

Barker K (2005). *At the bench: a laboratory navigator*, 2nd edn. Cold Spring Harbor Laboratory Press.

- Baar K and Esser K (1999). Phosphorylation of p70(S6k) correlates with increased skeletal muscle mass following resistance exercise. *Am J Physiol* 276, C120–C127.
- Baldwin KM (2000). Research in the exercise sciences: where do we go from here? *J Appl Physiol* 88, 332–336.
- Barker K (2005). *At the bench: a laboratory navigator*, 2nd edn. Cold Spring Harbor Laboratory Press.
- Booth FW (1988). Perspectives on molecular and cellular exercise physiology. *J Appl Physiol* 65, 1461–1471.
- Bouchard C, Chagnon M, ibault MC, Boulay MR, Marcotte M, Cote C and Simoneau JA (1989). Muscle genetic variants and relationship with performance and trainability. *Med Sci Sports Exerc* 21, 71–77.
- Bouchard C, Malina RM and Perusse L (1997). Genetics of fitness and physical performance. *Human Kinetics*, Champaign, IL.
- Bouchard C, Sarzynski MA, Rice TK, Kraus WE, Church TS, Sung YJ, et al. (2011). Genomic predictors of the maximal O uptake response to standardized exercise training programs. *J Appl Physiol* 110, 1160–1170.
- Campbell WG, Gordon SE, Carlson CJ, Pattison JS, Hamilton MT and Booth FW (2001). Differential global gene expression in red and white skeletal muscle. *Am J Physiol Cell Physiol* 280, C763–C768.
- Chin ER, Olson EN, Richardson JA, Yang Q, Humphries C, Shelton JM, et al. (1998). A calcineurin-dependent transcriptional pathway controls skeletal muscle fiber type. *Genes Dev* 12, 2499–2509.
- Collins CA and Zammit PS (2009). Isolation and grafting of single muscle fibres. *Methods Mol Biol* 482, 319–330.
- de la Chapelle A, Traskelin AL and Juvonen E (1993). Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis. *Proc Natl Acad Sci U S A* 90, 4495–4499.
- Deriaz O, Dionne F, Perusse L, Tremblay A, Vohl MC, Cote G and Bouchard C (1994). DNA variation in the genes of the Na,K-adenosine triphosphatase and its relation with resting metabolic rate, respiratory quotient, and body fat. *J Clin Invest* 93, 838–843.
- Dionne FT, Turcotte L, ibault MC, Boulay MR, Skinner JS and Bouchard C (1991). Mitochondrial DNA sequence polymorphism, V.O₂max, and response to endurance training. *Med Sci Sports Exerc* 23, 177–185.
- Garry DJ, Ordway GA, Lorenz JN, Radford NB, Chin ER, Grange RW, et al. (1998). Mice without myoglobin. *Nature* 395, 905–908.
- Gibson DG, Benders GA, Andrews-Pfannkoch C, Denisova EA, Baden-Tillson H, Zaveri J, et al. (2008). Complete chemical synthesis, assembly, and cloning of a *Mycoplasma genitalium* genome. *Science* 319, 1215–1220.
- Hamilton MT and Booth FW (2000). Skeletal muscle adaptation to exercise: a century of progress. *J Appl Physiol* 88, 327–331.
- Hayot M, Michaud A, Koechlin C, Caron MA, Leblanc P, Prefaut C, and Maltais F (2005). Skeletal muscle microbiopsy: a validation study of a minimally invasive technique. *Eur Respir J* 25, 431–440.
- Hood DA, Balaban A, Connor MK, Craig EE, Nishio ML, Rezvani M and Takahashi M (1994). Mitochondrial biogenesis in striated muscle. *Can J Appl Physiol* 19, 12–48.
- Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, et al. (2002). Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres. *Nature* 418, 797–801.
- Mauro A (1961). Satellite cell of skeletal muscle fibers. *J Biophys Biochem Cytol* 9, 493–495.
- McPherron AC, Lawler AM and Lee SJ (1997). Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. *Nature* 387, 83–90.
- Morange M (2009). History of molecular biology. In *Encyclopedia of life sciences*. John Wiley & Sons, Chichester.
- Murgia M, Serrano AL, Calabria E, Pallafacchina G, Lomo T and Schiaffino S (2000). Ras is involved in nerve-activity-dependent regulation of muscle genes. *Nat Cell Biol* 2, 142–147.
- Pallafacchina G, Calabria E, Serrano AL, Kalhovde JM and Schiaffino S (2002). A protein kinase B-dependent and rapamycin-sensitive pathway controls skeletal muscle growth but not fiber type specification. *Proc Natl Acad Sci U S A* 99, 9213–9218.
- Puigserver P, Wu Z, Park CW, Graves R, Wright M and Spiegelman BM (1998). A cold-inducible coactivator of nuclear receptors linked to adaptive thermogenesis. *Cell* 92, 829–839.

- Scarpulla RC (1997). Nuclear control of respiratory chain expression in mammalian cells. *J Bioenerg Biomembr* 29, 109–119.
- Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, et al. (2004). Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 350, 2682–2688.
- Spurway NC and Wackerhage H (2006). *Genetics and molecular biology of muscle adaptation*. Elsevier/Churchill Livingstone, Edinburgh.
- omason DB and Booth FW (1990). Stable incorporation of a bacterial gene into adult rat skeletal muscle in vivo. *Am J Physiol* 258, C578–C581.
- Timmons JA, Knudsen S, Rankinen T, Koch LG, Sarzynski M, Jensen T, et al. (2010). Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* 108, 1487–1496.
- Wackerhage H, Miah A, Harris RC, Montgomery HE and Williams AG (2009). Genetic research and testing in sport and exercise science: A review of the issues. *J Sports Sci* 1–8.
- Watson PA, Stein JP and Booth FW (1984). Changes in actin synthesis and alpha-actin-mRNA content in rat muscle during immobilization. *Am J Physiol* 247, C39–C44.
- Wheeler DA, Srinivasan M, Egholm M, Shen Y, Chen L, McGuires A, et al. (2008). e complete genome of an individual by massively parallel DNA sequencing. *Nature* 452, 872–876.
- Williams AG, Rayson MP, Jubbs M, World M, Woods DR, Hayward M, et al. (2000). e ACE gene and muscle performance. *Nature* 403, 614.
- Winder WW and Hardie DG (1996). Inactivation of acetyl-CoA carboxylase and activation of AMP-activated protein kinase in muscle during exercise. *Am J Physiol* 270, E299–E304.
- Wolff JA, Malone RW, Williams P, Chong W, Acsadi G, Jani A and Felgner PL (1990). Direct gene transfer into mouse muscle in vivo. *Science* 247, 1465–1468.
- Yamaguchi M, Nakayama Y and Nishikawa J (1985). Studies on exercise and an elastic protein “connectin” in hindlimb muscle of growing rat. *Jpn J Physiol* 35, 21–32.
- Zammit PS, Golding JP, Nagata Y, Hudon V, Partridge TA and Beauchamp JR (2004). Muscle satellite cells adopt divergent fates: a mechanism for self-renewal? *J Cell Biol* 166, 347–357.

■ جهت مطالعه بیشتر

- Bouchard C, Malina RM, and Perusse L (1997). *Genetics of fitness and physical performance*. Human Kinetics, Champaign, IL.
- Bouchard C and Hoffman EP (2011). Genetic and molecular aspects of sports performance, Vol. 18 of *Encyclopedia of sports medicine*. John Wiley & Sons, Chichester.
- Pescatello LS and Roth SM (2011). *Exercise genomics*. Springer, New York.
- Roth SM (2007). *Genetics primer for exercise science and health*. Human Kinetics, Champaign, IL.
- Roth SM (2008). Perspective on the future use of genomics in exercise prescription. *J Appl Physiol* 104, 1243–1245.
- Wackerhage H, Miah A, Harris RC, Montgomery HE and Williams AG (2009). Genetic research and testing in sport and exercise science: A review of the issues. *J Sports Sci* 1–8.

■ منابع

- Ahmetov II, Williams AG, Popov DV, Lyubaeva EV, Hakimullina AM, Fedotovskaya ON, et al. (2009). The combined impact of metabolic gene polymorphisms on elite endurance athlete status and related phenotypes. *Hum Genet* 126, 751–761.
- Altmuller J, Palmer LJ, Fischer G, Scherb H and Wjst M (2001). Genomewide scans of complex human diseases: true linkage is hard to find. *Am J Hum Genet* 69, 936–950.
- Bernstein BE, Birney E, Dunham I, Green ED, Gunter C and Snyder M (2012). An integrated encyclopedia of DNA elements in the human genome. *Nature* 489, 57–74.
- Bouchard C (2011). Overcoming barriers to progress in exercise genomics. *Exerc Sport Sci Rev* 39, 212–217.

- Bouchard C, Leon AS, Rao DC, Skinner JS, Wilmore JH and Gagnon J (1995). the HERITAGE family study. Aims, design, and measurement protocol. *Med Sci Sports Exerc* 27, 721–729.
- Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, et al. (1999). Familial aggregation of V.O₂(max) response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 87, 1003–1008.
- Bouchard C, Sarzynski MA, Rice TK, Kraus WE, Church TS, Sung YJ, et al. (2011). Genomic predictors of the maximal O uptake response to standardized exercise training programs. *J Appl Physiol* 110, 1160–1170.
- Bouchard C, Blair SN, Church TS, Earnest CP, Hagberg JM, Hakkinen K, et al. (2012). Adverse metabolic response to regular exercise: is it a rare or common occurrence? *PLoS ONE* 7, e37887.
- Bray MS, Hagberg JM, Perusse L, Rankinen T, Roth SM, Wolfarth B, et al. (2009). the human gene map for performance and health-related fitness phenotypes: the 2006–2007 update. *Med Sci Sports Exerc* 41, 35–73.
- Bruder CE, Piotrowski A, Gijsbers AA, Andersson R, Erickson S, Diaz de Ståhl T, et al. (2008). Phenotypically concordant and discordant monozygotic twins display different DNA copy-number-variation profiles. *Am J Hum Genet* 82, 763–771.
- Chanock SJ, Manolio T, Boehnke M, Boerwinkle E, Hunter DJ, omas G, et al. (2007). Replicating genotype-phenotype associations. *Nature* 447, 655–660.
- de la Chapelle A, Traskelin AL and Juvonen E (1993). Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis. *Proc Natl Acad Sci U S A* 90, 4495–4499.
- Falconer DS and MacKay TFS (2011). Introduction to quantitative genetics, 4 ed. Longmans Green, Harlow, Essex.
- Friedmann T (2010). How close are we to gene doping? *Hastings Cent Rep* 40, 20–22.
- Genetic Technologies Ltd (2007). ACTN3 sport performance test TM . <http://www.gtg.com.au/archives/migration/2/010/5/ACTN3%20web%20brochure.pdf>.
- Hakimi P, Yang J, Casadesus G, Massillon D, Tolentino-Silva F, Nye CK, et al. (2007). Overexpression of the cytosolic form of phosphoenolpyruvate carboxykinase (GTP) in skeletal muscle repatterns energy metabolism in the mouse. *J Biol Chem* 282, 32844–32855.
- Kidd JM, Cooper GM, Donahue WF, Hayden HS, Sampas N, Graves T, et al. (2008). Mapping and sequencing of structural variation from eight human genomes. *Nature* 453, 56–64.
- Lette G, Jackson AU, Gieger C, Schumacher FR, Berndt SI, Sanna S, et al. (2008). Identification of ten loci associated with height highlights new biological pathways in human growth. *Nat Genet* 40, 584–591.
- Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, et al. (2002). Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres. *Nature* 418, 797–801.
- Lionikas A, Cheng R, Lim JE, Palmer AA and Blizard DA (2010). Fine-mapping of muscle weight QTL in LG/J and SM/J intercrosses. *Physiol Genomics* 42A, 33–38.
- McPherron AC, Lawler AM and Lee SJ (1997). Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. *Nature* 387, 83–90.
- Mullis KB (1990). the unusual origin of the polymerase chain reaction. *Sci Am* 262, 64–65.
- North KN, Yang N, Wattanasirichaigoon D, Mills M, Eastal S and Beggs AH (1999). A common nonsense mutation results in alpha-actinin-3 deficiency in the general population. *Nat Genet* 21, 353–354.
- Pray LA (2008). DNA replication and causes of mutation. *Nature Education* 1.
- Rigat B, Hubert C, Alhenc-Gelas F, Cambien F, Corvol P and Soubrier F (1990). An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. *J Clin Invest* 86, 1343–1346.
- Roth SM (2008). Perspective on the future use of genomics in exercise prescription. *J Appl Physiol* 104, 1243–1245.
- Saiki RK, Gelfand DH, Stoffel S, Scharf SJ, Higuchi R, Horn GT, et al. (1988). Primer-directed enzymatic amplification of DNA with a thermostable DNA polymerase. *Science* 239, 487–491.
- Schork NJ, Murray SS, Frazer KA and Topol EJ (2009). Common vs. rare allele hypotheses for complex diseases. *Curr Opin Genet Dev* 19, 212–219.
- Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, et al. (2004). Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 350, 2682–2688.
- Smits J and Monden C (2011). Twinning across the developing world. *PLoS ONE* 6, e25239.
- Strachan T and Read AP (2004). Human molecular genetics, 3rd edn. Garland Science, New York, Oxford.
- Strittmatter WJ, Saunders AM, Schmechel D, Pericak-Vance M, Enghild J, Salvesen GS, et al. (1993). Apolipoprotein E: high-avidity binding to beta-amyloid and increased frequen-

- cy of type 4 allele in late-onset familial Alzheimer disease. *Proc Natl Acad Sci U S A* 90, 1977–1981.
- Tamaki K and Jeffreys AJ (2005). Human tandem repeat sequences in forensic DNA typing. *Leg Med (Tokyo)* 7, 244–250.
- Thomas S, Reading J and Shephard RJ (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Can J Sport Sci* 17, 338–345.
- Thomis MA, Beunen GP, Maes HH, Blimkie CJ, Van LM, Claessens AL, et al. (1998). Strength training: importance of genetic factors. *Med Sci Sports Exerc* 30, 724–731.
- Timmons JA, Knudsen S, Rankinen T, Koch LG, Sarzynski M, Jensen T, et al. (2010). Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* 108, 1487–1496.
- Wackerhage H, Miah A, Harris RC, Montgomery HE and Williams AG (2009). Genetic research and testing in sport and exercise science: A review of the issues. *J Sports Sci* 1–8.
- Consortium (2007). Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 447, 661–678.
- Wheeler DA, Srinivasan M, Egholm M, Shen Y, Chen L, McGuire A, et al. (2008). The complete genome of an individual by massively parallel DNA sequencing. *Nature* 452, 872–876.
- World Anti-Doping Code (2009). <http://www.wada-ama.org/en/world-anti-doping-program/sports-and-anti-doping-organizations/the-code/>.
- Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Eastal S, et al. (2003). ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet* 73, 627–631.

■ جهت مطالعه بیشتر

- Burniston JG and Hoffman EP (2011). Proteomic responses of skeletal and cardiac muscle to exercise. *Exp Rev Proteomics* 8, 361–77.

■ منابع

- Aldridge GM, Podrebarac DM, Greenough WT and Weiler IJ (2008). The use of total protein stains as loading controls: an alternative to high-abundance single-protein controls in semi-quantitative immunoblotting. *J Neurosci Methods* 172, 250–254.
- Alonso A, Sasin J, Bottini N, Friedberg I, Friedberg I, Osterman A, et al. (2004). Protein tyrosine phosphatases in the human genome. *Cell* 117, 699–711.
- Baar K and Esser K (1999). Phosphorylation of p70(S6k) correlates with increased skeletal muscle mass following resistance exercise. *Am J Physiol* 276, C120–C127.
- Bergstrom J and Hultman E (1966). Muscle glycogen synthesis after exercise: an enhancing factor localized to the muscle cells in man. *Nature* 210, 309–310.
- Bodine SC, Latres E, Baumhueter S, Lai VK, Nunez L, Clarke BA, et al. (2001). Identification of ubiquitin ligases required for skeletal muscle atrophy. *Science* 294, 1704–1708.
- Burnette WN (1981). “Western blotting”: electrophoretic transfer of proteins from sodium dodecyl sulfate—polyacrylamide gels to unmodified nitrocellulose and radiographic detection with antibody and radioiodinated protein A. *Anal Biochem* 112, 195–203.
- Burniston JG (2008). Changes in the rat skeletal muscle proteome induced by moderate-intensity endurance exercise. *Biochim Biophys Acta* 1784, 1077–1086.
- Burniston JG, Meek TH, Pandey SN, Broitman-Maduro G, Maduro MF, Bronikowski AM, et al. (2013). Gene expression profiling of gastrocnemius of “minimuscle” mice. *Physiol Genomics* 45, 228–236.

