skeletal muscle	Treadmill exercise	↑
	Tang et al., 2010	VEGF luciferase reporter gene mice	Brain/lung/skeletal muscle	Treadmill exercise	↑
	Aksu et al., 2012	Pregnant rats	Prefrontal cortex	Treadmill exercise	↑ in the offspring rats' prefrontal cortex
	Tsai et al., 2013	C57BL/6 mice	Serum	Aerobic interval/continuous exercise	↑
	Voss et al., 2013	Older adults	Serum	Aerobic walking	↑
	Ross et al., 2014	Trained young men	Serum	Endurance exercise	↑
	Uysal et al., 2015	Adolescent Wistar rats	Hippocampus	Treadmill exercise	↑
	Eldomiaty et al., 2017	Depression model rats	Hippocampus	Voluntary running	↑
	Morland et al., 2017	Wild-type mice	Hippocampus	High intensity interval exercise	↑
	Muñoz et al., 2018	Elderly Sprague-Dawley rats	Substantia nigra	Treadmill exercise	↑
	Fiorenza et al., 2019	Subjects with essential hypertension	Skeletal muscle	High intensity interval training	↑
	Kujach et al., 2019	Young males	Serum	Sprint interval exercise	↑
	Boyne et al., 2020	Chronic stroke patients	Serum	High intensity interval training/medium intensity continuous treadmill	↑ (High intensity interval training > medium intensity continuous treadmill)
IGF-1	Hoier et al., 2020	Healthy young subjects	Skeletal muscle	Endurance training	↑
	Roh et al., 2020	Obese elderly women	Serum	Resistance exercise	↑
	Wu et al., 2020	Young males	Skeletal muscle	Aerobic exercise	↑
	Bayod et al., 2011	Sprague-Dawley rats	Cortex/hippocampus	Long-term treadmill exercise	↑
	Cassilhas et al., 2012a	Wistar rats	Hippocampus/serum	Resistance exercise	↑
	Cassilhas et al., 2012b	Wistar rats	Hippocampus	Aerobic training	↑
	Kohman et al., 2012	Aged BALB/c mice	Hippocampus	Voluntary running	↑ IGF-1 positive microglia
	Luo et al., 2013	Aged Sprague-Dawley rats	Gastrocnemius muscle	Resistance exercise training	↑
	Park and Höke, 2014	Mice with median nerve transection	Serum/nerve/muscle	Treadmill exercise	↑
	Annibalini et al., 2017	Patients with advanced type 2 diabetes mellitus	Serum/leukocyte	Aerobic and resistance training	↑
	Chen et al., 2017	Elder with sarcopenic obesity	Serum	Resistance training	↑
	de Almeida et al., 2017	Chronic epileptic model rats	Hippocampus	Resistance exercise	↑
	Vanzella et al., 2017	Aged Wistar rats	Hippocampus	Treadmill exercise	↑
	Martins et al., 2018	Sciatic nerve crush-subjected mice	Sciatic nerve	Regular eccentric training	↑
Fragoso et al., 2020	Pregnant rats	Cerebellum	Voluntary running	↑	
Niu et al., 2020	BALB/c mice	Hippocampus/serum	Voluntary running	↑	
Tai et al., 2020	Sleep-deprived mice	Hippocampus	Treadmill exercise	↑	

	Taş Dürmüş et al., 2020	Inpatients with opioid use disorder	Serum	High intensity interval training	↑
FNDC5/irisin	Huh et al., 2012	Young healthy adults	Serum	Acute exercise	↑
	Lecker et al., 2012	Patients with heart failure	Skeletal muscle	Cardiopulmonary exercise test	↑
	Wrann et al., 2013	C57BL/6 mice	Hippocampus	Endurance exercise	↑
	Brenmoehl et al., 2014	High treadmill performance mice	Skeletal muscle/serum	Acute exercise	↑
	Samy et al., 2015	Rats with thyroid dysfunction	Serum	Swimming	↑
	Tsuchiya et al., 2015	Healthy males	Plasma	Resistance/endurance exercise	↑ (Resistance > endurance)
