Additional Table 5 Potential molecular mechanisms underlying the exercise-induced upregulation of exerkines

Exerkine	Study	Reported molecular mechanism
BDNF	Chen et al., 2006	Nitric oxide synthase pathway
	Chen and Russo-Neustadt, 2007	IGF-1 pathway
	Chen and Russo-Neustadt, 2009; Aguiar et al., 2011; Taheri et al., 2018; Wu et al., 2020)	p-CREB pathway
	Aguiar et al., 2011	AKT/p-CREB pathway
	Wrann et al., 2013; Azimi et al., 2018; Belviranlı and Okudan, 2018; Babaei et al., 2021)	PGC1-α/FNDC5 pathway
	Ferreira-Vieira et al., 2014	Endocannabinoid pathway
	Marosi et al., 2016	3-Hydroxybutyrate pathway
	Moon et al., 2016	Cathepsin B pathway
	Sleiman et al., 2016	β-Hydroxybutyrate/class I histone deacetylases (HDAC2/HDAC3) pathway
	Chou et al., 2018	Heat shock protein 20 pathway
	Niu et al., 2018	NF-κB/miR-503 pathway
	Chen et al., 2019	Caveolin-1/VEGF pathway
	El Hayek et al., 2019	Lactate/SIRT1/PGC1-α/FNDC5 pathway
	Lang et al., 2020	SIRT1/PGC1-α/FNDC5 pathway
	Lee et al., 2020	ERK/Akt/p-CREB pathway
	Niu et al., 2021	CircRIMS2/miR-186 pathway
NGF	Murase et al., 2010	B2 bradykinin pathway
IGF-1	Gomes et al., 2006	Growth hormone pathway
	Salgueiro et al., 2014	Lactate/growth hormone pathway
	Delfan et al., 2020	miR-1 pathway
ADN	Tang et al., 2013	IL-6 pathway
	Meziat et al., 2019	NO/PKG pathway
	Yang et al., 2019	FGF21 pathway
VEGF\	Arany et al., 2008; Chinsomboon et al., 2009; Leick et al., 2009	PGC1-α pathway
	Gao et al., 2014; Zhao et al., 2017; Chen et al., 2019; Xie et al., 2019	Caveolin-1 pathway
	Fentz et al., 2015	AMPK-dependent pathway
	Rodriguez-Miguelez et al., 2015; Halliday et al., 2019; Tian et al., 2020	Hypoxia-inducible factor 1α pathway
	Morland et al., 2017	Lactate pathway
	Bao et al., 2020	PI3K/AKT/mTOR pathway
	Saboory et al., 2020	IGF-1 pathway
	Sabzevari Rad et al., 2020	miR-126 pathway
FNDC5/irisin	Boström et al., 2012; Yang et al., 2016; Azimi et al., 2018; Belviranlı and Okudan, 2018; Kazeminasab et al., 2018; Pang et al., 2018; He et al., 2020; Babaei et al., 2021; Cho et al., 2021	PGC1-α pathway
	Pekkala et al., 2013; Lang et al., 2020	SIRT1/PGC1-α pathway
	El Hayek et al., 2019	Lactate/SIRT1/PGC1-α pathway
IDE	Kurauti et al., 2016	AMPK-acetyl CoA carboxylase pathway

	Kurauti et al., 2017	IL-6 pathway
GSH and SOD	Merry and Ristow, 2016; Liu et al., 2020	Nrf2/SOD pathway
	Wang et al., 2016	Redox effector factor-1/Nrf2/GSH pathway
	Wen et al., 2019	Silent information regulator 2/FoxO/SOD pathway
	Yamada et al., 2019	p62 and Nrf2/SOD pathway
Metabolites of the kynurenine pathway	Agudelo et al., 2014; Mudry et al., 2016; Schlittler et al., 2016	PGC1-α/KAT pathway
Lactate	Wasserman et al., 1973; Kinni et al., 2011; Wang et al., 2015; Peek et al., 2017	Hypoxic induced anaerobic glycolysis
	Parolin et al., 1999	Imbalance between glycogen phosphorylase and pyruvate dehydrogenase
	Bishop et al., 2007; Takimoto and Hamada, 2014; Opitz et al., 2015	Alteration of MCT

ADN: Adiponectin; AKT: protein kinase B; AMPK: adenosine monophosphate-activated protein kinase; BDNF: brain-derived neurotrophic factor; CircRIMS2: Regulating synaptic membrane exocytosis 2 circRNA; CoA: coenzyme A; ERK: extracellular regulated protein kinase; FGF21: fibroblast growth factor 21; FNDC5: fibronectin type III domain containing 5; FoxO: forkhead box O; GSH: nerve growth factor; HDAC: histone deacetylase; IDE: insulin-degrading enzyme; IGF-1: insulin-like growth factor 1; IL-6: interleukin-6; KAT: kynurenine aminotransferase; MCT: monocarboxylate transporter; miR: microRNA; mTOR: mammalian target of rapamycin; NF-κB: nuclear factor kappa β; NGF: nerve growth factor; NO: nitric oxide; Nrf2: nuclear factor erythroid 2-related factor 2; p-CREB: phosphorylated cyclic adenosine monophosphate response element-binding protein; PGC1-α: proliferator-activated receptor - co-activator 1 α; PI3K: phosphatidylinositol 3-kinase; PKG: protein kinase G; SIRT1: silent information regulator 1; SOD: superoxide dismutase; VEGF: vascular endothelial growth factor.

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