- Campbell WG, Gordon SE, Carlson CJ, Pattison JS, Hamilton MT and Booth FW (2001). Differential global gene expression in red and white skeletal muscle. *Am J Physiol Cell Physiol* 280, C763–C768.
- Cao Y, Yao Z, Sarkar D, Lawrence M, Sanchez GJ, Parker MH, et al. (2010). Genome-wide MyoD binding in skeletal muscle cells: a potential for broad cellular reprogramming. *Dev Cell* 18, 662–674.
- Chin ER, Olson EN, Richardson JA, Yang Q, Humphries C, Shelton JM, et al. (1998). A calcineurin-dependent transcriptional pathway controls skeletal muscle fiber type. *Genes Dev* 12, 2499–2509.
- Chomczynski P and Sacchi N (1987). Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal Biochem* 162, 156–159.
- Cohen P (2002). The origins of protein phosphorylation. *Nat Cell Biol* 4, E127–E130.
- Davidson PK, Gallagher IJ, Hartman JW, Tarnopolsky MA, Dela F, Helge JW, et al. (2011). High responders to resistance exercise training demonstrate differential regulation of skeletal muscle microRNA expression. *J Appl Physiol* 110, 309–317.
- Dunham I, Kundaje A, Aldred SF, Collins PJ, Davis CA, Doyle F, et al. (2012). An integrated encyclopedia of DNA elements in the human genome. *Nature* 489, 57–74.
- Erce MA, Pang CN, Hart-Smith G and Wilkins MR (2012). The methylproteome and the intracellular methylation network. *Proteomics* 12, 564–586.
- Fischer EH and Krebs EG (1955). Conversion of phosphorylase b to phosphorylase a in muscle extracts. *J Biol Chem* 216, 121–132.
- Fuda NJ, Ardehali MB and Lis JT (2009). Defining mechanisms that regulate RNA polymerase II transcription in vivo. *Nature* 461, 186–192.
- Glickman MH and Ciechanover A (2002). The ubiquitin-proteasome proteolytic pathway: destruction for the sake of construction. *Physiol Rev* 82, 373–428.
- Gordon PM, Liu D, Sartor MA, IglayRager HB, Pistilli EE, Gutmann L, et al. (2012). Resistance exercise training influences skeletal muscle immune activation: a microarray analysis. *J Appl Physiol* 112, 443–453.
- Hardie DG, Ross FA and Hawley SA (2012). AMPK: a nutrient and energy sensor that maintains energy homeostasis. *Nat Rev Mol Cell Biol* 13, 251–262.
- He C, Sumpter R, Jr. and Levine B (2012). Exercise induces autophagy in peripheral tissues and in the brain. *Autophagy* 8, 1548–1551.
- Henriksson J, Salmons S and Lowry OH (1989). Chronic stimulation of mammalian muscle: enzyme and metabolic changes in individual fibres. *Biomed Biochim Acta* 48, S445–S454.
- Holloway KV, O’Gorman M, Woods P, Morton JP, Evans L, Cable NT, et al. (2009). Proteomic investigation of changes in human vastus lateralis muscle in response to interval-exercise training. *Proteomics* 9, 5155–5174.
- Hornberger TA (2011). Mechanotransduction and the regulation of mTORC1 signaling in skeletal muscle. *Int J Biochem Cell Biol* 43, 1267–1276.
- Ilsley JL, Sudol M and Winder SJ (2002). The WW domain: linking cell signalling to the membrane cytoskeleton. *Cell Signal* 14, 183–189.
- Johnson ES (2004). Protein modification by SUMO. *Annu Rev Biochem* 73, 355–382.
- Keller P, Vollaard NB, Gustafsson T, Gallagher IJ, Sundberg CJ, Rankinen T, et al. (2011). A transcriptional map of the impact of endurance exercise training on skeletal muscle phenotype. *J Appl Physiol* 110, 46–59.
- Koutedakis Y, Metsios GS and Stavropoulos-Kalinoglou A (2006). Periodization of exercise training in sport. In *The physiology of training*, ed. MacLaren D, pp. 1–21. Elsevier, Edinburgh.
- Laemmli UK (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227, 680–685.
- Li W, Bengtson MH, Ulbrich A, Matsuda A, Reddy VA, Orth A, et al. (2008). Genome-wide and functional annotation of human E3 ubiquitin ligases identifies MULAN, a mitochondrial E3 that regulates the organelle’s dynamics and signaling. *PLoS ONE* 3, e1487.
- Manning G, Whyte DB, Martinez R, Hunter T and Sudarsanam S (2002). The protein kinase complement of the human genome. *Science* 298, 1912–1934.
- McCarthy JJ and Esser KA (2007). MicroRNA-1 and microRNA-133a expression are decreased during skeletal muscle hypertrophy. *J Appl Physiol* 102, 306–313.
- McGee SL and Hargreaves M (2011). Histone modifications and exercise adaptations. *J Appl Physiol* 110, 258–263.
- Mischerikow N and Heck AJ (2011). Targeted large-scale analysis of protein acetylation. *Proteomics* 11, 571–589.

Ohtsubo K and Marth JD (2006). Glycosylation in cellular mechanisms of health and disease. *Cell* 126, 855–867.

Park KD, Park J, Ko J, Kim BC, Kim HS, Ahn K, et al. (2012). Whole transcriptome analyses of six thoroughbred horses before and after exercise using RNA-Seq. *BMC Genomics* 13, 473.

Parker KC, Walsh RJ, Salajegheh M, Amato AA, Krastins B, Sarracino DA, et al. (2009). Characterization of human skeletal muscle biopsy samples using shotgun proteomics. *J Proteome Res* 8, 3265–3277.

Pearen MA, Myers SA, Raichur S, Ryall JG, Lynch GS and Muscat GE (2008). The orphan nuclear receptor, NOR-1, a target of beta-adrenergic signaling, regulates gene expression that controls oxidative metabolism in skeletal muscle. *Endocrinology* 149, 2853–2865.

Renart J, Reiser J and Stark GR (1979). Transfer of proteins from gels to diazobenzoyloxymethyl-paper and detection with antisera: a method for studying antibody specificity and antigen structure. *Proc Natl Acad Sci U S A* 76, 3116–3120.

Resh MD (2006). Trafficking and signaling by fatty-acylated and prenylated proteins. *Nat Chem Biol* 2, 584–590.

Roff M, Thompson J, Rodriguez MS, Jacque JM, Baleux F, Arenzana-Seisdedos F, et al. (1996). Role of I κ B α ubiquitination in signal-induced activation of NF κ B in vivo. *J Biol Chem* 271, 7844–7850.

Safdar A, Abadi A, Akhtar M, Hettinga BP and Tarnopolsky MA (2009). miRNA in the regulation of skeletal muscle adaptation to acute endurance exercise in C57Bl/6J male mice. *PLoS ONE* 4, e5610.

Sanyal A, Lajoie BR, Jain G and Dekker J (2012). A long-range interaction landscape of gene promoters. *Nature* 489, 109–113.

Scarpulla RC (2002). Nuclear activators and coactivators in mammalian mitochondrial biogenesis. *Biochim Biophys Acta* 1576, 1–14.

Tintignac LA, Lagirand J, Batonnet S, Sirri V, Leibovitch MP and Leibovitch SA (2005). Degradation of MyoD mediated by the SCF (MAFbx) ubiquitin ligase. *J Biol Chem* 280, 2847–2856.

Toole BJ and Cohen PT (2007). The skeletal muscle-specific glycogen-targeted protein phosphatase 1 plays a major role in the regulation of glycogen metabolism by adrenaline in vivo. *Cell Signal* 19, 1044–1055.

Towbin H, Staehelin T and Gordon J (1979). Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. *Proc Natl Acad Sci U S A* 76, 4350–4354.

Ulbricht A and Hohfeld J (2013). Tension-induced autophagy: May the chaperone be with you. *Autophagy* 9.

Valencia-Sanchez MA, Liu J, Hannon GJ and Parker R (2006). Control of translation and mRNA degradation by miRNAs and siRNAs. *Genes Dev* 20, 515–524.

Vaquerez JM, Kummerfeld SK, Teichmann SA and Luscombe NM (2009). A census of human transcription factors: function, expression and evolution. *Nat Rev Genet* 10, 252–263.

Wolff J (1892). *Das Gesetz der Transformation der Knochen*. Springer, Berlin.

Yang S, Alnaqeeb M, Simpson H and Goldspink G (1996). Cloning and characterization of an IGF-1 isoform expressed in skeletal muscle subjected to stretch. *J Muscle Res Cell Motil* 17, 487–495.

■ جهت مطالعه بیشتر

Egan B and Zierath JR (2013). Exercise metabolism and the molecular regulation of skeletal muscle adaptation. *Cell Metab* 17, 162–184.

Hardie DG (2011). Energy sensing by the AMP-activated protein kinase and its effects on muscle metabolism. *Proc Nutr Soc* 70, 92–99.

Schiaffino S (2010). Fibre types in skeletal muscle: a personal account. *Acta Physiol (Oxford)* 199, 451–463.

■ منابع

Ameln H, Gustafsson T, Sundberg CJ, Okamoto K, Jansson E, Poellinger L, et al. (2005). Physiological activation of hypoxia inducible factor-1 in human skeletal muscle. *FASEB J* 19, 1009–1011.

Andersen P and Henriksson J (1977). Capillary supply of the quadriceps femoris muscle of man: adaptive response to exercise. *J Physiol* 270, 677–690.

- Arany Z, Foo SY, Ma Y, Ruas JL, Bommi-Reddy A, Girnun G, et al. (2008). HIF-independent regulation of VEGF and angiogenesis by the transcriptional coactivator PGC-1 α . *Nature* 451, 1008–1012.
- Asp P, Blum R, Vethantham V, Parisi F, Micsinai M, Cheng J, et al. (2011). Genome-wide remodeling of the epigenetic landscape during myogenic differentiation. *Proc Natl Acad Sci U S A* 108, E149–E158.
- Baar K, Wende AR, Jones TE, Marison M, Nolte LA, Chen M, et al. (2002). Adaptations of skeletal muscle to exercise: rapid increase in the transcriptional coactivator PGC-1. *FASEB J* 16, 1879–1886.
- Barany M (1967). ATPase activity of myosin correlated with speed of muscle shortening. *J Gen Physiol* 50, Suppl 218.
- Barres R, Yan J, Egan B, Trebak JT, Rasmussen M, Fritz T, et al. (2012). Acute exercise remodels promoter methylation in human skeletal muscle. *Cell Metab* 15, 405–411.
- Bassett DR, Jr. and Howley ET (2000). Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Med Sci Sports Exerc* 32, 70–84.
- Berchtold MW, Brinkmeier H and Muntener M (2000). Calcium ion in skeletal muscle: its crucial role for muscle function, plasticity, and disease. *Physiol Rev* 80, 1215–1265.
- Bernardo BC, Weeks KL, Pretorius L and McMullen JR (2010). Molecular distinction between physiological and pathological cardiac hypertrophy: experimental findings and therapeutic strategies. *Pharmacol Ther* 128, 191–227.
- Biering-Sorensen B, Kristensen IB, Kjaer M and Biering-Sorensen F (2009). Muscle after spinal cord injury. *Muscle Nerve* 40, 499–519.
- Blomqvist CG and Saltin B (1983). Cardiovascular adaptations to physical training. *Annu Rev Physiol* 45, 169–189.
- Bostrom P, Mann N, Wu J, Quintero PA, Plovie ER, Panakova D, et al. (2010). C/EBP β controls exercise-induced cardiac growth and protects against pathological cardiac remodeling. *Cell* 143, 1072–1083.
- Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, et al. (1999). Familial aggregation of $\dot{V}O_{2\max}$ response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 87, 1003–1008.
- Bouchard C, Sarzynski MA, Rice TK, Kraus WE, Church TS, Sung YJ, et al. (2011). Genomic predictors of the maximal $\dot{V}O_{2\max}$ response to standardized exercise training programs. *J Appl Physiol* 110, 1160–1170.
- Bouchard C, Blair SN, Church TS, Earnest CP, Hagberg JM, Hakkinen K, et al. (2012). Adverse metabolic response to regular exercise: is it a rare or common occurrence? *PLoS ONE* 7, e37887.
- Brodal P, Ingjer F and Hermansen L (1977). Capillary supply of skeletal muscle fibers in untrained and endurance-trained men. *Am J Physiol* 232, H705–H712.
- Bueno OF, De Windt LJ, Tymitz KM, Witt SA, Kimball TR, Kleivitsky R, et al. (2000). The MEK1-ERK1/2 signaling pathway promotes compensated cardiac hypertrophy in transgenic mice. *EMBO J* 19, 6341–6350.
- Buller AJ, Eccles JC and Eccles RM (1960). Interactions between motoneurons and muscles in respect of the characteristic speeds of their responses. *J Physiol* 150, 417–439.
- Canto C, Gerhart-Hines Z, Feige JN, Lagouge M, Noriega L, Milne JC, et al. (2009). AMPK regulates energy expenditure by modulating NAD metabolism and SIRT1 activity. *Nature* 458, 1056–1060.
- Carling D, Thornton C, Woods A and Sanders MJ (2012). AMP-activated protein kinase: new regulation, new roles? *Biochem J* 445, 11–27.
- Carroll SL, Klein MG and Schneider MF (1997). Decay of calcium transients after electrical stimulation in rat fast- and slow-twitch skeletal muscle fibres. *J Physiol* 501 (Pt 3), 573–588.
- Chin ER (2005). Role of Ca²⁺/calmodulin-dependent kinases in skeletal muscle plasticity. *J Appl Physiol* 99, 414–423.
- Chin ER, Olson EN, Richardson JA, Yang Q, Humphries C, Shelton JM, et al. (1998). A calcineurin-independent transcriptional pathway controls skeletal muscle fiber type. *Genes Dev* 12, 2499–2509.
- Costill DL, Daniels J, Evans W, Fink W, Krahenbuhl G and Saltin B (1976a). Skeletal muscle enzymes and fiber composition in male and female track athletes. *J Appl Physiol* 40, 149–154.
- Costill DL, Fink WJ and Pollock ML (1976b). Muscle fiber composition and enzyme activities of elite distance runners. *Med Sci Sports* 8, 96–100.
- DeBosch B, Treskov I, Lupu TS, Weinheimer C, Kovacs A, Courtois M, et al. (2006). Akt1 is required for physiological cardiac growth. *Circulation* 113, 2097–2104.
- Egan B and Zierath JR (2013). Exercise metabolism and the molecular regulation of skeletal muscle adaptation. *Cell Metab* 17, 162–184.
- Eklom B (1968). Effect of physical training on oxygen transport system in man. *Acta Physiol Scand Suppl* 328, 1–45.
- Gan Z, Burkart-Hartman EM, Han DH, Finck B, Leone TC, Smith EY, et al. (2011). The nuclear receptor PPAR β / δ programs muscle glucose metabolism in cooperation with AMPK and MEF2. *Genes Dev* 25, 2619–2630.

- Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 43, 1334–1359.
- Gibala MJ, Little JP, MacDonald MJ and Hawley JA (2012). Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J Physiol* 590, 1077–1084.
- Gollnick PD, Armstrong RB, Saltin B, Saubert CW, Sembrowich WL and Shepherd RE (1973). Effect of training on enzyme activity and fiber composition of human skeletal muscle. *J Appl Physiol* 34, 107–111.
- Haas TL, Milkiewicz M, Davis SJ, Zhou AL, Egginton S, Brown MD, et al. (2000). Matrix metalloproteinase activity is required for activity-induced angiogenesis in rat skeletal muscle. *Am J Physiol Heart Circ Physiol* 279, H1540–H1547.
- Hardie DG and Sakamoto K (2006). AMPK: a key sensor of fuel and energy status in skeletal muscle. *Physiology (Bethesda)* 21, 48–60.
- Harridge SD, Bottinelli R, Canepari M, Pellegrino MA, Reggiani C, Esbjornsson M, et al. (1996). Whole-muscle and single-fibre contractile properties and myosin heavy chain isoforms in humans. *Pflügers Arch* 432, 913–920.
- Hennig R and Lomo T (1985). Firing patterns of motor units in normal rats. *Nature* 314, 164–166.
- Holloszy JO (1967). Biochemical adaptations in muscle. Effects of exercise on mitochondrial oxygen uptake and respiratory enzyme activity in skeletal muscle. *J Biol Chem* 242, 2278–2282.
- Hudlicka O, Brown MD and Silgram H (2000). Inhibition of capillary growth in chronically stimulated rat muscles by N(G)-nitro-L-arginine, nitric oxide synthase inhibitor. *Microvasc Res* 59, 45–51.
- Hughes SM, Chi MM, Lowry OH and Gundersen K (1999). Myogenin induces a shift of enzyme activity from glycolytic to oxidative metabolism in muscles of transgenic mice. *J Cell Biol* 145, 633–642.
- Ingalls CP (2004). Nature vs. nurture: can exercise really alter fiber type composition in human skeletal muscle? *J Appl Physiol* 97, 1591–1592.
- Ingjer F (1979). Effects of endurance training on muscle fibre ATP-ase activity, capillary supply and mitochondrial content in man. *J Physiol* 294, 419–432.
- Jager S, Handschin C, St-Pierre J and Spiegelman BM (2007). AMP-activated protein kinase (AMPK) action in skeletal muscle via direct phosphorylation of PGC-1 α . *Proc Natl Acad Sci U S A* 104, 12017–12022.
- Jansson E and Kaijser L (1977). Muscle adaptation to extreme endurance training in man. *Acta Physiol Scand* 100, 315–324.
- Jenuwein T and Allis CD (2001). Translating the histone code. *Science* 293, 1074–1080.
- Johnson MA, Polgar J, Weightman D and Appleton D (1973). Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. *J Neurol Sci* 18, 111–129.
- Jones D, Round J and de Haan A (2004). *Skeletal muscle. From molecules to movement*. Churchill Livingstone, Edinburgh.
- Knutti D, Kressler D and Kralli A (2001). Regulation of the transcriptional coactivator PGC-1 via MAPK-sensitive interaction with a repressor. *Proc Natl Acad Sci U S A* 98, 9713–9718.
- Lassar AB, Paterson BM and Weintraub H (1986). Transfection of a DNA locus that mediates the conversion of 10T1/2 fibroblasts to myoblasts. *Cell* 47, 649–656.
- Lexell J, Taylor CC and Sjoström M (1988). What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 84, 275–294.
- Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, et al. (2002). Transcriptional co-activator PGC-1 α drives the formation of slow-twitch muscle fibres. *Nature* 418, 797–801.
- Mason SD, Howlett RA, Kim MJ, Olfert IM, Hogan MC, McNulty W, et al. (2004). Loss of skeletal muscle HIF-1 α results in altered exercise endurance. *PLoS Biol* 2, e288.
- McKinsey TA, Zhang CL and Olson EN (2001). Control of muscle development by dueling HATs and HDACs. *Curr Opin Genet Dev* 11, 497–504.
- McMullen JR, Shioi T, Zhang L, Tarnavski O, Sherwood MC, Kang PM, et al. (2003). Phosphoinositide 3-kinase (p110 α) plays a critical role for the induction of physiological, but not pathological, cardiac hypertrophy. *Proc Natl Acad Sci U S A* 100, 12355–12360.
- McPhee JS, Williams AG, Stewart C, Baar K, Schindler JP, Aldred S, et al. (2009). The training stimulus experienced

- by the leg muscles during cycling in humans. *Exp Physiol* 94, 684–694.
- Meyer RA and Foley JM (1996). Cellular processes integrating the metabolic response to exercise. In *Handbook of Physiology. Section 12. Exercise: Regulation and Integration of multiple Systems*, eds. Rowell LB and Shepherd JT, pp. 841–869. Oxford University Press, Oxford.
- Midgley AW, McNaughton LR and Jones AM (2007). Training to enhance the physiological determinants of long-distance running performance: can valid recommendations be given to runners and coaches based on current scientific knowledge? *Sports Med* 37, 857–880.
- Molkentin JD, Lu JR, Antos CL, Markham B, Richardson J, Robbins J, et al. (1998). A calcineurin-dependent transcriptional pathway for cardiac hypertrophy. *Cell* 93, 215–228.
- Murgia M, Serrano AL, Calabria E, Pallafacchina G, Lomo T and Schiaffino S (2000). Ras is involved in nerve-activity-dependent regulation of muscle genes. *Nat Cell Biol* 2, 142–147.
- Naya FJ, Mercer B, Shelton J, Richardson JA, Williams RS and Olson EN (2000). Stimulation of slow skeletal muscle fiber gene expression by calcineurin in vivo. *J Biol Chem* 275, 4545–4548.
- Ouchi N, Shibata R and Walsh K (2005). AMP-activated protein kinase signaling stimulates VEGF expression and angiogenesis in skeletal muscle. *Circ Res* 96, 838–846.
- Pandorf CE, Haddad F, Wright C, Bodell PW and Baldwin KM (2009). Differential epigenetic modifications of histones at the myosin heavy chain genes in fast and slow skeletal muscle fibers and in response to muscle unloading. *Am J Physiol Cell Physiol* 297, C6–16.
- Parsons SA, Wilkins BJ, Bueno OF and Molkentin JD (2003). Altered skeletal muscle phenotypes in calcineurin A α and Abeta gene-targeted mice. *Mol Cell Biol* 23, 4331–4343.
- Parsons SA, Millay DP, Wilkins BJ, Bueno OF, Tsika GL, Neilson JR, et al. (2004). Genetic loss of calcineurin blocks mechanical overload-induced skeletal muscle fiber-type switching but not hypertrophy. *J Biol Chem* 279, 26192–26220.
- Pette D and Vrbova G (1992). Adaptation of mammalian skeletal muscle fibers to chronic electrical stimulation. *Rev Physiol Biochem Pharmacol* 120, 115–202.
- Philp A, Chen A, Lan D, Meyer GA, Murphy AN, Knapp AE, et al. (2011). Sirtuin 1 (SIRT1) deacetylase activity is not required for mitochondrial biogenesis or peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α) deacetylation following endurance exercise. *J Biol Chem* 286, 30561–30570.
- Pilegaard H, Saltin B and Neufer PD (2003). Exercise induces transient transcriptional activation of the PGC-1 α gene in human skeletal muscle. *J Physiol* 546, 851–858.
- Poyton RO and McEwen JE (1996). Crosstalk between nuclear and mitochondrial genomes. *Annu Rev Biochem* 65, 563–607.
- Quiat D, Voelker KA, Pei J, Grishin NV, Grange RW, Bassel-Duby R, et al. (2011). Concerted regulation of myofiber-specific gene expression and muscle performance by the transcriptional repressor Sox6. *Proc Natl Acad Sci U S A* 108, 10196–10201.
- Rose AJ, Kiens B and Richter EA (2006). Ca²⁺-calmodulin-dependent protein kinase expression and signalling in skeletal muscle during exercise. *J Physiol* 574, 889–903.
- Saltin B, Radegran G, Koskolou MD and Roach RC (1998). Skeletal muscle blood flow in humans and its regulation during exercise. *Acta Physiol Scand* 162, 421–436.
- Sawka MN, Convertino VA, Eichner ER, Schnieder SM and Young AJ (2000). Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. *Med Sci Sports Exerc* 32, 332–348.
- Scarpulla RC (2010). Metabolic control of mitochondrial biogenesis through the PGC-1 family regulatory network. *Biochim Biophys Acta* 1813, 1269–1278.
- Scharhag J, Schneider G, Urhausen A, Rochette V, Kramann B and Kindermann W (2002). Athlete's heart: right and left ventricular mass and function in male endurance athletes and untrained individuals determined by magnetic resonance imaging. *J Am Coll Cardiol* 40, 1856–1863.
- Schiaffino S (2010). Fibre types in skeletal muscle: a personal account. *Acta Physiol (Oxford)* 199, 451–463.
- Shioi T, Kang PM, Douglas PS, Hampe J, Yballe CM, Lawitts J, et al. (2000). The conserved phosphoinositide 3-kinase pathway determines heart size in mice. *EMBO J* 19, 2537–2548.
- Shioi T, McMullen JR, Kang PM, Douglas PS, Obata T, Franke TF, et al. (2002). Akt/protein kinase B promotes organ growth in transgenic mice. *Mol Cell Biol* 22, 2799–2809.
- Simoneau JA and Bouchard C (1995). Genetic determinism of fiber type proportion in human skeletal muscle. *FASEB*

J 9, 1091–1095.

- Smerdu V, Karsch-Mizrachi I, Campione M, Leinwand L and Schiaffino S (1994). Type IIX myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle. *Am J Physiol* 267, C1723–C1728.
- Spurway NC and Wackerhage H (2006). *Genetics and molecular biology of muscle adaptation*. Elsevier/Churchill Livingstone, Edinburgh.
- Suwa M, Nakano H and Kumagai S (2003). Effects of chronic AICAR treatment on fiber composition, enzyme activity, UCP3, and PGC-1 in rat muscles. *J Appl Physiol* 95, 960–968.
- Timmons JA, Knudsen S, Rankinen T, Koch LG, Sarzynski M, Jensen T, et al. (2010). Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* 108, 1487–1496.
- Tothova J, Blaauw B, Pallafacchina G, Rudolf R, Argentini C, Reggiani C, et al. (2006). NFATc1 nucleocytoplasmic shuttling is controlled by nerve activity in skeletal muscle. *J Cell Sci* 119, 1604–1611.
- Towler MC and Hardie DG (2007). AMP-activated protein kinase in metabolic control and insulin signaling. *Circ Res* 100, 328–341.
- Trappe SW, Costill DL, Fink WJ and Pearson DR (1995). Skeletal muscle characteristics among distance runners: a 20-yr follow-up study. *J Appl Physiol* 78, 823–829.
- Tseng BS, Kasper CE and Edgerton VR (1994). Cytoplasm-to-myonucleus ratios and succinate dehydrogenase activities in adult rat slow and fast muscle fibers. *Cell Tissue Res* 275, 39–49.
- Tsika RW, Schramm C, Simmer G, Fitzsimons DP, Moss RL and Ji J (2008). Overexpression of TEAD-1 in transgenic mouse striated muscles produces a slower skeletal muscle contractile phenotype. *J Biol Chem* 283, 36154–36167.
- van Rooij E., Quiat D, Johnson BA, Sutherland LB, Qi X, Richardson JA, et al. (2009). A family of microRNAs encoded by myosin genes governs myosin expression and muscle performance. *Dev Cell* 17, 662–673.
- Wagner PD (2011). The critical role of VEGF in skeletal muscle angiogenesis and blood flow. *Biochem Soc Trans* 39, 1556–1559.
- Weiss A, McDonough D, Wertman B, Acakpo-Satchivi L, Montgomery K, Kucherlapati R, et al. (1999). Organization of human and mouse skeletal myosin heavy chain gene clusters is highly conserved. *Proc Natl Acad Sci U S A* 96, 2958–2963.
- Wu H, Kanatous SB, Thurmond FA, Gallardo T, Isotani E, Bassel-Duby R, et al. (2002). Regulation of mitochondrial biogenesis in skeletal muscle by CaMK. *Science* 296, 349–352.
- Xiao B, Sanders MJ, Underwood E, Heath R, Mayer FV, Carmena D, et al. (2011). Structure of mammalian AMPK and its regulation by ADP. *Nature* 472(7342), 230–233.
- Xie K, Wei D, Shi Q and Huang S (2004). Constitutive and inducible expression and regulation of vascular endothelial growth factor. *Cytokine Growth Factor Rev* 15, 297–324.
- Yancopoulos GD, Davis S, Gale NW, Rudge JS, Wiegand SJ and Holash J (2000). Vascular-specific growth factors and blood vessel formation. *Nature* 407, 242–248.

■ جهت مطالعه بیشتر

- Bouchard C and Hoffman EP (2011). Genetic and molecular aspects of sports performance, Vol. 18 of *Encyclopedia of sports medicine*. John Wiley & Sons, Chichester.
- Bray MS, Hagberg JM, Perusse L, Rankinen T, Roth SM, Wolfarth B, et al. (2009). The human gene map for performance and health-related fitness phenotypes: the 2006–2007 update. *Med Sci Sports Exerc* 41, 35–73.
- de la Chapelle A, Traskelin AL and Juvonen E (1993). Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis. *Proc Natl Acad Sci U S A* 90, 4495–4499.
- Hagberg JM, Rankinen T, Loos RJ, Perusse L, Roth SM, Wolfarth B, et al. (2011). Advances in exercise, fitness, and performance genomics in 2010. *Med Sci Sports Exerc* 43, 743–752.
- Peeters MW, Thomis MA, Beunen GP and Malina RM (2009). Genetics and sports: an overview of the

pre-molecular biology era. *Med Sport Sci* 54, 28–42.

Pescatello LS and Roth SM (2011). *Exercise genomics*. Springer, New York.

■ منابع

- Ahmetov II, Williams AG, Popov DV, Lyubaeva EV, Hakimullina AM, Fedotovskaya ON, et al. (2009). The combined impact of metabolic gene polymorphisms on elite endurance athlete status and related phenotypes. *Hum Genet* 126, 751–761.
- Altmuller J, Palmer LJ, Fischer G, Scherb H and Wjst M (2001). Genomewide scans of complex human diseases: true linkage is hard to find. *Am J Hum Genet* 69, 936–950.
- Anderson S, Bankier AT, Barrell BG, de Bruijn MH, Coulson AR, Drouin J, et al. (1981). Sequence and organization of the human mitochondrial genome. *Nature* 290, 457–465.
- Bassett DR, Jr. and Howley ET (2000). Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Med Sci Sports Exerc* 32, 70–84.
- Bouchard C, Lesage R, Lortie G, Simoneau JA, Hamel P, Boulay MR, et al. (1986a). Aerobic performance in brothers, dizygotic and monozygotic twins. *Med Sci Sports Exerc* 18, 639–646.
- Bouchard C, Simoneau JA, Lortie G, Boulay MR, Marcotte M and Thibault MC (1986b). Genetic effects in human skeletal muscle fiber type distribution and enzyme activities. *Can J Physiol Pharmacol* 64, 1245–1251.
- Bouchard C, Daw EW, Rice T, Perusse L, Gagnon J, Province MA, et al. (1998). Familial resemblance for $\dot{V}O_2\max$ in the sedentary state: the HERITAGE family study. *Med Sci Sports Exerc* 30, 252–258.
- Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, et al. (1999). Familial aggregation of $\dot{V}O_2\max$ response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 87, 1003–1008.
- Bouchard C, Sarzynski MA, Rice TK, Kraus WE, Church TS, Sung YJ, et al. (2011). Genomic predictors of the maximal $\dot{V}O_2$ uptake response to standardized exercise training programs. *J Appl Physiol* 110, 1160–1170.
- Bray MS, Hagberg JM, Perusse L, Rankinen T, Roth SM, Wolfarth B, et al. (2009). The human gene map for performance and health-related fitness phenotypes: the 2006–2007 update. *Med Sci Sports Exerc* 41, 35–73.
- Bueno OF, De Windt LJ, Tymitz KM, Witt SA, Kimball TR, Klevitsky R, et al. (2000). The MEK1-ERK1/2 signaling pathway promotes compensated cardiac hypertrophy in transgenic mice. *EMBO J* 19, 6341–6350.
- Castro MG, Terrados N, Reguero JR, Alvarez V and Coto E (2007). Mitochondrial haplogroup T is negatively associated with the status of elite endurance athlete. *Mitochondrion* 7, 354–357.
- hanock SJ, Manolio T, Boehnke M, Boerwinkle E, Hunter DJ, Thomas G, et al. (2007). Replicating genotype-phenotype associations. *Nature* 447, 655–660.
- Cooper CE (2008). The biochemistry of drugs and doping methods used to enhance aerobic sport performance. *Essays Biochem* 44, 63–83.
- Costill DL, Daniels J, Evans W, Fink W, Krahenbuhl G and Saltin B (1976a). Skeletal muscle enzymes and fiber composition in male and female track athletes. *J Appl Physiol* 40, 149–154.
- Costill DL, Fink WJ and Pollock ML (1976b). Muscle fiber composition and enzyme activities of elite distance runners. *Med Sci Sports* 8, 96–100.
- de la Chapelle A, Traskelin AL and Juvonen E (1993). Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis. *Proc Natl Acad Sci U S A* 90, 4495–4499.
- Defoor J, Martens K, Zielinska D, Matthijs G, Van NH, Schepers D, et al. (2006). The CAREGENE study: polymorphisms of the beta1-adrenoceptor gene and aerobic power in coronary artery disease. *Eur Heart J* 27, 808–816.