	Rocha-Rodrigues et al., 2016	High fat diet rats	Skeletal muscle	Voluntary running	↑
	Zhang et al., 2017	C57BL/6J mice	Bone tissue/serum	Voluntary running	Bone ↑; Serum ↓
	Azimi et al., 2018	Aβ1-42-induced AD model mice	Hippocampus	Moderate treadmill exercise	↑
	Eaton et al., 2018	Healthy males	Skeletal muscle	High intensity interval exercise	↑
	Schaalan et al., 2018	High fat diet rats	Serum	Swimming	↑
	Lourenco et al., 2019	Aβ oligomers induced AD model mice	Hippocampus	Swimming	↑
VADN	Shirvani et al., 2019	Sprague-Dawley rats	Serum	Eccentric resistance training	↑
	He et al., 2020	Aged C57BL/6 mice	Skeletal muscle	Treadmill exercise	↑
	Lang et al., 2020	Type 2 diabetes mellitus mice	Hippocampus	Treadmill exercise	↑
	Siteneski et al., 2020	Swiss mice	Hippocampus	Treadmill exercise	↑ FNDC5 positive cells
	Fukao et al., 2010	High fat diet ApoE <sup>-/-</sup> mice	Serum	Voluntary running	↑
	Qi et al., 2011	Type 2 diabetes mellitus rats (Goto-Kakizaki)	Serum	Treadmill exercise	↑
	Teixeira de Lemos et al., 2011	Type 2 diabetes mellitus rats	Serum	Swimming/acute extenuating exercise	↑
	Oh et al., 2013	Obese adult men	Serum	Aerobic training	↑
	Markofski et al., 2014	Elderly health participant	Serum	Endurance and resistance training	↑
	Yau et al., 2014	C57BL/6J mice	Hippocampus	Voluntary running	↑
	Wasinski et al., 2015	Pregnant C57BL/6 mice	Skeletal muscle	Swimming training	↑ in offspring mice
	Chan et al., 2017	Women with chronic fatigue syndrome-like illness	Serum	Baduanjin Qigong exercise	↑
	Inoue et al., 2017	SAMP10 mice	Plasma	Treadmill exercise	↑
	Mazur-Bialy et al., 2017	Ulcerative colitis mice with high fat diet	Plasma	Voluntary running	↑
de Castro et al., 2018	Type 2 diabetes mellitus rats	Serum	Resistance/aerobic/combined training	↑	
Supriya et al., 2018	Patients with hypertension and	Serum	Yoga training	↑	

	metabolic syndrome			
Kim et al., 2020	ApoE <sup>-/-</sup> mice on a Western diet	Plasma	Treadmill exercise	↑
Li et al., 2019	Aged Sprague-Dawley rats	Gastrocnemius muscle	Long-term high intensity interval training/medium intensity continuous treadmill	↑
Zelikovich et al., 2019	Mdx mice	Serum	Treadmill exercise	↑
Wang et al., 2020	Corticosterone injection induces depression model mice	Hippocampus/serum	Voluntary running	↑

AD: Alzheimer's disease; ADN: adiponectin; ApoE: apolipoprotein E; A $\beta$ : beta-amyloid peptide; BDNF: brain-derived neurotrophic factor; FNDC5: fibronectin type III domain containing 5; IGF-1: insulin-like growth factor 1; NGF: nerve growth factor; SAMP10: senescence-accelerated mice prone 10; VEGF: vascular endothelial growth factor.

## References

- Aksu I, Baykara B, Ozbal S, Cetin F, Sisman AR, Dayi A, Gencoglu C, Tas A, Büyük E, Gonenc-Arda S, Uysal N (2012) Maternal treadmill exercise during pregnancy decreases anxiety and increases prefrontal cortex VEGF and BDNF levels of rat pups in early and late periods of life. *Neurosci Lett* 516:221-225.
- Ando I, Karasawa K, Matsuda H, Tanaka A (2016) Changes in serum NGF levels after the exercise load in dogs: a pilot study. *J Vet Med Sci* 78:1709-1712.
- Annibalini G, Lucertini F, Agostini D, Vallorani L, Gioacchini A, Barbieri E, Guescini M, Casadei L, Passalia A, Del Sal M, Piccoli G, Andreani M, Federici A, Stocchi V (2017) Concurrent aerobic and resistance training has anti-inflammatory effects and increases both plasma and leukocyte levels of IGF-1 in late middle-aged type 2 diabetic patients. *Oxid Med Cell Longev* 2017:3937842.
- Azimi M, Gharakhanlou R, Naghdi N, Khodadadi D, Heysieattalab S (2018) Moderate treadmill exercise ameliorates amyloid- $\beta$ -induced learning and memory impairment, possibly via increasing AMPK activity and up-regulation of the PGC-1 $\alpha$ /FNDC5/BDNF pathway. *Peptides* 102:78-88.
- Bayod S, Del Valle J, Canudas AM, Lalanza JF, Sanchez-Roige S, Camins A, Escorihuela RM, Pallàs M (2011) Long-term treadmill exercise induces neuroprotective molecular changes in rat brain. *J Appl Physiol* (1985) 111:1380-1390.
- Berchtold NC, Castello N, Cotman CW (2010) Exercise and time-dependent benefits to learning and memory. *Neuroscience* 167:588-597.
- Bonini M, Fioretti D, Sargentini V, Del Giacco S, Rinaldi M, Tranquilli C, Bonini S (2013) Increased nerve growth factor serum levels in top athletes. *Clin J Sport Med* 23:228-231.
- Boyne P, Meyrose C, Westover J, Whitesel D, Hatter K, Reisman DS, Carl D, Khoury JC, Gerson M, Kissela B, Dunning K (2020) Effects of exercise intensity on acute circulating molecular responses poststroke. *Neurorehabil Neural Repair* 34:222-234.
- Brenmoehl J, Albrecht E, Komolka K, Schering L, Langhammer M, Hoeflich A, Maak S (2014) Irisin is elevated in skeletal muscle and serum of mice immediately after acute exercise. *Int J Biol Sci* 10:338-349.
- Cassilhas RC, Lee KS, Venâncio DP, Oliveira MG, Tufik S, de Mello MT (2012a) Resistance exercise improves hippocampus-dependent memory. *Braz J Med Biol Res* 45:1215-1220.
- Cassilhas RC, Lee KS, Fernandes J, Oliveira MG, Tufik S, Meeusen R, de Mello MT (2012b) Spatial memory is improved by aerobic and resistance exercise through divergent molecular mechanisms. *Neuroscience* 202:309-317.

- Chae CH, Kim HT (2009) Forced, moderate-intensity treadmill exercise suppresses apoptosis by increasing the level of NGF and stimulating phosphatidylinositol 3-kinase signaling in the hippocampus of induced aging rats. *Neurochem Int* 55:208-213.
- Chan JS, Li A, Ng SM, Ho RT, Xu A, Yao TJ, Wang XM, So KF, Chan CL (2017) Adiponectin potentially contributes to the antidepressive effects of Baduanjin Qigong exercise in women with chronic fatigue syndrome-like illness. *Cell Transplant* 26:493-501.
- Chen HT, Chung YC, Chen YJ, Ho SY, Wu HJ (2017) Effects of different types of exercise on body composition, muscle strength, and IGF-1 in the elderly with sarcopenic obesity. *J Am Geriatr Soc* 65:827-832.
- de Almeida AA, Gomes da Silva S, Lopim GM, Vannucci Campos D, Fernandes J, Cabral FR, Arida RM (2017) Resistance exercise reduces seizure occurrence, attenuates memory deficits and restores BDNF signaling in rats with chronic epilepsy. *Neurochem Res* 42:1230-1239.
- de Castro CA, da Silva KA, Rocha MC, Sene-Fiorese M, Nonaka KO, Malavazi I, Anibal FF, Duarte A (2018) Exercise and omentin: their role in the crosstalk between muscle and adipose tissues in type 2 diabetes mellitus rat models. *Front Physiol* 9:1881.