- Eynon N, Meckel Y, Sagiv M, Yamin C, Amir R, Sagiv M, et al. (2010). Do PPARGC1A and PPARalpha polymorphisms influence sprint or endurance phenotypes? *Scand J Med Sci Sports* 20, e145–e150.
- Eynon N, Moran M, Birk R and Lucia A (2011). The champions' mitochondria: is it genetically determined? A review on mitochondrial DNA and elite athletic performance. *Physiol Genomics* 43, 789–798.
- Franks PW, Barroso I, Luan J, Ekelund U, Crowley VE, Brage S, et al. (2003). PGC-1alpha genotype modifies the association of volitional energy expenditure with [OV0312]O₂max. *Med Sci Sports Exerc* 35, 1998–2004.
- Hakimi P, Yang J, Casadesus G, Massillon D, Tolentino-Silva F, Nye CK, et al. (2007). Overexpression of the cytosolic form of phosphoenolpyruvate carboxykinase (GTP) in skeletal muscle repatterns energy metabolism in the mouse. *J Biol Chem* 282, 32844–32855.
- Hautala AJ, Leon AS, Skinner JS, Rao DC, Bouchard C and Rankinen T (2007). Peroxisome proliferator-activated receptor-delta polymorphisms are associated with physical performance and plasma lipids: the HERITAGE Family Study. *Am J Physiol Heart Circ Physiol* 292, H2498–H2505.
- Hill AV and Lupton H (1923). Muscular exercise, lactic acid and the supply and utilization of oxygen. *Q J Med* 16, 135–171.
- Johnson MA, Polgar J, Weightman D and Appleton D (1973). Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. *J Neurol Sci* 18, 111–129.
- Klissouras V (1971). Heritability of adaptive variation. *J Appl Physiol* 31, 338–344.
- Komi PV, Viitasalo JH, Havu M, Thorstensson A, Sjodin B and Karlsson J (1977). Skeletal muscle fibres and muscle enzyme activities in monozygous and dizygous twins of both sexes. *Acta Physiol Scand* 100, 385–392.
- Lightfoot JT, Leamy L, Pomp D, Turner MJ, Fodor AA, Knab A, et al. (2010). Strain screen and haplotype association mapping of wheel running in inbred mouse strains. *J Appl Physiol* 109, 623–634.
- Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, et al. (2002). Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres. *Nature* 418, 797–801.
- Lucia A, Gomez-Gallego F, Barroso I, Rabadan M, Bandres F, San Juan AF, et al. (2005). PPARGC1A genotype (Gly482Ser) predicts exceptional endurance capacity in European men. *J Appl Physiol* 99, 344–348.
- MacArthur DG, Seto JT, Chan S, Quinlan KG, Raftery JM, Turner N, et al. (2008). An Actn3 knockout mouse provides mechanistic insights into the association between alpha-actinin-3 deficiency and human athletic performance. *Hum Mol Genet* 17, 1076–1086.
- Manchester J, Skurat AV, Roach P, Hauschka SD and Lawrence JC, Jr. (1996). Increased glycogen accumulation in transgenic mice overexpressing glycogen synthase in skeletal muscle. *Proc Natl Acad Sci U S A* 93, 10707–10711.
- Martinez-Redondo D, Marcuello A, Casajus JA, Ara I, Dahmani Y, Montoya J, et al. (2010). Human mitochondrial haplogroup H: the highest V. O₂max consumer – is it a paradox? *Mitochondrion* 10, 102–107.
- McCole SD, Shuldiner AR, Brown MD, Moore GE, Ferrell RE, Wilund KR, et al. (2004). Beta2- and beta3-adrenergic receptor polymorphisms and exercise hemodynamics in postmenopausal women. *J Appl Physiol* 96, 526–530.
- Montgomery HE, Clarkson P, Dollery CM, Prasad K, Losi MA, Hemingway H, et al. (1997). Association of angiotensin-converting enzyme gene I/D polymorphism with change in left ventricular mass in response to physical training. *Circulation* 96, 741–747.
- Montgomery HE, Marshall R, Hemingway H, Myerson S, Clarkson P, Dollery C, et al. (1998). Human gene for physical performance. *Nature* 393, 221–222.
- Moore GE, Shuldiner AR, Zmuda JM, Ferrell RE, McCole SD and Hagberg JM (2001). Obesity gene variant and elite endurance performance. *Metabolism* 50, 1391–1392.
- Murgia M, Serrano AL, Calabria E, Pallafacchina G, Lomo T and Schiaffino S (2000). Ras is involved in nerve-activity-dependent regulation of muscle genes. *Nat Cell Biol* 2, 142–147.

- Parsons SA, Wilkins BJ, Bueno OF and Molkentin JD (2003). Altered skeletal muscle phenotypes in calcineurin A α and A β gene-targeted mice. *Mol Cell Biol* 23, 4331–4343.
- Parsons SA, Millay DP, Wilkins BJ, Bueno OF, Tsika GL, Neilson JR, et al. (2004). Genetic loss of calcineurin blocks mechanical overload-induced skeletal muscle fiber-type switching but not hypertrophy. *J Biol Chem* 279, 26192–26200.
- Prior SJ, Hagberg JM, Phares DA, Brown MD, Fairfull L, Ferrell RE, et al. (2003). Sequence variation in hypoxia-inducible factor 1 α (HIF1A): association with maximal oxygen consumption. *Physiol Genomics* 15, 20–26.
- Prior SJ, Hagberg JM, Paton CM, Douglass LW, Brown MD, McLenithan JC, et al. (2006). DNA sequence variation in the promoter region of the VEGF gene impacts VEGF gene expression and maximal oxygen consumption. *Am J Physiol Heart Circ Physiol* 290, H1848–H1855.
- Quiat D, Voelker KA, Pei J, Grishin NV, Grange RW, Bassel-Duby R and Olson EN (2011). Concerted regulation of myofiber-specific gene expression and muscle performance by the transcriptional repressor Sox6. *Proc Natl Acad Sci U S A* 108, 10196–10201.
- Rankinen T, Perusse L, Gagnon J, Chagnon YC, Leon AS, Skinner JS, et al. (2000a). Angiotensin-converting enzyme ID polymorphism and fitness phenotype in the HERITAGE Family Study. *J Appl Physiol* 88, 1029–1035.
- Rankinen T, Wolfarth B, Simoneau JA, Maier-Lenz D, Rauramaa R, Rivera MA, et al. (2000b). No association between the angiotensin-converting enzyme ID polymorphism and elite endurance athlete status. *J Appl Physiol* 88, 1571–1575.
- Rico-Sanz J, Rankinen T, Joanisse DR, Leon AS, Skinner JS, Wilmore JH, et al. (2003). Associations between cardiorespiratory responses to exercise and the C34T AMPD1 gene polymorphism in the HERITAGE Family Study. *Physiol Genomics* 14, 161–166.
- Rigat B, Hubert C, Ahenc-Gelas F, Cambien F, Corvol P and Soubrier F (1990). An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. *J Clin Invest* 86, 1343–1346.
- Rivera MA, Dionne FT, Simoneau JA, Perusse L, Chagnon M, Chagnon Y, et al. (1997). Musclespecific creatine kinase gene polymorphism and V. O₂max in the HERITAGE Family Study. *Med Sci Sports Exerc* 29, 1311–1317.
- Roth SM (2008). Perspective on the future use of genomics in exercise prescription. *J Appl Physiol* 104, 1243–1245.
- Saunders CJ, Xenophontos SL, Cariolou MA, Anastassiades LC, Noakes TD and Collins M (2006). The bradykinin beta 2 receptor (BDKRB2) and endothelial nitric oxide synthase 3 (NOS3) genes and endurance performance during Ironman Triathlons. *Hum Mol Genet* 15, 979–987.
- Scott RA, Fuku N, Onywera VO, Boit M, Wilson RH, Tanaka M, et al. (2009). Mitochondrial haplogroups associated with elite Kenyan athlete status. *Med Sci Sports Exerc* 41, 123–128.
- Shriver MD and Kittles RA (2004). Genetic ancestry and the search for personalized genetic histories. *Nat Rev Genet* 5, 611–618.
- Simoneau JA and Bouchard C (1995). Genetic determinism of fiber type proportion in human skeletal muscle. *FASEB J* 9, 1091–1095.
- Smerdu V, Karsch-Mizrachi I, Campione M, Leinwand L and Schiaffino S (1994). Type IIX myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle. *Am J Physiol* 267, C1723–C1728.
- Timmons JA, Knudsen S, Rankinen T, Koch LG, Sarzynski M, Jensen T, et al. (2010). Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* 108, 1487–1496.
- van Oven M and Kayser M (2009). Updated comprehensive phylogenetic tree of global human mitochondrial DNA variation. *Hum Mutat* 30, E386–E394.

- van Rooij E., Quiat D, Johnson BA, Sutherland LB, Qi X, Richardson JA, et al. (2009). A family of microRNAs encoded by myosin genes governs myosin expression and muscle performance. *Dev Cell* 17, 662–673.
- Wagoner LE, Craft LL, Zengel P, McGuire N, Rathz DA, Dorn GW and Liggett SB (2002). Poly morphisms of the beta1-adrenergic receptor predict exercise capacity in heart failure. *Am Heart J* 144, 840–846.
- Wang YX, Zhang CL, Yu RT, Cho HK, Nelson MC, Bayuga-Ocampo CR, et al. (2004). Regulation of muscle fiber type and running endurance by PPARdelta. *PLoS Biol* 2, e294.
- Wheeler DA, Srinivasan M, Egholm M, Shen Y, Chen L, McGuire A, et al. (2008). The complete genome of an individual by massively parallel DNA sequencing. *Nature* 452, 872–876.
- Williams AG and Folland JP (2008). Similarity of polygenic profiles limits the potential for elite human physical performance. *J Physiol* 586, 113–121.
- Williams AG, Dhamrait SS, Wootton PT, Day SH, Hawe E, Payne JR, et al. (2004). Bradykinin receptor gene variant and human physical performance. *J Appl Physiol* 96, 938–942.
- Wisloff U, Najjar SM, Ellingsen O, Haram PM, Swoap S, Al Share Q, et al. (2005). Cardiovascular risk factors emerge after artificial selection for low aerobic capacity. *Science* 307, 418–420.
- Wolfarth B, Rankinen T, Muhlbauer S, Scherr J, Boulay MR, Perusse L, et al. (2007). Association between a beta2-adrenergic receptor polymorphism and elite endurance performance. *Metabolism* 56, 1649–1651.

Egan B and Zierath JR (2013). Exercise metabolism and the molecular regulation of skeletal muscle adaptation. *Cell Metab* 17, 162–184.

- ACSM (2009). American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 41, 687–708.
- Allen DL, Roy RR, and Edgerton VR (1999). Myonuclear domains in muscle adaptation and disease. *Muscle Nerve* 22, 1350–1360.
- Amthor H, Otto A, Vulin A, Rochat A, Dumonceaux J, Garcia L, et al. (2009). Muscle hypertrophy driven by myostatin blockade does not require stem/precursor-cell activity. *Proc Natl Acad Sci U S A* 106, 7479–7484.
- Arnold HH and Braun T (1996). Targeted inactivation of myogenic factor genes reveals their role during mouse myogenesis: a review. *Int J Dev Biol* 40, 345–353.
- Baar K and Esser K (1999). Phosphorylation of p70 (S6k) correlates with increased skeletal muscle mass following resistance exercise. *Am J Physiol* 276, C120–C127.
- Bentzinger CF, von Maltzahn J and Rudnicki MA (2010). Extrinsic regulation of satellite cell specification. *Stem Cell Res* 1, 27.
- Blaauw B, Canato M, Agatea L, Toniolo L, Mammucari C, Masiero E, et al. (2009). Inducible activation of Akt increases skeletal muscle mass and force without satellite cell activation. *FASEB J* 23, 3896–3905.
- Bodine SC, Stitt TN, Gonzalez M, Kline WO, Stover GL, Bauerlein R, et al. (2001). Akt/mTOR pathway is a crucial regulator of skeletal muscle hypertrophy and can prevent muscle atrophy in vivo. *Nat Cell Biol* 3, 1014–1019.
- Bohe J, Low JF, Wolfe RR and Rennie MJ (2001). Latency and duration of stimulation of human muscle protein synthesis during continuous infusion of amino acids. *J Physiol* 532, 575–579.
- Cao Y, Yao Z, Sarkar D, Lawrence M, Sanchez GJ, Parker MH, et al. (2010). Genome-wide MyoD binding in skeletal muscle cells: a potential for broad cellular reprogramming. *Dev Cell* 18, 662–674.
- Carpinelli RN (2009). Challenging the American College of Sports Medicine 2009 position stand on resistance training. *Medicina Sportiva* 13, 131–137.
- Carpinelli RF, Otto RM and Winett RA (2004). A critical analysis of the ACSM position stand on resistance training: Insufficient evidence to support recommended training protocols. *J Exerc Physiol* 7, 1–60.
- Carroll CC, Carrithers JA and Trappe TA (2004). Contractile protein concentrations in human single muscle fibers. *J*