- Eaton M, Granata C, Barry J, Safdar A, Bishop D, Little JP (2018) Impact of a single bout of high-intensity interval exercise and short-term interval training on interleukin-6, FNDC5, and METRN mRNA expression in human skeletal muscle. *J Sport Health Sci* 7:191-196.
- Eldomiaty MA, Almasry SM, Desouky MK, Algaidi SA (2017) Voluntary running improves depressive behaviours and the structure of the hippocampus in rats: A possible impact of myokines. *Brain Res* 1657:29-42.
- Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM, Wojcicki TR, Mailey E, Vieira VJ, Martin SA, Pence BD, Woods JA, McAuley E, Kramer AF (2011) Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A* 108:3017-3022.
- Fiorenza M, Gunnarsson TP, Ehlers TS, Bangsbo J (2019) High-intensity exercise training ameliorates aberrant expression of markers of mitochondrial turnover but not oxidative damage in skeletal muscle of men with essential hypertension. *Acta Physiol (Oxf)* 225:e13208.
- Fragoso J, Carvalho Jurema Santos G, Thomaz da Silva H, Oliveira Nogueira V, Loizon E, Vidal H, Costa-Silva JH, da Silva Aragão R, Pirola L, Leandro CG (2020) Maternal physical activity-induced adaptive transcriptional response in brain and placenta of mothers and rat offspring. *J Dev Orig Health Dis* 11:108-117.
- Franzoni F, Federighi G, Fusi J, Agosta V, Cerri E, Banducci R, Petrocchi A, Bernardi R, Innocenti A, Pruneti C, Daniele S, Pellegrini S, Martini C, Scuri R, Galetta F (2017) Physical exercise improves total antioxidant capacity and gene expression in rat hippocampal tissue. *Arch Ital Biol* 155:1-10.
- Fukao K, Shimada K, Naito H, Sumiyoshi K, Inoue N, Iesaki T, Kume A, Kiyonagi T, Hiki M, Hirose K, Matsumori R, Ohsaka H, Takahashi Y, Toyoda S, Itoh S, Miyazaki T, Tada N, Daida H (2010) Voluntary exercise ameliorates the progression of atherosclerotic lesion formation via anti-inflammatory effects in apolipoprotein E-deficient mice. *J Atheroscler Thromb* 17:1226-1236.
- Gómez-Pinilla F, Ying Z, Opazo P, Roy RR, Edgerton VR (2001) Differential regulation by exercise of BDNF and NT-3 in rat spinal cord and skeletal muscle. *Eur J Neurosci* 13:1078-1084.
- Hall JM, Gomez-Pinilla F, Savage LM (2018) Nerve growth factor is responsible for exercise-induced recovery of septohippocampal cholinergic structure and function. *Front Neurosci* 12:773.

- He W, Wang P, Chen Q, Li C (2020) Exercise enhances mitochondrial fission and mitophagy to improve myopathy following critical limb ischemia in elderly mice via the PGC1a/FNDC5/irisin pathway. *Skelet Muscle* 10:25.
- Hoffman JR, Ostfeld I, Kaplan Z, Zohar J, Cohen H (2015) Exercise enhances the behavioral responses to acute stress in an animal model of PTSD. *Med Sci Sports Exerc* 47:2043-2052.
- Hoier B, Olsen K, Hanskov DJA, Jorgensen M, Norup LR, Hellsten Y (2020) Early time course of change in angiogenic proteins in human skeletal muscle and vascular cells with endurance training. *Scand J Med Sci Sports* 30:1117-1131.
- Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, Mantzoros CS (2012) 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* 61:1725-1738.
- Inoue A, Cheng XW, Huang Z, Hu L, Kikuchi R, Jiang H, Piao L, Sasaki T, Itakura K, Wu H, Zhao G, Lei Y, Yang G, Zhu E, Li X, Sato K, Koike T, Kuzuya M (2017) Exercise restores muscle stem cell mobilization, regenerative capacity and muscle metabolic alterations via adiponectin/AdipoR1 activation in SAMP10 mice. *J Cachexia Sarcopenia Muscle* 8:370-385.
- Kim J, Jang HJ, Schellingerhout D, Kang JW, Choi S, Oh H, Kim EJ, Lee SK, Lee JS, Kwon IC, Kim K, Koh YJ, Ryu WS, Kim DE (2020) Effects of exercise training and detraining on atheromatous matrix metalloproteinase activity in mice. *Atherosclerosis* 299:15-23.
- Kohman RA, DeYoung EK, Bhattacharya TK, Peterson LN, Rhodes JS (2012) Wheel running attenuates microglia proliferation and increases expression of a proneurogenic phenotype in the hippocampus of aged mice. *Brain Behav Immun* 26:803-810.
- Kujach S, Olek RA, Byun K, Suwabe K, Sitek EJ, Ziemann E, Laskowski R, Soya H (2019) Acute sprint interval exercise increases both cognitive functions and peripheral neurotrophic factors in humans: the possible involvement of lactate. *Front Neurosci* 13:1455.
- Lang X, Zhao N, He Q, Li X, Li X, Sun C, Zhang X (2020) Treadmill exercise mitigates neuroinflammation and increases BDNF via activation of SIRT1 signaling in a mouse model of T2DM. *Brain Res Bull* 165:30-39.
- Lecker SH, Zavin A, Cao P, Arena R, Allsup K, Daniels KM, Joseph J, Schulze PC, Forman DE (2012) Expression of the irisin precursor FNDC5 in skeletal muscle correlates with aerobic exercise performance in patients with heart failure. *Circ Heart Fail* 5:812-818.
- Leick L, Hellsten Y, Fentz J, Lyngby SS, Wojtaszewski JF, Hidalgo J, Pilegaard H (2009) PGC-1alpha mediates exercise-induced skeletal muscle VEGF expression in mice. *Am J Physiol Endocrinol Metab* 297:E92-103.
- Li FH, Sun L, Wu DS, Gao HE, Min Z (2019) Proteomics-based identification of different training adaptations of aged skeletal muscle following long-term high-intensity interval and moderate-intensity continuous training in aged rats. *Aging (Albany NY)* 11:4159-4182.
- Lourenco MV, Frozza RL, de Freitas GB, Zhang H, Kincheski GC, Ribeiro FC, Gonçalves RA, Clarke JR, Beckman D, Staniszewski A, Berman H, Guerra LA, Fornhy-Germano L, Meier S, Wilcock DM, de Souza JM, Alves-Leon S, Prado VF, Prado MAM, Abisambra JF, et al. (2019) Exercise-linked FNDC5/irisin rescues synaptic plasticity and memory defects in Alzheimer's models. *Nat Med* 25:165-175.
- Luo L, Lu AM, Wang Y, Hong A, Chen Y, Hu J, Li X, Qin ZH (2013) Chronic resistance training activates autophagy and reduces apoptosis of muscle cells by modulating IGF-1 and

- its receptors, Akt/mTOR and Akt/FOXO3a signaling in aged rats. *Exp Gerontol* 48:427-436.
- Markofski MM, Carrillo AE, Timmerman KL, Jennings K, Coen PM, Pence BD, Flynn MG (2014) Exercise training modifies ghrelin and adiponectin concentrations and is related to inflammation in older adults. *J Gerontol A Biol Sci Med Sci* 69:675-681.
- Martins DF, Martins TC, Batisti AP, Dos Santos Leonel L, Bobinski F, Belmonte LAO, Mazzardo-Martins L, Cargnin-Ferreira E, Santos ARS (2018) Long-Term Regular Eccentric Exercise Decreases Neuropathic Pain-like Behavior and Improves Motor Functional Recovery in an Axonotmesis Mouse Model: the Role of Insulin-like Growth Factor-1. *Mol Neurobiol* 55:6155-6168.
- Mazur-Bialy AI, Bilski J, Wojcik D, Brzozowski B, Surmiak M, Hubalewska-Mazgaj M, Chmura A, Magierowski M, Magierowska K, Mach T, Brzozowski T (2017) Beneficial effect of voluntary exercise on experimental colitis in mice fed a high-fat diet: the role of irisin, adiponectin and proinflammatory biomarkers. *Nutrients* 9:410.