- Muscle Res Cell Motil 25, 55–59.
- Coleman ME, DeMayo F, Yin KC, Lee HM, Geske R, Montgomery C, et al. (1995). Myogenic vector expression of insulin-like growth factor I stimulates muscle cell differentiation and myofiber hypertrophy in transgenic mice. *J Biol Chem* 270, 12109–12116.
- Collins CA, Olsen I, Zammit PS, Heslop L, Petrie A, Partridge TA, et al. (2005). Stem cell function, self-renewal, and behavioral heterogeneity of cells from the adult muscle satellite cell niche. *Cell* 122, 289–301.
- Conboy IM and Rando TA (2002). The regulation of Notch signaling controls satellite cell activation and cell fate determination in postnatal myogenesis. *Dev Cell* 3, 397–409.
- Davies SP, Reddy H, Caivano M and Cohen P (2000). Specificity and mechanism of action of some commonly used protein kinase inhibitors. *Biochem J* 351, 95–105.
- Davis RL, Weintraub H and Lassar AB (1987). Expression of a single transfected cDNA converts fibroblasts to myoblasts. *Cell* 51, 987–1000.
- Drummond MJ, Fry CS, Glynn EL, Dreyer HC, Dhanani S, Timmerman KL, et al. (2009). Rapamycin administration in humans blocks the contraction-induced increase in skeletal muscle protein synthesis. *J Physiol* 587, 1535–1546.
- Edmondson DG and Olson EN (1989). A gene with homology to the myc similarity region of MyoD1 is expressed during myogenesis and is sufficient to activate the muscle differentiation program. *Genes Dev* 3, 628–640.
- Ferrari G, Cusella-De Angelis G, Coletta M, Paolucci E, Stornaiuolo A, Cossu G, et al. (1998). Muscle regeneration by bone marrow-derived myogenic progenitors. *Science* 279, 1528–1530.
- Forsberg AM, Nilsson E, Werneman J, Bergstrom J and Hultman E (1991). Muscle composition in relation to age and sex. *Clin Sci (Lond)* 81, 249–256.
- Goodman CA, Miu MH, Frey JW, Mabrey DM, Lincoln HC, Ge Y, et al. (2010). A phosphatidylinositol 3-kinase/protein kinase B-independent activation of mammalian target of rapamycin signaling is sufficient to induce skeletal muscle hypertrophy. *Mol Biol Cell* 21, 3258–3268.
- Goodman CA, Frey JW, Mabrey DM, Jacobs BL, Lincoln HC, You JS, et al. (2011). The role of skeletal muscle mTOR in the regulation of mechanical load-induced growth. *J Physiol* 589, 5485–5501.
- Heron MI and Richmond FJ (1993). In-series fiber architecture in long human muscles. *J Morphol* 216, 35–45.
- Holz MK, Ballif BA, Gygi SP and Blenis J (2005). mTOR and S6K1 mediate assembly of the translation preinitiation complex through dynamic protein interchange and ordered phosphorylation events. *Cell* 123, 569–580.
- Hornberger TA (2011). Mechanotransduction and the regulation of mTORC1 signaling in skeletal muscle. *Int J Biochem Cell Biol* 43, 1267–1276.
- Hubal MJ, Gordish-Dressman H, Hompson PD, Price TB, Hoffman EP, Angelopoulos TJ, et al. (2005). Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc* 37, 964–972.
- Inoki K, Zhu T and Guan KL (2003). TSC2 mediates cellular energy response to control cell growth and survival. *Cell* 115, 577–590.
- Janssen I, Heymsfield SB, Wang ZM and Ross R (2000). Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol* 89, 81–88.
- Judson RN, Tremblay AM, Knopp P, White RB, Urcia R, De BC, et al. (2012). The Hippo pathway member Yap plays a key role in influencing fate decisions in muscle satellite cells. *J Cell Sci* 125, 6009–6019.
- Kadi F, Charifi N, Denis C, Lexell J, Andersen JL, Schjerling P, et al. (2005). The behaviour of satellite cells in response to exercise: what have we learned from human studies? *Pflugers Arch* 451, 319–327.
- Katz B (1961). The terminations of the afferent nerve fibre in the muscle spindle of the frog. *Philos Trans R Soc Lond B Biol Sci* 243, 221–240.
- Kelley G (1996). Mechanical overload and skeletal muscle fiber hyperplasia: a meta-analysis. *J Appl Physiol* 81, 1584–1588.
- Kim E and Guan KL (2009). RAG GTPases in nutrient-mediated TOR signaling pathway. *Cell Cycle* 8, 1014–1018.
- Kim PL, Staron RS and Phillips SM (2005). Fasted-state skeletal muscle protein synthesis after resistance exercise is altered with training. *J Physiol* 568, 283–290.
- Kim JS, Petrella JK, Cross JM and Bamman MM (2007). Load-mediated downregulation of myostatin mRNA is not sufficient to promote myofiber hypertrophy in humans: a cluster analysis. *J Appl Physiol* 103, 1488–1495.
- Kraemer WJ, Adams K, Cafarelli E, Dudley GA, Dooly C, Feigenbaum MS, et al. (2002). American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 34, 364–380.
- Lai KM, Gonzalez M, Poueymirou WT, Kline WO, Na E, Zlotchenko E, et al. (2004). Conditional activation of akt in adult skeletal muscle induces rapid hypertrophy. *Mol Cell Biol* 24, 9295–9304.
- Lassar AB, Paterson BM and Weintraub H (1986). Transfection of a DNA locus that mediates the conversion of 10T1/2 fibroblasts to myoblasts. *Cell* 47, 649–656.
- Lee SJ (2004). Regulation of muscle mass by myostatin. *Annu Rev Cell Dev Biol* 20, 61–86. Lee SJ (2007). Quadrupling

muscle mass in mice by targeting TGF-beta signaling pathways. *PLoS ONE* 2, e789.

Lee SJ (2010). Extracellular regulation of myostatin: a molecular rheostat for muscle mass. *Immunol Endocr Metab Agents Med Chem* 10, 183–194.

Lepper C, Partridge TA and Fan CM (2011). An absolute requirement for Pax7-positive satellite cells in acute injury-induced skeletal muscle regeneration. *Development* 138, 3639–3646.

Lexell J, Taylor CC and Sjöström M (1988). What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 84, 275–294.

Louis E, Raue U, Yang Y, Jemiolo B and Trappe S (2007). Time course of proteolytic, cytokine, and myostatin gene expression after acute exercise in human skeletal muscle. *J Appl Physiol* 103, 1744–1751.

Mauro A (1961). Satellite cell of skeletal muscle fibers. *J Biophys Biochem Cytol* 9, 493–495.

McCarthy JJ, Mula J, Miyazaki M, Erfani R, Garrison K, Farooqui AB, et al. (2011). Effective fiber hypertrophy in satellite cell-depleted skeletal muscle. *Development* 138, 3657–3666.

McCroskery S, Thomas M, Maxwell L, Sharma M and Kambadur R (2003). Myostatin negatively regulates satellite cell activation and self-renewal. *J Cell Biol* 162, 1135–1147.

McPherron AC, Lawler AM and Lee SJ (1997). Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. *Nature* 387, 83–90.

Mendias CL, Marciniak JE, Calderon DR and Faulkner JA (2006). Contractile properties of EDL and soleus muscles of myostatin-deficient mice. *J Appl Physiol* 101, 898–905.

Miller BF, Olesen JL, Hansen M, Dossing S, Cramer RM, Welling RJ, et al. (2005). Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. *J Physiol* 567, 1021–1033.

Mosher DS, Quignon P, Bustamante CD, Sutter NB, Mellers CS, Parker HG, et al. (2007). A mutation in the myostatin gene increases muscle mass and enhances racing performance in heterozygote dogs. *PLoS Genet* 3, e79.

Mourikis P, Sambasivan R, Castel D, Rocheteau P, Bizzarro V and Tajbakhsh S (2012). A critical requirement for notch signaling in maintenance of the quiescent skeletal muscle stem cell state. *Stem Cells* 30, 243–252.

O'Connor RS and Pavlath GK (2007). Point: Counterpoint: Satellite cell addition is/is not obligatory for skeletal muscle hypertrophy. *J Appl Physiol* 103, 1099–1100.

Ono Y, Calhabeu F, Morgan JE, Katagiri T, Amthor H and Zammit PS (2011). BMP signalling permits population expansion by preventing premature myogenic differentiation in muscle satellite cells. *Cell Death Differ* 18, 222–234.

Otto A, Schmidt C, Luke G, Allen S, Valasek P, Muntoni F, et al. (2008). Canonical Wnt signaling induces satellite-cell proliferation during adult skeletal muscle regeneration. *J Cell Sci* 121, 2939–2950.

Otto A, Collins-Hooper H, Patel A, Dash PR and Patel K (2011). Adult skeletal muscle stem cell migration is mediated by a blebbing/amoeboid mechanism. *Rejuvenation Res* 14, 249–260.

Pallafacchina G, Calabria E, Serrano AL, Kalhovde JM and Schiaffino S (2002). A protein kinase B-dependent and rapamycin-sensitive pathway controls skeletal muscle growth but not fiber type specification. *Proc Natl Acad Sci U S A* 99, 9213–9218.

Phillips SM, Tipton KD, Aarsland A, Wolf SE and Wolfe RR (1997). Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am J Physiol* 273, E99–107.

Philp A, Hamilton DL and Baar K (2011). Signals mediating skeletal muscle remodeling by resistance exercise: PI3-kinase independent activation of mTORC1. *J Appl Physiol* 110, 561–568.

Rosenblatt JD and Parry DJ (1992). Gamma irradiation prevents compensatory hypertrophy of overloaded mouse extensor digitorum longus muscle. *J Appl Physiol* 73, 2538–2543.

Sacco A, Doyonnas R, Kraft P, Vitorovic S and Blau HM (2008). Self-renewal and expansion of single transplanted muscle stem cells. *Nature* 456, 502–506.

Sale DG (1988). Neural adaptation to resistance training. *Med Sci Sports Exerc* 20, S135–S145.

Scharner J and Zammit PS (2011). The muscle satellite cell at 50: the formative years. *Skelet Muscle* 1, 28.

Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, et al. (2004). Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 350, 2682–2688.

Seale P, Sabourin LA, Girgis-Gabardo A, Mansouri A, Gruss P and Rudnicki MA (2000). Pax7 is required for the specification of myogenic satellite cells. *Cell* 102, 777–786.

Sherwood RI, Christensen JL, Conboy IM, Conboy MJ, Rando TA, Weissman IL, et al. (2004). Isolation of adult mouse myogenic progenitors: functional heterogeneity of cells within and engrafting skeletal muscle. *Cell* 119, 543–554.

Spangenburg EE, Le RD, Ward CW and Bodine SC (2008). A functional insulin-like growth factor receptor is not necessary for load-induced skeletal muscle hypertrophy. *J Physiol* 586, 283–291.

Studitsky AN (1964). Free auto- and homografts of muscle tissue in experiments on animals. *Ann N Y Acad Sci* 120, 789–801.

Sutrave P, Kelly AM and Hughes SH (1990). Ski can cause selective growth of skeletal muscle in transgenic mice. *Genes Dev* 4, 1462–1472.

Tipton KD, Ferrando AA, Phillips SM, Doyle D, Jr. and Wolfe RR (1999). Postexercise net pro-

- tein synthesis in human muscle from orally administered amino acids. *Am J Physiol* 276, E628–E634.
- Tseng BS, Kasper CE and Edgerton VR (1994). Cytoplasm-to-myonucleus ratios and succinate dehydrogenase activities in adult rat slow and fast muscle fibers. *Cell Tissue Res* 275, 39–49.
- Van CM, Duchateau J and Hainaut K (1998). Changes in single motor unit behaviour contribute to the increase in contraction speed after dynamic training in humans. *J Physiol* 513 Pt 1, 295–305.
- Weintraub H, Tapscott SJ, Davis RL, Hayer MJ, Adam MA, Lassar AB, et al. (1989). Activation of muscle-specific genes in pigment, nerve, fat, liver, and fibroblast cell lines by forced expression of MyoD. *Proc Natl Acad Sci U S A* 86, 5434–5438.
- Welle S, Bhatt K and Pinkert CA (2006). Myofibrillar protein synthesis in myostatin-deficient mice. *Am J Physiol Endocrinol Metab* 290, E409–E415.
- Welle S, Bhatt K, Pinkert CA, Tawil R and Horton CA (2007). Muscle growth after postdevelopmental myostatin gene knockout. *Am J Physiol Endocrinol Metab* 292, E985–E991.
- Welle S, Mehta S and Burgess K (2011). Effect of postdevelopmental myostatin depletion on myofibrillar protein metabolism. *Am J Physiol Endocrinol Metab* 300, E993–E1001.
- Whitmore LA, Song K, Li X, Aghajanian J, Davies M, Girgenrath S, et al. (2003). Inhibition of myostatin in adult mice increases skeletal muscle mass and strength. *Biochem Biophys Res Commun* 300, 965–971.
- Winbanks CE, Weeks KL, Homson RE, Sepulveda PV, Beyer C, Qian H, et al. (2012). Follistatin-mediated skeletal muscle hypertrophy is regulated by Smad3 and mTOR independently of myostatin. *J Cell Biol* 197, 997–1008.
- Zammit PS, Golding JP, Nagata Y, Hudon V, Partridge TA and Beauchamp JR (2004). Muscle satellite cells adopt divergent fates: a mechanism for self-renewal? *J Cell Biol* 166, 347–357.

■ جهت مطالعه بیشتر

- Bouchard C and Houman EP (2011). Genetic and molecular aspects of sports performance, Vol. 18 of *Encyclopedia of sports medicine*. John Wiley & Sons, Chichester.
- Peeters MW, Homis MA, Beunen GP and Malina RM (2009). Genetics and sports: an overview of the pre-molecular biology era. *Med Sport Sci* 54, 28–42.
- Pescatello LS and Roth SM (2011). *Exercise genomics* Springer, New York.
- Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, et al. (2004). Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 350, 2682–2688.
- Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, et al. (2003). ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet* 73, 627–631.

■ منابع

- Alfred T, Ben-Shlomo Y, Cooper R, Hardy R, Cooper C, Deary IJ, et al. (2011). ACTN3 genotype, athletic status, and life course physical capability: meta-analysis of the published literature and findings from nine studies. *Hum Mutat* 32, 1008–1018.
- Amthor H, Macharia R, Navarrete R, Schuelke M, Brown SC, Otto A, et al. (2007). Lack of myostatin results in excessive muscle growth but impaired force generation. *Proc Natl Acad Sci U S A* 104, 1835–1840.
- Binns MM, Boehler DA and Lambert DH (2010). Identification of the myostatin locus (MSTN) as having a major effect on optimum racing distance in the thoroughbred horse in the USA. *Anim Genet* 41 Suppl 2, 154–158.
- Bogl LH, Latvala A, Kaprio J, Sovijarvi O, Rissanen A and Pietilainen KH (2011). An investigation into the relationship between soft tissue body composition and bone mineral density in a young adult twin sample. *J Bone Miner Res* 26, 79–87.
- Coleman ME, DeMayo F, Yin KC, Lee HM, Geske R, Montgomery C, et al. (1995). Myogenic vector expression of insulin-like growth factor I stimulates muscle cell differentiation and myofiber hypertrophy in transgenic mice. *J Biol Chem* 270, 12109–12116.
- Dahiya S, Bhatnagar S, Hindi SM, Jiang C, Paul PK, Kuang S and Kumar A (2011). Elevated levels of active matrix metalloproteinase-9 cause hypertrophy in skeletal muscle of normal and dystrophin-deficient mdx mice. *Hum Mol*

- Genet 20, 4345–4359.
- De Mars G, Windelinckx A, Huygens W, Peeters MW, Beunen GP, Aerssens J, et al. (2008). Genome-wide linkage scan for maximum and length-dependent knee muscle strength in young men: significant evidence for linkage at chromosome 14q24.3. *J Med Genet* 45, 275–283.
- Delmonico MJ, Kostek MC, Doldo NA, Hand BD, Walsh S, Conway JM, et al. (2007). Alpha-actinin-3 (ACTN3) R577X polymorphism influences knee extensor peak power response to strength training in older men and women. *J Gerontol A Biol Sci Med Sci* 62, 206–212.
- Grundberg E, Brandstrom H, Ribom EL, Ljunggren O, Mallmin H and Kindmark A (2004). Genetic variation in the human vitamin D receptor is associated with muscle strength, fat mass and body weight in Swedish women. *Eur J Endocrinol* 150, 323–328.
- Hall KD (2010). Mathematical modelling of energy expenditure during tissue deposition. *Br J Nutr* 104, 4–7.
- Haq S, Kilter H, Michael A, Tao J, O’Leary E, Sun XM, et al. (2003). Deletion of cytosolic phospholipase A2 promotes striated muscle growth. *Nat Med* 9, 944–951.
- Hsu FC, Lenchik L, Nicklas BJ, Lohman K, Register TC, Mychaleckyj J, et al. (2005). Heritability of body composition measured by DXA in the diabetes heart study. *Obes Res* 13, 312–319.
- Hubal MJ, Gordish-Dressman H, hompson PD, Price TB, Hoffman EP, Angelopoulos TJ, et al. (2005). Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc* 37, 964–972.
- Hughes DC, Day SH, Ahmetov II and Williams AG (2011). Genetics of muscle strength and power: Polygenic profile similarity limits skeletal muscle performance. *J Sports Sci* 29, 1425–1434.
- Huygens W, homis MA, Peeters MW, Aerssens J, Janssen R, Vlietinck RF, et al. (2004a). Linkage of myostatin pathway genes with knee strength in humans. *Physiol Genomics* 17, 264–270.
- Huygens W, homis MA, Peeters MW, Vlietinck RF and Beunen GP (2004b). Determinants and upper-limit heritabilities of skeletal muscle mass and strength. *Can J Appl Physiol* 29, 186–200.
- Huygens W, homis MA, Peeters MW, Aerssens J, Vlietinck R and Beunen GP (2005). Quantitative trait loci for human muscle strength: linkage analysis of myostatin pathway genes. *Physiol Genomics* 22, 390–397.
- Janssen I, Heymsfield SB, Wang ZM and Ross R (2000). Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol* 89, 81–88.
- Kostek MC, Delmonico MJ, Reichel JB, Roth SM, Douglass L, Ferrell RE, et al. (2005). Muscle strength response to strength training is influenced by insulin-like growth factor 1 genotype in older adults. *J Appl Physiol* 98, 2147–2154.
- Lai KM, Gonzalez M, Poueymirou WT, Kline WO, Na E, Zlotchenko E, et al. (2004). Conditional activation of akt in adult skeletal muscle induces rapid hypertrophy. *Mol Cell Biol* 24, 9295–9304.
- Lee SJ (2007). Quadrupling muscle mass in mice by targeting TGF-beta signaling pathways. *PLoS ONE* 2, e789.
- Lexell J, Taylor CC and Sjostrom M (1988). What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 84, 275–294.
- Lionikas A, Cheng R, Lim JE, Palmer AA and Blizard DA (2010). Fine-mapping of muscle weight QTL in LG/J and SM/J intercrosses. *Physiol Genomics* 42A, 33–38.
- Liu D, Metter EJ, Ferrucci L and Roth SM (2008). TNF promoter polymorphisms associated with muscle phenotypes in humans. *J Appl Physiol* 105, 859–867.
- MacArthur DG, Seto JT, Chan S, Quinlan KG, Raftery JM, Turner N, et al. (2008). An Actn3 knockout mouse provides mechanistic insights into the association between alpha-actinin-3 deficiency and human athletic performance. *Hum Mol Genet* 17, 1076–1086.
- McPherron AC and Lee SJ (1997). Double muscling in cattle due to mutations in the myostatin gene. *Proc Natl Acad Sci U S A* 94, 12457–12461.
- McPherron AC and Lee SJ (2002). Suppression of body fat accumulation in myostatin-deficient mice. *J Clin Invest* 109, 595–601.
- McPherron AC, Lawler AM and Lee SJ (1997). Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. *Nature* 387, 83–90.
- Mills M, Yang N, Weinberger R, Vander Woude DL, Beggs AH, Eastale S and North K (2001). Differential expression of the actin-binding proteins, alpha-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. *Hum Mol Genet* 10, 1335–1346.
- Mosher DS, Quignon P, Bustamante CD, Sutter NB, Mellersh CS, Parker HG, et al. (2007). A mutation in the myostatin gene increases muscle mass and enhances racing performance in heterozygote dogs. *PLoS Genet* 3, e79.