- Morland C, Andersson KA, Haugen Ø P, Hadzic A, Kleppa L, Gille A, Rinholm JE, Palibrk V, Diget EH, Kennedy LH, Stølen T, Hennestad E, Moldestad O, Cai Y, Puchades M, Offermanns S, Vervaeke K, Bjørås M, Wisløff U, Storm-Mathisen J, et al. (2017) Exercise induces cerebral VEGF and angiogenesis via the lactate receptor HCAR1. *Nat Commun* 8:15557.
- Müller P, Rehfeld K, Schmicker M, Hökelmann A, Dordevic M, Lessmann V, Brigadski T, Kaufmann J, Müller NG (2017) Evolution of neuroplasticity in response to physical activity in old age: the case for dancing. *Front Aging Neurosci* 9:56.
- Muñoz A, Corrêa CL, Lopez-Lopez A, Costa-Besada MA, Diaz-Ruiz C, Labandeira-Garcia JL (2018) Physical exercise improves aging-related changes in angiotensin, IGF-1, SIRT1, SIRT3, and VEGF in the substantia nigra. *J Gerontol A Biol Sci Med Sci* 73:1594-1601.
- Niu X, Zhao Y, Yang N, Zhao X, Zhang W, Bai X, Li A, Yang W, Lu L (2020) Proteasome activation by insulin-like growth factor-1/nuclear factor erythroid 2-related factor 2 signaling promotes exercise-induced neurogenesis. *Stem Cells* 38:246-260.
- O'Callaghan RM, Griffin EW, Kelly AM (2009) Long-term treadmill exposure protects against age-related neurodegenerative change in the rat hippocampus. *Hippocampus* 19:1019-1029.
- Oh S, Tanaka K, Warabi E, Shoda J (2013) Exercise reduces inflammation and oxidative stress in obesity-related liver diseases. *Med Sci Sports Exerc* 45:2214-2222.
- Okudan N, Belviranlı M (2017) Long-term voluntary exercise prevents post-weaning social isolation-induced cognitive impairment in rats. *Neuroscience* 360:1-8.
- Paddock N, Sheppard P, Gardiner P (2018) Chronic increases in daily neuromuscular activity promote changes in gene expression in small and large dorsal root ganglion neurons in rat. *Neuroscience* 388:171-180.
- Park JS, Höke A (2014) Treadmill exercise induced functional recovery after peripheral nerve repair is associated with increased levels of neurotrophic factors. *PLoS One* 9:e90245.
- Patel DI, White LJ, Lira VA, Criswell DS (2016) Forced exercise increases muscle mass in EAE despite early onset of disability. *Physiol Res* 65:1013-1017.
- Peake JM, Roberts LA, Figueiredo VC, Egner I, Krog S, Aas SN, Suzuki K, Markworth JF, Coombes JS, Cameron-Smith D, Raastad T (2017) The effects of cold water immersion and active recovery on inflammation and cell stress responses in human skeletal muscle after resistance exercise. *J Physiol* 595:695-711.
- Qi Z, He J, Zhang Y, Shao Y, Ding S (2011) Exercise training attenuates oxidative stress and decreases p53 protein content in skeletal muscle of type 2 diabetic Goto-Kakizaki rats. *Free Radic Biol Med* 50:794-800.



- Rocha-Rodrigues S, Rodríguez A, Gouveia AM, Gonçalves IO, Becerril S, Ramírez B, Beleza J, Frühbeck G, Ascensão A, Magalhães J (2016) Effects of physical exercise on myokines expression and brown adipose-like phenotype modulation in rats fed a high-fat diet. *Life Sci* 165:100-108.
- Roh HT, Cho SY, So WY (2020) A cross-sectional study evaluating the effects of resistance exercise on inflammation and neurotrophic factors in elderly women with obesity. *J Clin Med* 9:842.
- Roh HT, Cho SY, Yoon HG, So WY (2017) Effect of exercise intensity on neurotrophic factors and blood-brain barrier permeability induced by oxidative-nitrosative stress in male college students. *Int J Sport Nutr Exerc Metab* 27:239-246.
- Rosa JM, Pazini FL, Olescowicz G, Camargo A, Moretti M, Gil-Mohapel J, Rodrigues ALS (2019) Prophylactic effect of physical exercise on A $\beta$ (1-40)-induced depressive-like behavior: Role of BDNF, mTOR signaling, cell proliferation and survival in the hippocampus. *Prog Neuropsychopharmacol Biol Psychiatry* 94:109646.
- Ross MD, Wekesa AL, Phelan JP, Harrison M (2014) Resistance exercise increases endothelial progenitor cells and angiogenic factors. *Med Sci Sports Exerc* 46:16-23.
- Samy DM, Ismail CA, Nassra RA (2015) Circulating irisin concentrations in rat models of thyroid dysfunction -- effect of exercise. *Metabolism* 64:804-813.
- Saucedo Marquez CM, Vanaudenaerde B, Troosters T, Wenderoth N (2015) High-intensity interval training evokes larger serum BDNF levels compared with intense continuous exercise. *J Appl Physiol* (1985) 119:1363-1373.
- Schaalan MF, Ramadan BK, Abd Elwahab AH (2018) Synergistic effect of carnosine on browning of adipose tissue in exercised obese rats; a focus on circulating irisin levels. *J Cell Physiol* 233:5044-5057.
- Shirvani H, Rahmati-Ahmadabad S, Broom DR, Mirnejad R (2019) Eccentric resistance training and  $\beta$ -hydroxy- $\beta$ -methylbutyrate free acid affects muscle PGC-1 $\alpha$  expression and serum irisin, nesfatin-1 and resistin in rats. *J Exp Biol* 222:jeb198424.
- Siteneski A, Olescowicz G, Pazini FL, Camargo A, Fraga DB, Brocardo PS, Gil-Mohapel J, Cunha MP, Rodrigues ALS (2020) Antidepressant-like and pro-neurogenic effects of physical exercise: the putative role of FNDC5/irisin pathway. *J Neural Transm (Vienna)* 127:355-370.
- Supriya R, Yu AP, Lee PH, Lai CW, Cheng KK, Yau SY, Chan LW, Yung BY, Siu PM (2018) Yoga training modulates adipokines in adults with high-normal blood pressure and metabolic syndrome. *Scand J Med Sci Sports* 28:1130-1138.
- Tai F, Wang C, Deng X, Li R, Guo Z, Quan H, Li S (2020) Treadmill exercise ameliorates chronic REM sleep deprivation-induced anxiety-like behavior and cognitive impairment in C57BL/6J mice. *Brain Res Bull* 164:198-207.
- Tang K, Xia FC, Wagner PD, Breen EC (2010) Exercise-induced VEGF transcriptional activation in brain, lung and skeletal muscle. *Respir Physiol Neurobiol* 170:16-22.
- Taş Dürmüş P, Vardar ME, Kaya O, Tayfur P, Süt N, Vardar SA (2020) Evaluation of the effects of high intensity interval training on cytokine levels and clinical course in treatment of opioid use disorder. *Turk Psikiyatri Dergisi* 31:151-158.
- Teixeira de Lemos E, Pinto R, Oliveira J, Garrido P, Sereno J, Mascarenhas-Melo F, Páscoa-Pinheiro J, Teixeira F, Reis F (2011) Differential effects of acute (extenuating) and chronic (training) exercise on inflammation and oxidative stress status in an animal model of type 2 diabetes mellitus. *Mediators Inflamm* 2011:253061.
- Tsai MS, Kuo ML, Chang CC, Wu YT (2013) The effects of exercise training on levels of vascular endothelial growth factor in tumor-bearing mice. *Cancer Biomark* 13:307-313.
- Tsuchiya Y, Ando D, Takamatsu K, Goto K (2015) Resistance exercise induces a greater irisin response than endurance exercise. *Metabolism* 64:1042-1050.



- Um HS, Kang EB, Koo JH, Kim HT, Jin L, Kim EJ, Yang CH, An GY, Cho IH, Cho JY (2011) Treadmill exercise represses neuronal cell death in an aged transgenic mouse model of Alzheimer's disease. *Neurosci Res* 69:161-173.