- Nimmo MA, Wilson RH and Snow DH (1985). The inheritance of skeletal muscle fibre composition in mice. *Comp Biochem Physiol A Comp Physiol* 81, 109–115.
- North KN, Yang N, Wattanasirichaigoon D, Mills M, Eastale S and Beggs AH (1999). A common non-sense mutation results in alpha-actinin-3 deficiency in the general population. *Nat Genet* 21, 353–354.
- Ohanna M, Sobering AK, Lapointe T, Lorenzo L, Praud C, Petroulakis E, et al. (2005). Atrophy of S6K1(-/-) skeletal muscle cells reveals distinct mTOR effectors for cell cycle and size control. *Nat Cell Biol* 7, 286–294.
- Ontell MP, Sopper MM, Lyons G, Buckingham M and Ontell M (1993). Modulation of contractile protein gene expression in fetal murine crural muscles: emergence of muscle diversity. *Dev Dyn* 198, 203–213.
- Peeters MW, homis MA, Beunen GP and Malina RM (2009). Genetics and sports: an overview of the pre-molecular biology era. *Med Sport Sci* 54, 28–42.
- Proud CG (2004). mTOR-mediated regulation of translation factors by amino acids. *Biochem Biophys Res Commun* 313, 429–436.
- Riechman SE, Balasekaran G, Roth SM and Ferrell RE (2004). Association of interleukin-15 protein and interleukin-15 receptor genetic variation with resistance exercise training responses. *J Appl Physiol* 97, 2214–2219.
- Roth SM, Schrager MA, Ferrell RE, Riechman SE, Metter EJ, Lynch NA, et al. (2001). CNTF genotype is associated with muscular strength and quality in humans across the adult age span. *J Appl Physiol* 90, 1205–1210.
- Santiago C, Ruiz JR, Rodríguez-Romo G, Fiuza-Luces C, Yvert T, Gonzalez-Freire M, et al. (2011). The K153R polymorphism in the myostatin gene and muscle power phenotypes in young, non-athletic men. *PLoS ONE* 6, e16323.
- Sayer AA, Syddall H, O'Dell SD, Chen XH, Briggs PJ, Briggs R, et al. (2002). Polymorphism of the IGF2 gene, birth weight and grip strength in adult men. *Age Ageing* 31, 468–470.
- Schrager MA, Roth SM, Ferrell RE, Metter EJ, Russek-Cohen E, Lynch NA, et al. (2004). Insulin-like growth factor-2 genotype, fat-free mass, and muscle performance across the adult life span. *J Appl Physiol* 97, 2176–2183.
- Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, et al. (2004). Myostatin mutation associated with gross muscle hypertrophy in a child. *N Engl J Med* 350, 2682–2688.
- Seale P, Sabourin LA, Girgis-Gabardo A, Mansouri A, Gruss P and Rudnicki MA (2000). Pax7 is required for the specification of myogenic satellite cells. *Cell* 102, 777–786.
- Silventoinen K, Magnusson PK, Tynelius P, Kaprio J and Rasmussen F (2008). Heritability of body size and muscle strength in young adulthood: a study of one million Swedish men. *Genet Epidemiol* 32, 341–349.
- Smerdu V, Karsch-Mizrachi I, Campione M, Leinwand L and Schiaffino S (1994). Type Iix myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle. *Am J Physiol* 267, C1723–C1728.
- Souren NY, Paulussen AD, Loos RJ, Gielen M, Beunen G, Fagard R, et al. (2007). Anthropometry, carbohydrate and lipid metabolism in the East Flanders Prospective Twin Survey: heritabilities. *Diabetologia* 50, 2107–2116.
- Sutrave P, Kelly AM and Hughes SH (1990). ski can cause selective growth of skeletal muscle in transgenic mice. *Genes Dev* 4, 1462–1472.
- Totsuka Y, Nagao Y, Horii T, Yonekawa H, Imai H, Hatta H, et al. (2003). Physical performance and soleus muscle fiber composition in wild-derived and laboratory inbred mouse strains. *J Appl Physiol* 95, 720–727.
- Vincent B, De Bock K, Ramaekers M, Van den Eede E, Van Leemputte M, Hespel P, et al. (2007). ACTN3 (R577X) genotype is associated with fiber type distribution. *Physiol Genomics* 32, 58–63.
- Wang P, Ma LH, Wang HY, Zhang W, Tian Q, Cao DN, Zheng GX and Sun YL (2006). Association between polymorphisms of vitamin D receptor gene Apal, BsmI and TaqI and muscular strength in young Chinese women. *Int J Sports Med* 27, 182–186.
- Welle S, Mehta S and Burgess K (2011). Effect of postdevelopmental myostatin depletion on myofibrillar protein metabolism. *Am J Physiol Endocrinol Metab* 300, E993–E1001.
- Wheeler DA, Srinivasan M, Egholm M, Shen Y, Chen L, McGuire A, et al. (2008). The complete genome of an individual by massively parallel DNA sequencing. *Nature* 452, 872–876.
- Whittemore LA, Song K, Li X, Aghajanian J, Davies M, Girgenrath S, et al. (2003). Inhibition of myostatin in adult mice increases skeletal muscle mass and strength. *Biochem Biophys Res Commun* 300, 965–971.
- Windelinckx A, De Mars G, Huygens W, Peeters MW, Vincent B, Wijmenga C, et al. (2011). Comprehensive fine mapping of chr12q12–14 and follow-up replication identify activin receptor 1B (ACVR1B) as a muscle strength gene. *Eur J Hum Genet* 19, 208–215.
- Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Eastale S, and North K (2003). ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet* 73, 627–631.

- Atherton PJ and Smith K (2012). Muscle protein synthesis in response to nutrition and exercise. *J Physiol* 590, 1049–1057.
- Bilan PJ, Samokhvalov V, Koshkina A, Schertzer JD, Samaan MC and Klip A (2009). Direct and macrophage-mediated actions of fatty acids causing insulin resistance in muscle cells. *Arch Physiol Biochem* 115, 176–190.
- Gallen IW, Hume C and Lumb A (2011). Fuelling the athlete with type 1 diabetes. *Diabetes Obes Metab* 13, 130–136.
- Cummings DE and Overduin J (2007). Gastrointestinal regulation of food intake. *J Clin Invest* 117, 13–23.
- Hawley JA, Schabort EJ, Noakes TD and Dennis SC (1997). Carbohydrate-loading and exercise performance. An update. *Sports Med* 24, 73–81.
- Philp A, Hargreaves M and Baar K (2012). More than a store: regulatory roles for glycogen in skeletal muscle adaptation to exercise. *Am J Physiol Endocrinol Metab* 302, E1343–E1351.
- Watt MJ and Hoy AJ (2012). Lipid metabolism in skeletal muscle: generation of adaptive and maladaptive intracellular signals for cellular function. *Am J Physiol Endocrinol Metab* 302, E1315–E1328.

- Al MO, Pardo M, Roca-Rivada A, Castela C, Casanueva FF and Seoane LM (2010b). Macronutrients act directly on the stomach to regulate gastric ghrelin release. *J Endocrinol Invest* 33, 599–602.
- Allirot X, Saulais L, Seyssel K, Graeppi-Dulac J, Roth H, Charrie A, et al. (2013b). An isocaloric increase of eating episodes in the morning contributes to decrease energy intake at lunch in lean men. *Physiol Behav* 110–111, 169–178.
- Andrali SS, Sampley ML, Vanderford NL and Ozcan S (2008). Glucose regulation of insulin gene expression in pancreatic beta-cells. *Biochem J* 415, 1–10.
- Andre C and Cota D (2012). Coupling nutrient sensing to metabolic homeostasis: the role of the mammalian target of rapamycin complex 1 pathway. *Proc Nutr Soc* 71, 502–510.
- Areta JL, Burke LM, Ross ML, Camera DM, West DW, Broad EM, et al. (2013b). Timing and distribution of protein ingestion during prolonged recovery from resistance exercise alters myofibrillar protein synthesis. *J Physiol* 591, 2319–2331.
- Ashford M, Beall C and McCrimmon R (2012). Hypoglycaemia: exercise for the brain? *J Neuroendocrinol* 24, 1365–1366.
- Banks WA, Coon AB, Robinson SM, Moinuddin A, Shultz JM, Nakaoke R, et al. (2004). Triglycerides induce leptin resistance at the blood–brain barrier. *Diabetes* 53, 1253–1260.
- Bansal P and Wang Q (2008a). Insulin as a physiological modulator of glucagon secretion. *Am J Physiol Endocrinol Metab* 295, E751–E761.
- Batterham RL and Bloom SR (2003a). The gut hormone peptide YY regulates appetite. *Ann N Y Acad Sci* 994, 162–168.
- Beall C, Ashford ML and McCrimmon RJ (2012a). The physiology and pathophysiology of the neural control of the counterregulatory response. *Am J Physiol Regul Integr Comp Physiol* 302, R215–R223.
- Beelen M, Berghuis J, Bonaparte B, Ballak SB, Jeukendrup AE and van Loon LJ (2009). Carbohydrate mouth rinsing in the fed state: lack of enhancement of time-trial performance. *Int J Sport Nutr Exerc Metab* 19, 400–409.
- Bergstrom J and Hultman E (1966). Muscle glycogen synthesis after exercise: an enhancing factor localized to the muscle cells in man. *Nature* 210, 309–310.
- Bergstrom J and Hultman E (1967). A study of the glycogen metabolism during exercise in man. *Scand J Clin Lab Invest* 19, 218–228.
- Bjorbaek C, Elmquist JK, Frantz JD, Shoelson SE and Flier JS (1998). Identification of SOCS-3 as a potential mediator of central leptin resistance. *Mol Cell* 1, 619–625.
- Blundell JE (2006). Perspective on the central control of appetite. *Obesity (Silver Spring)* 14 Suppl 4, 160S–163S.
- Bohe J, Low JF, Wolfe RR and Rennie MJ (2001). Latency and duration of stimulation of human muscle protein synthesis during continuous infusion of amino acids. *J Physiol* 532, 575–579.
- Bohe J, Low A, Wolfe RR and Rennie MJ (2003). Human muscle protein synthesis is modulated by extracellular, not intramuscular amino acid availability: a dose-response study. *J Physiol* 552, 315–324.
- Boirie Y, Dangin M, Gachon P, Vasson MP, Maubois JL and Beaufriere B (1997). Slow and fast dietary proteins differentially modulate postprandial protein accretion. *Proc Natl Acad Sci U S A* 94, 14930–14935.
- Brazeau AS, Rabasa-Lhoret R, Strychar I and Mircescu H (2008). Barriers to physical activity among patients with type 1 diabetes. *Diabetes Care* 31, 2108–2109.

- Burke LM, Millet G and Tarnopolsky MA (2007). Nutrition for distance events. *J Sports Sci* 25 Suppl 1, S29–S38.
- Chambers ES, Bridge MW and Jones DA (2009). Carbohydrate sensing in the human mouth: effects on exercise performance and brain activity. *J Physiol* 587, 1779–1794.
- Chen K, Li F, Li J, Cai H, Strom S, Bisello A, et al. (2006). Induction of leptin resistance through direct interaction of C-reactive protein with leptin. *Nat Med* 12, 425–432.
- Christie GR, Hajdudich E, Hundal HS, Proud CG and Taylor PM (2002). Intracellular sensing of amino acids in *Xenopus laevis* oocytes stimulates p70 S6 kinase in a target of rapamycin-dependent manner. *J Biol Chem* 277, 9952–9957.
- Churchward-Venne TA, Burd NA and Phillips SM (2012). Nutritional regulation of muscle protein synthesis with resistance exercise: strategies to enhance anabolism. *Nutr Metab (Lond)* 9, 40.
- Crozier SJ, Kimball SR, Emmert SW, Anthony JC and Jefferson LS (2005). Oral leucine administration stimulates protein synthesis in rat skeletal muscle. *J Nutr* 135, 376–382.
- Cryer PE (2005). Mechanisms of hypoglycemia-associated autonomic failure and its component syndromes in diabetes. *Diabetes* 54, 3592–3601.
- Cryer PE (2008). Hypoglycemia: still the limiting factor in the glycemic management of diabetes. *Endocr Pract* 14, 750–756.
- Cryer PE (2009). Exercise-related hypoglycemia-associated autonomic failure in diabetes. *Diabetes* 58, 1951–1952.
- Cummings DE and Overduin J (2007). Gastrointestinal regulation of food intake. *J Clin Invest* 117, 13–23.
- Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, et al. (2005). Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. *FASEB J* 19, 422–424.
- D'Alessio DA, Kahn SE, Leusner CR and Ensink JW (1994). Glucagon-like peptide 1 enhances glucose tolerance both by stimulation of insulin release and by increasing insulin-independent glucose disposal. *J Clin Invest* 93, 2263–2266.
- Dickinson JM, Fry CS, Drummond MJ, Gundermann DM, Walker DK, Glynn EL, et al. (2011). Mammalian target of rapamycin complex 1 activation is required for the stimulation of human skeletal muscle protein synthesis by essential amino acids. *J Nutr* 141, 856–862.
- Dodd KM and Tee AR (2012). Leucine and mTORC1: a complex relationship. *Am J Physiol Endocrinol Metab* 302, E1329–E1342.
- Drummond MJ, Dickinson JM, Fry CS, Walker DK, Gundermann DM, Reidy PT, et al. (2012). Bed rest impairs skeletal muscle amino acid transporter expression, mTORC1 signaling, and protein synthesis in response to essential amino acids in older adults. *Am J Physiol Endocrinol Metab* 302, E1113–E1122.
- Fares EJ and Kayser B (2011). Carbohydrate mouth rinse effects on exercise capacity in pre- and postprandial states. *J Nutr Metab* 2011, 385962.
- Friedman JM and Halaas JL (1998). Leptin and the regulation of body weight in mammals. *Nature* 395, 763–770.
- Galassetti P, Tate D, Neill RA, Richardson A, Leu SY and Davis SN (2006). Effect of differing antecedent hypoglycemia on counterregulatory responses to exercise in type 1 diabetes. *Am J Physiol Endocrinol Metab* 290, E1109–E1117.
- Gallen IW, Hume C and Lumb A (2011). Fuelling the athlete with type 1 diabetes. *Diabetes Obes Metab* 13, 130–136.
- Gant N, Stinear CM and Byblow WD (2010). Carbohydrate in the mouth immediately facilitates motor output. *Brain Res* 1350, 151–158.
- Hawley JA, Schabort EJ, Noakes TD and Dennis SC (1997). Carbohydrate-loading and exercise performance. An update. *Sports Med* 24, 73–81.
- Hawley JA, Burke LM, Phillips SM and Spriet LL (2011). Nutritional modulation of training-induced skeletal muscle adaptations. *J Appl Physiol* 110, 834–845.
- Henquin JC (2009). Regulation of insulin secretion: a matter of phase control and amplitude modulation. *Diabetologia* 52, 739–751.
- Holloszy JO (2005). Exercise-induced increase in muscle insulin sensitivity. *J Appl Physiol* 99, 338–343.
- Holst JJ (2007). The physiology of glucagon-like peptide 1. *Physiol Rev* 87, 1409–1439.
- Hyde R, Peyrollier K and Hundal HS (2002). Insulin promotes the cell surface recruitment of the SAT2/ATA2 system A amino acid transporter from an endosomal compartment in skeletal muscle cells. *J Biol Chem* 277, 13628–13634.
- Jewell JL, Russell RC and Guan KL (2013). Amino acid signalling upstream of mTOR. *Nat Rev Mol Cell Biol* 14, 133–139.
- Jiang G and Zhang BB (2003). Glucagon and regulation of glucose metabolism. *Am J Physiol Endocrinol Metab* 284, E671–E678.
- Jordan SD, Konner AC and Bruning JC (2010). Sensing the fuels: glucose and lipid signaling in the CNS controlling energy homeostasis. *Cell Mol Life Sci* 67, 3255–3273.
- Jorpes E, Mutt V and Olbe L (1959). On the biological assay of cholecystokinin and its dosage in cholecystography. *Acta Physiol Scand* 47, 109–114.
- Kim E and Guan KL (2009). RAG GTPases in nutrient-mediated TOR signaling pathway. *Cell Cycle* 8, 1014–1018.