- Uysal N, Kiray M, Sisman AR, Camsari UM, Gencoglu C, Baykara B, Cetinkaya C, Aksu I (2015) Effects of voluntary and involuntary exercise on cognitive functions, and VEGF and BDNF levels in adolescent rats. *Biotech Histochem* 90:55-68.
- Vanzella C, Neves JD, Vizuete AF, Aristimunha D, Kolling J, Longoni A, Gonçalves CAS, Wyse ATS, Netto CA (2017) Treadmill running prevents age-related memory deficit and alters neurotrophic factors and oxidative damage in the hippocampus of Wistar rats. *Behav Brain Res* 334:78-85.
- Voss MW, Erickson KI, Prakash RS, Chaddock L, Kim JS, Alves H, Szabo A, Phillips SM, Wójcicki TR, Mailey EL, Olson EA, Gothe N, Vieira-Potter VJ, Martin SA, Pence BD, Cook MD, Woods JA, McAuley E, Kramer AF (2013) Neurobiological markers of exercise-related brain plasticity in older adults. *Brain Behav Immun* 28:90-99.
- Wang BL, Jin H, Han XQ, Xia Y, Liu NF (2018) Involvement of brain-derived neurotrophic factor in exercise-induced cardioprotection of post-myocardial infarction rats. *Int J Mol Med* 42:2867-2880.
- Wang P, Liang Y, Chen K, Yau SY, Sun X, Cheng KK, Xu A, So KF, Li A (2020) Potential involvement of adiponectin signaling in regulating physical exercise-elicited hippocampal neurogenesis and dendritic morphology in stressed mice. *Front Cell Neurosci* 14:189.
- Wasinski F, Bacurau RF, Estrela GR, Klempin F, Arakaki AM, Batista RO, Mafra FF, do Nascimento LF, Hiyane MI, Velloso LA, Câmara NO, Araujo RC (2015) Exercise during pregnancy protects adult mouse offspring from diet-induced obesity. *Nutr Metab (Lond)* 12:56.
- Woo J, Shin KO, Park SY, Jang KS, Kang S (2013) Effects of exercise and diet change on cognition function and synaptic plasticity in high fat diet induced obese rats. *Lipids Health Dis* 12:144.
- Wrann CD, White JP, Salogiannis J, Laznik-Bogoslavski D, Wu J, Ma D, Lin JD, Greenberg ME, Spiegelman BM (2013) Exercise induces hippocampal BDNF through a PGC-1 $\alpha$ /FNDC5 pathway. *Cell Metab* 18:649-659.
- Wu J, Cheng IS, Saovieng S, Jean WH, Kao CL, Liu YY, Huang CY, Lee TXY, Ivy JL, Kuo CH (2020) Aerobic exercise induces tumor suppressor p16(INK4a) expression of endothelial progenitor cells in human skeletal muscle. *Aging (Albany NY)* 12:20226-20234.
- Yau SY, Li A, Hoo RL, Ching YP, Christie BR, Lee TM, Xu A, So KF (2014) Physical exercise-induced hippocampal neurogenesis and antidepressant effects are mediated by the adipocyte hormone adiponectin. *Proc Natl Acad Sci U S A* 111:15810-15815.
- Yu T, Chang Y, Gao XL, Li H, Zhao P (2017) Dynamic expression and the role of BDNF in exercise-induced skeletal muscle regeneration. *Int J Sports Med* 38:959-966.
- Zelikovich AS, Quattrocchi M, Salamone IM, Kuntz NL, McNally EM (2019) Moderate exercise improves function and increases adiponectin in the mdx mouse model of muscular dystrophy. *Sci Rep* 9:5770.
- Zhang J, Valverde P, Zhu X, Murray D, Wu Y, Yu L, Jiang H, Dard MM, Huang J, Xu Z, Tu Q, Chen J (2017) Exercise-induced irisin in bone and systemic irisin administration reveal new regulatory mechanisms of bone metabolism. *Bone Res* 5:16056.