- Kimball SR and Jefferson LS (2005). Role of amino acids in the translational control of protein synthesis in mammals. *Semin Cell Dev Biol* 16, 21–27.
- Kissileff HR, Carretta JC, Geliebter A and Pi-Sunyer FX (2003b). Cholecystokinin and stomach distension combine to reduce food intake in humans. *Am J Physiol Regul Integr Comp Physiol* 285, R992–R998.
- Kristensen M and Jensen MG (2011). Dietary fibres in the regulation of appetite and food intake. Importance of viscosity. *Appetite* 56, 65–70.
- Lane SC, Bird SR, Burke LM and Hawley JA (2013). Effect of a carbohydrate mouth rinse on simulated cycling time-trial performance commenced in a fed or fasted state. *Appl Physiol Nutr Metab* 38, 134–139.
- Lewis LD and Williams JA (1990). Regulation of cholecystokinin secretion by food, hormones, and neural pathways in the rat. *Am J Physiol* 258, G512–G518.
- Luyckx AS and Lefebvre PJ (1974). Mechanisms involved in the exercise-induced increase in glucagon secretion in rats. *Diabetes* 23, 81–93.
- Lyly M, Ohls N, Lahteenmaki L, Salmenkallio-Marttila M, Liukkonen KH, Karhunen L, et al. (2010). The effect of fibre amount, energy level and viscosity of beverages containing oat fibre supplement on perceived satiety. *Food Nutr Res* 54. Mangelsdorf DJ and Evans RM (1995). The RXR heterodimers and orphan receptors. *Cell* 83, 841–850.
- Massa ML, Gagliardino JJ and Francini F (2011). Liver glucokinase: An overview on the regulatory mechanisms of its activity. *IUBMB Life* 63, 1–6.
- Mettler S, Mitchell N and Tipton KD (2010). Increased protein intake reduces lean body mass loss during weight loss in athletes. *Med Sci Sports Exerc* 42, 326–337.
- Miller BF, Olesen JL, Hansen M, Dossing S, Cramer RM, Welling RJ, et al. (2005). Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. *J Physiol* 567, 1021–1033.
- Moore DR, Robinson MJ, Fry JL, Tang JE, Glover EI, Wilkinson SB, et al. (2009). Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. *Am J Clin Nutr* 89, 161–168.
- Moran TH (2000). Cholecystokinin and satiety: current perspectives. *Nutrition* 16, 858–865.
- Mountjoy PD and Rutter GA (2007). Glucose sensing by hypothalamic neurones and pancreatic islet cells: AMPle evidence for common mechanisms? *Exp Physiol* 92, 311–319.
- Newsholme P, Gaudel C and McClenaghan NH (2010). Nutrient regulation of insulin secretion and beta-cell functional integrity. *Adv Exp Med Biol* 654, 91–114.
- Nicklin P, Bergman P, Zhang B, Triantafellow E, Wang H, Nyfeler B, et al. (2009). Bidirectional transport of amino acids regulates mTOR and autophagy. *Cell* 136, 521–534.
- Nilsson LH and Hultman E (1973). Liver glycogen in man—the effect of total starvation or a carbohydrate-poor diet followed by carbohydrate refeeding. *Scand J Clin Lab Invest* 32, 325–330.
- Pasiakos SM, Vislocky LM, Carbone JW, Altieri N, Konopelski K, Freake HC, et al. (2010b). Acute energy deprivation affects skeletal muscle protein synthesis and associated intracellular signaling proteins in physically active adults. *J Nutr* 140, 745–751.
- Pennings B, Boirie Y, Senden JM, Gijsen AP, Kuipers H and van Loon LJ (2011). Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. *Am J Clin Nutr* 93, 997–1005.
- Petersen KF, Dufour S, Savage DB, Bilz S, Solomon G, Yonemitsu S, et al. (2007). The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome. *Proc Natl Acad Sci U S A* 104, 12587–12594.
- Peyrollier K, Hajduch E, Blair AS, Hyde R and Hundal HS (2000). L-Leucine availability regulates phosphatidylinositol 3-kinase, p70 S6 kinase and glycogen synthase kinase-3 activity in L6 muscle cells: evidence for the involvement of the mammalian target of rapamycin (mTOR) pathway in the L-leucine-induced up-regulation of system A amino acid transport. *Biochem J* 350 Pt 2, 361–368.
- Plaisancie P, Dumoulin V, Chayvialle JA and Cuber JC (1996). Luminal peptide YY-releasing factors in the isolated vascularly perfused rat colon. *J Endocrinol* 151, 421–429.
- Ramnanan CJ, Edgerton DS, Kraft G and Cherrington AD (2011). Physiologic action of glucagon on liver glucose metabolism. *Diabetes Obes Metab* 13 Suppl 1, 118–125.
- Rocha DM, Faloona GR and Unger RH (1972). Glucagon-stimulating activity of 20 amino acids in dogs. *J Clin Invest* 51, 2346–2351.
- Rollo I and Williams C (2011). Effect of mouth-rinsing carbohydrate solutions on endurance performance. *Sports Med* 41, 449–461.
- Sancak Y, Bar-Peled L, Zoncu R, Markhard AL, Nada S and Sabatini DM (2010). Ragulator-Rag complex targets mTORC1 to the lysosomal surface and is necessary for its activation by amino acids. *Cell* 141, 290–303.
- Schwartz MW (2000). Biomedicine. Staying slim with insulin in mind. *Science* 289, 2066–2067.
- Simpson KA, Martin NM and Bloom SR (2009). Hypothalamic regulation of food intake and clinical therapeutic applications. *Arq Bras Endocrinol Metabol* 53, 120–128.

- Spanswick D, Smith MA, Mirshamsi S, Routh VH and Ashford ML (2000). Insulin activates ATP- sensitive K⁺ channels in hypothalamic neurons of lean, but not obese rats. *Nat Neurosci* 3, 757–758.
- Strader AD and Woods SC (2005). Gastrointestinal hormones and food intake. *Gastroenterology* 128, 175–191.
- Suzuki K, Simpson KA, Minnion JS, Shillito JC and Bloom SR (2010). The role of gut hormones and the hypothalamus in appetite regulation. *Endocr J* 57, 359–372.
- Tanaka K, Inoue S, Nagase H and Takamura Y (1990). Modulation of arginine-induced insulin and glucagon secretion by the hepatic vagus nerve in the rat: effects of celiac vagotomy and administration of atropine. *Endocrinology* 127, 2017–2023.
- Tang JE, Moore DR, Kujbida GW, Tarnopolsky MA and Phillips SM (2009a). Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. *J Appl Physiol* 107, 987–992.
- Tipton KD, Ferrando AA, Phillips SM, Doyle D, Jr. and Wolfe RR (1999a). Postexercise net protein synthesis in human muscle from orally administered amino acids. *Am J Physiol* 276, E628–E634.
- Vuksan V, Panahi S, Lyon M, Rogovik AL, Jenkins AL and Leiter LA (2009). Viscosity of fiber preloads affects food intake in adolescents. *Nutr Metab Cardiovasc Dis* 19, 498–503.
- Walberg JL, Leidy MK, Sturgill DJ, Hinkle DE, Ritchey SJ and Sebolt DR (1988). Macronutrient content of a hypoenergy diet affects nitrogen retention and muscle function in weight lifters. *Int J Sports Med* 9, 261–266.
- Wang GJ, Tomasi D, Backus W, Wang R, Telang F, Geliebter A, et al. (2008). Gastric distention activates satiety circuitry in the human brain. *Neuroimage* 39, 1824–1831.
- Westertep-Plantenga MS, Lemmens SG and Westertep KR (2012). Dietary protein – its role in satiety, energetics, weight loss and health. *Br J Nutr* 108 Suppl 2, S105–S112.
- Winder WW, Wilson HA, Hardie DG, Rasmussen BB, Hutber CA, Call GB, et al. (1997). Phosphorylation of rat muscle acetyl-CoA carboxylase by AMP-activated protein kinase and protein kinase A. *J Appl Physiol* 82, 219–225.
- Winder WW, Holmes BF, Rubink DS, Jensen EB, Chen M and Holloszy JO (2000). Activation of AMP-activated protein kinase increases mitochondrial enzymes in skeletal muscle. *J Appl Physiol* 88, 2219–2226.
- Yang Y, Breen L, Burd NA, Hector AJ, Churchward-Venne TA, Josse AR, et al. (2012). Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. *Br J Nutr* 1–9.
- Yeo WK, Carey AL, Burke L, Spriet LL and Hawley JA (2011). Fat adaptation in well-trained athletes: effects on cell metabolism. *J Appl Physiol Nutr Metab* 36, 12–22.
- Zhang Y, Proenca R, Maffei M, Barone M, Leopold L and Friedman JM (1994). Positional cloning of the mouse obese gene and its human homologue. *Nature* 372, 425–432.

■ جهت مطالعه بیشتر

- Abdul-Ghani MA and DeFronzo RA (2010). Pathogenesis of insulin resistance in skeletal muscle. *J Biomed Biotechnol* 2010, 476279.
- Bramble DM and Lieberman DE (2004). Endurance running and the evolution of homo. *Nature* 432, 345–352.
- Kahn SE, Hull RL and Utzschneider KM (2006). Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature* 444, 840–846.
- Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346, 393–403.
- Muoio DM and Newgard CB (2008). Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. *Nat Rev Mol Cell Biol* 9, 193–205.
- Rose AJ and Richter EA (2005). Skeletal muscle glucose uptake during exercise: how is it regulated? *Physiology (Bethesda)* 20, 260–270.

■ منابع

- Abdul-Ghani MA and DeFronzo RA (2010). Pathogenesis of insulin resistance in skeletal muscle. *J Biomed Biotechnol* 2010, 476279.

- Amati F, Dubé JJ, Alvarez-Carnero E, Edreira MM, Chomentowski P, Coen PM, et al. (2011). Skeletal muscle triglycerides, diacylglycerols, and ceramides in insulin resistance: another paradox in endurance-trained athletes? *Diabetes* 60, 2588–2597.
- ADA (American Diabetes Association) (2013). Standards of medical care in diabetes – 2013. *Diabetes Care* 36 Suppl 1, S11–S66.
- Archer E and Blair SN (2011). Physical activity and the prevention of cardiovascular disease: from evolution to epidemiology. *Prog Cardiovasc Dis* 53, 387–396.
- Barker DJ (1997). Maternal nutrition, fetal nutrition, and disease in later life. *Nutrition* 13, 807–813.
- Baur JA, Pearson KJ, Price NL, Jamieson HA, Lerin C, Kalra A, et al. (2006). Resveratrol improves health and survival of mice on a high-calorie diet. *Nature* 444, 337–342.
- Bergstrom J and Hultman E (1966). Muscle glycogen synthesis after exercise: an enhancing factor localized to the muscle cells in man. *Nature* 210, 309–310.
- Bersaglieri T, Sabeti PC, Patterson N, Vanderploeg T, Schanner SF, Drake JA, et al. (2004). Genetic signatures of strong recent positive selection at the lactase gene. *Am J Hum Genet* 74, 1111–1120.
- Billings LK and Florez JC (2010). The genetics of type 2 diabetes: what have we learned from GWAS? *Ann N Y Acad Sci* 1212, 59–77.
- Blair SN, Kampert JB, Kohl HW, III, Barlow CE, Macera CA, Paffenbarger RS, Jr., et al. (1996). Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA* 276, 205–210.
- Boule NG, Weisnagel SJ, Lakka TA, Tremblay A, Bergman RN, Rankinen T, et al. (2005). Effects of exercise training on glucose homeostasis: the HERITAGE Family Study. *Diabetes Care* 28, 108–114.
- Bramble DM and Lieberman DE (2004). Endurance running and the evolution of homo. *Nature* 432, 345–352.
- Cerling TE, Wynn JG, Andanje SA, Bird MI, Korir DK, Levin NE, et al. (2011). Woody cover and hominin environments in the past 6 million years. *Nature* 476, 51–56.
- Chakravarthy MV and Booth FW (2004). Eating, exercise, and “thrifty” genotypes: connecting the dots toward an evolutionary understanding of modern chronic diseases. *J Appl Physiol* 96, 3–10.
- Cnop M, Foufelle F and Velloso LA (2011). Endoplasmic reticulum stress, obesity and diabetes. *Trends Mol Med* 18, 59–68.
- Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. (2011). National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet* 378, 31–40.
- Danforth WH (1965). Glycogen synthetase activity in skeletal muscle. Interconversion of two forms and control of glycogen synthesis. *J Biol Chem* 240, 588–593.
- DeFronzo RA, Ferrannini E, Sato Y, Felig P and Wahren J (1981). Synergistic interaction between exercise and insulin on peripheral glucose uptake. *J Clin Invest* 68, 1468–1474.
- Diamond J (2003). The double puzzle of diabetes. *Nature* 423, 599–602.
- Dolinoy DC (2008). The agouti mouse model: an epigenetic biosensor for nutritional and environmental alterations on the fetal epigenome. *Nutr Rev* 66 Suppl 1, S7–11.
- Elia M (2000). Hunger disease. *Clin Nutr* 19, 379–386.
- Ferrannini E, Barrett EJ, Bevilacqua S and DeFronzo RA (1983). Effect of fatty acids on glucose production and utilization in man. *J Clin Invest* 72, 1737–1747.
- Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. (2011). National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 377, 557–567.
- George S, Rochford JJ, Wolfrum C, Gray SL, Schinner S, Wilson JC, et al. (2004). A family with severe insulin resistance and diabetes due to a mutation in AKT2. *Science* 304, 1325–1328.
- Gluckman PD, Hanson MA, Buklijas T, Low FM and Beedle AS (2009). Epigenetic mechanisms that underpin metabolic and cardiovascular diseases. *Nat Rev Endocrinol* 5, 401–408.
- Goh KP and Sum CF (2010). Connecting the dots: molecular and epigenetic mechanisms in type 2 diabetes. *Curr Diabetes Rev* 6, 255–265.
- Gollnick PD, Piehl K and Saltin B (1974). Selective glycogen depletion pattern in human muscle fibres after exercise of varying intensity and at varying pedalling rates. *J Physiol* 241, 45–57.

- Gordon BA, Benson AC, Bird SR and Fraser SF (2009). Resistance training improves metabolic health in type 2 diabetes: a systematic review. *Diabetes Res Clin Pract* 83, 157–175.
- Gresham D, Desai MM, Tucker CM, Jenq HT, Pai DA, Ward A, et al. (2008). e repertoire and dynamics of evolutionary adaptations to controlled nutrient-limited environments in yeast. *PLoS Genet* 4, e1000303.
- Hansen PA, Gulve EA, Marshall BA, Gao J, Pessin JE, Holloszy JO and Mueckler M (1995). Skeletal muscle glucose transport and metabolism are enhanced in transgenic mice overexpressing the Glut4 glucose transporter. *J Biol Chem* 270, 1679–1684.
- Hardie DG, Scott JW, Pan DA and Hudson ER (2003). Management of cellular energy by the AMP-activated protein kinase system. *FEBS Lett* 546, 113–120.
- Hart GW, Slawson C, Ramirez-Correa G and Lagerlof O (2011). Cross talk between O-GlcNAcylation and phosphorylation: roles in signaling, transcription, and chronic disease. *Annu Rev Biochem* 80, 825–858.
- Hill AM, Fleming JA and Kris-Etherton PM (2009). the role of diet and nutritional supplements in preventing and treating cardiovascular disease. *Curr Opin Cardiol* 24, 433–441.
- Holloszy JO (2008). Regulation by exercise of skeletal muscle content of mitochondria and GLUT4. *J Physiol Pharmacol* 59 Suppl 7, 5–18.
- Holloszy JO (2009). Skeletal muscle ‘mitochondrial deficiency’ does not mediate insulin resistance. *Am J Clin Nutr* 89, 463S–466S.
- Houtkooper RH, Canto C, Wanders RJ and Auwerx J (2010). the secret life of NAD⁺: an old metabolite controlling new metabolic signaling pathways. *Endocr Rev* 31, 194–223.
- Hu FB, Stampfer MJ, Solomon C, Liu S, Colditz GA, Speizer FE, et al. (2001). Physical activity and risk for cardiovascular events in diabetic women. *Ann Intern Med* 134, 96–105.
- Hu FB, Li TY, Colditz GA, Willett WC and Manson JE (2003). Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 289, 1785–1791.
- Huang S and Czech MP (2007). the GLUT4 glucose transporter. *Cell Metab* 5, 237–252.
- Hudson ER, Pan DA, James J, Lucocq JM, Hawley SA, Green KA, et al. (2003). A novel domain in AMP-activated protein kinase causes glycogen storage bodies similar to those seen in hereditary cardiac arrhythmias. *Curr Biol* 13, 861–866.
- Isbell LA and Young TP (1996). the evolution of bipedalism in hominids and reduced group size in chimpanzees: alternative responses to decreasing resource availability. *J Hum Evol* 30, 289–297.
- Kahn SE, Hull RL and Utzschneider KM (2006). Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature* 444, 840–846.
- Kahn SE, Zraika S, Utzschneider KM and Hull RL (2009). the beta cell lesion in type 2 diabetes: there has to be a primary functional abnormality. *Diabetologia* 52, 1003–1012.
- Kennedy JW, Hirshman MF, Gervino EV, Ocel JV, Forse RA, Hoening SJ, et al. (1999). Acute exercise induces GLUT4 translocation in skeletal muscle of normal human subjects and subjects with type 2 diabetes. *Diabetes* 48, 1192–1197.
- Kim JK, Gavrilova O, Chen Y, Reitman ML and Shulman GI (2000). Mechanism of insulin resistance in A-ZIP/F-1 fatless mice. *J Biol Chem* 275, 8456–8460.
- Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346, 393–403.
- Levy-Marchal C, Arslanian S, Cutfield W, Sinaiko A, Druet C, Marcovecchio ML, et al. (2010). Insulin resistance in children: consensus, perspective, and future directions. *J Clin Endocrinol Metab* 95, 5189–5198.
- Lopez AD, Mathers CD, Ezzati M, Jamison DT and Murray CJ (2006). Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 367, 1747–1757.
- Lowell BB and Shulman GI (2005). Mitochondrial dysfunction and type 2 diabetes. *Science* 307, 384–387.
- Maarbjerg SJ, Sylow L and Richter EA (2011). Current understanding of increased insulin sensitivity after exercise – emerging candidates. *Acta Physiol (Oxford)* 202, 323–335.
- Manchester J, Skurat AV, Roach P, Hauschka SD and Lawrence JC, Jr. (1996). Increased glycogen accumulation in transgenic mice overexpressing glycogen synthase in skeletal muscle. *Proc Natl Acad Sci U S A* 93, 10707–10711.
- Martin IK, Katz A and Wahren J (1995). Splanchnic and muscle metabolism during exercise in NIDDM patients. *Am J Physiol* 269, E583–E590.

- Milne JC, Lambert PD, Schenk S, Carney DP, Smith JJ, Gagne DJ, et al. (2007). Small molecule activators of SIRT1 as therapeutics for the treatment of type 2 diabetes. *Nature* 450, 712–716.
- Mootha VK, Lindgren CM, Eriksson KF, Subramanian A, Sihag S, Lehar J, et al. (2003). PGC-1 α -responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. *Nat Genet* 34, 267–273.
- Muoio DM and Newgard CB (2008). Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. *Nat Rev Mol Cell Biol* 9, 193–205.
- Myatt JP, Schilling N and Thorpe SK (2011). Distribution patterns of fibre types in the triceps surae muscle group of chimpanzees and orangutans. *J Anat* 218, 402–412.
- Narkar VA, Downes M, Yu RT, Embler E, Wang YX, Banayo E, et al. (2008). AMPK and PPAR δ agonists are exercise mimetics. *Cell* 134, 405–415.
- Neel JV (1962). Diabetes mellitus: a “thrifty” genotype rendered detrimental by “progress”? *Am J Hum Genet* 14, 353–362. Neel JV (1999). the “thrifty genotype” in 1998. *Nutr Rev* 57, S2–S9.
- O’Neill HM, Maarbjerg SJ, Crane JD, Jeppesen J, Jorgensen SB, Schertzer JD, et al. (2011). AMP-activated protein kinase (AMPK) β 1 β 2 muscle null mice reveal an essential role for AMPK in maintaining mitochondrial content and glucose uptake during exercise. *Proc Natl Acad Sci U S A* 108, 16092–16097.
- Patti ME, Butte AJ, Crunkhorn S, Cusi K, Berria R, Kashyap S, et al. (2003). Coordinated reduction of genes of oxidative metabolism in humans with insulin resistance and diabetes: Potential role of PGC1 and NRF1. *Proc Natl Acad Sci U S A* 100, 8466–8471.
- Petersen KF and Shulman GI (2006). Etiology of insulin resistance. *Am J Med* 119, S10–S16.
- Petrie JR, Pearson ER and Sutherland C (2011). Implications of genome wide association studies for the understanding of type 2 diabetes pathophysiology. *Biochem Pharmacol* 81, 471–477.
- Prentice AM, Hennig BJ and Fulford AJ (2008). Evolutionary origins of the obesity epidemic: natural selection of thrifty genes or genetic drift following predation release? *Int J Obes (Lond)* 32, 1607–1610.
- Randle PJ, Garland PB, Hales CN and Newsholme EA (1963). The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *Lancet* 1, 785–789.
- Reasner CA and DeFronzo RA (2001). Treatment of type 2 diabetes mellitus: a rational approach based on its pathophysiology. *Am Fam Physician* 63, 1687–2, 1694.
- Romijn JA, Coyle EF, Sidossis LS, Gastaldelli A, Horowitz JF, Endert E, et al. (1993). Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *Am J Physiol* 265, E380–E391.
- Rose AJ and Richter EA (2005). Skeletal muscle glucose uptake during exercise: how is it regulated? *Physiology (Bethesda)* 20, 260–270.
- Scholz MN, D’Aout K, Bobbert MF and Aerts P (2006). Vertical jumping performance of bonobo (*Pan paniscus*) suggests superior muscle properties. *Proc Biol Sci* 273, 2177–2184.
- Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C and White RD (2006). Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* 29, 1433–1438.
- Singh U and Jialal I (2008). Alpha-lipoic acid supplementation and diabetes. *Nutr Rev* 66, 646–657.
- Sinha R, Fisch G, Teague B, Tamborlane WV, Banyas B, Allen K, et al. (2002). Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *N Engl J Med* 346, 802–810.
- Soares P, Alshamali F, Pereira JB, Fernandes V, Silva NM, Afonso C, et al. (2012). The expansion of mtDNA haplogroup L3 within and out of Africa. *Mol Biol Evol* 29, 915–927.
- Speakman JR (2008). Thrifty genes for obesity, an attractive but flawed idea, and an alternative perspective: the ‘drifty gene’ hypothesis. *Int J Obes (Lond)* 32, 1611–1617.
- Stumvoll M, Goldstein BJ and van Haeften TW (2005). Type 2 diabetes: principles of pathogenesis and therapy. *Lancet* 365, 1333–1346.
- Suwa M, Egashira T, Nakano H, Sasaki H and Kumagai S (2006). Metformin increases the PGC-1 α protein and oxidative enzyme activities possibly via AMPK phosphorylation in skeletal muscle in vivo. *J Appl Physiol* 101, 1685–1692.
- The Wellcome Trust Case Control Consortium (2007). Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 447, 661–678.
- Thomson DM and Winder WW (2009). AMP-activated protein kinase control of fat metabolism in skeletal muscle. *Acta Physiol (Oxford)* 196, 147–154.

- Ungar PS and Sponheimer M (2011). The diets of early hominins. *Science* 334, 190–193.
- Wang Y, Simar D and Fiatarone Singh MA (2009). Adaptations to exercise training within skeletal muscle in adults with type 2 diabetes or impaired glucose tolerance: a systematic review. *Diabetes Metab Res Rev* 25, 13–40.
- Ward CV (2002). Interpreting the posture and locomotion of *Australopithecus afarensis*: where do we stand? *Am J Phys Anthropol Suppl* 35, 185–215.
- Watt MJ, Heigenhauser GJ and Spriet LL (2002). Intramuscular triacylglycerol utilization in human skeletal muscle during exercise: is there a controversy? *J Appl Physiol* 93, 1185–1195.
- Winder WW and Hardie DG (1999). AMP-activated protein kinase, a metabolic master switch: possible roles in type 2 diabetes. *Am J Physiol* 277, E1–10.
- Witczak CA, Jessen N, Warro DM, Toyoda T, Fujii N, Anderson ME, et al. (2010). CaMKII regulates contraction- but not insulin-induced glucose uptake in mouse skeletal muscle. *Am J Physiol Endocrinol Metab* 298, E1150–E1160.
- Xiao B, Sanders MJ, Underwood E, Heath R, Mayer FV, Carmena D, et al. (2011). Structure of mammalian AMPK and its regulation by ADP. *Nature* 472, 230–233.
- Zhang BB, Zhou G and Li C (2009). AMPK: an emerging drug target for diabetes and the metabolic syndrome. *Cell Metab* 9, 407–416.
- Zhou G, Myers R, Li Y, Chen Y, Shen X, Fenyk-Melody J, et al. (2001). Role of AMP-activated protein kinase in mechanism of metformin action. *J Clin Invest* 108, 1167–1174.
- Zimmet P, Alberti KG and Shaw J (2001). Global and societal implications of the diabetes epidemic. *Nature* 414, 782–787.

■ جهت مطالعه بیشتر

- Johnson SC, Rabinovitch PS and Kaeberlein M (2013). mTOR is a key modulator of ageing and age-related disease. *Nature* 493, 338–345.
- Narici MV and Maffulli N (2010). Sarcopenia: characteristics, mechanisms and functional significance. *Br Med Bull* 95, 139–159.
- Powers SK and Jackson MJ (2008). Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. *Physiol Rev* 88, 1243–1276.
- Shawi M and Autexier C (2008). Telomerase, senescence and ageing. *Mech Ageing Dev* 129, 3–10.
- Tyner SD, Venkatachalam S, Choi J, Jones S, Ghebranion N, Igelmann H, et al. (2002). p53 mutant mice that display early ageing-associated phenotypes. *Nature* 415, 45–53.

■ منابع

- Aagaard P, Suetta C, Caserotti P, Magnusson SP and Kjaer M (2010). Role of the nervous system in sarcopenia and muscle atrophy with aging: strength training as a countermeasure. *Scand J Med Sci Sports* 20, 49–64.
- Alsharidah M, Lazarus NR, George TE, Agle CC, Velloso CP and Harridge SD (2013). Primary human muscle precursor cells obtained from young and old donors produce similar proliferative, differentiation and senescent profiles in culture. *Aging Cell* 12, 333–344.
- Anisimov VN, Berstein LM, Egormin PA, Piskunova TS, Popovich IG, Zabezhinski MA, et al. (2008). Metformin slows down aging and extends life span of female SHR mice. *Cell Cycle* 7, 2769–2773.
- Baker DJ, Wijshake T, Tchkonian T, LeBrasseur NK, Childs BG, van de Sluis B, et al. (2011). Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. *Nature* 479, 232–236.
- Baur JA, Pearson KJ, Price NL, Jamieson HA, Lerin C, Kalra A, et al. (2006). Resveratrol improves health and survival of mice on a high-calorie diet. *Nature* 444, 337–342.
- Blair SN and Morris JN (2009). Healthy hearts – and the universal benefits of being physically active: physical activity and health. *Ann Epidemiol* 19, 253–256.
- Bodnar AG, Ouellette M, Frolkis M, Holt SE, Chiu CP, Morin GB, et al. (1998). Extension of life-span by introduction

of telomerase into normal human cells. *Science* 279, 349–352.

Carlson ME, Hsu M and Conboy IM (2008). Imbalance between pSmad3 and Notch induces CDK inhibitors in old muscle stem cells. *Nature* 454, 528–532.

Carlson ME, Suetta C, Conboy MJ, Aagaard P, Mackey A, Kjaer M, et al. (2009). Molecular aging and rejuvenation of human muscle stem cells. *EMBO Mol Med* 1, 381–391.

Caron E, Ghosh S, Matsuoka Y, Ashton-Beaucage D, Therrien M, Lemieux S, et al. (2010). A comprehensive map of the mTOR signaling network. *Mol Syst Biol* 6, 453.

Chakkalakal JV, Jones KM, Basson MA and Brack AS (2012). The aged niche disrupts muscle stem cell quiescence. *Nature* 490, 355–360.

Chen C, Liu Y, Liu Y and Zheng P (2009). mTOR regulation and therapeutic rejuvenation of aging hematopoietic stem cells. *Sci Signal* 2, ra75.

Cherkas LF, Hunkin JL, Kato BS, Richards JB, Gardner JP, Surdulescu GL, et al. (2008). The association between physical activity in leisure time and leukocyte telomere length. *Arch Intern Med* 168, 154–158. Christou DD and Seals DR (2008).

Decreased maximal heart rate with aging is related to reduced β -adrenergic responsiveness but is largely explained by a reduction in intrinsic heart rate. *J Appl Physiol* 105, 24–29. Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, et al. (2009). Caloric restriction delays disease onset and mortality in rhesus monkeys. *Science* 325, 201–204.

Conboy IM, Conboy MJ, Wagers AJ, Girma ER, Weissman IL and Rando TA (2005). Rejuvenation of aged progenitor cells by exposure to a young systemic environment. *Nature* 433, 760–764.

Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, et al. (2005). Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. *FASEB J* 19, 422–424.

Eklblom B (1968). Effect of physical training on oxygen transport system in man. *Acta Physiol Scand Suppl* 328, 1–45.

Fisher-Wellman K and Bloomer RJ (2009). Acute exercise and oxidative stress: a 30 year history. *Dyn Med* 8, 1.

Frontera WR, Meredith CN, O'Reilly KP and Evans WJ (1990). Strength training and determinants of $\dot{V}O_{2max}$ in older men. *J Appl Physiol* 68, 329–333.

Fullerton MD and Steinberg GR (2010). SIRT1 takes a backseat to AMPK in the regulation of insulin sensitivity by resveratrol. *Diabetes* 59, 551–553.

George T, Velloso CP, Alsharidah M, Lazarus NR and Harridge SD (2010). Sera from young and older humans equally sustain proliferation and differentiation of human myoblasts. *Exp Gerontol* 45, 875–881.

Gwinn DM, Shackelford DB, Egan DF, Mihaylova MM, Mery A, Vasquez DS, et al. (2008). AMPK phosphorylation of raptor mediates a metabolic checkpoint. *Mol Cell* 30, 214–226.

Harley CB, Futcher AB and Greider CW (1990). Telomeres shorten during ageing of human fibroblasts. *Nature* 345, 458–460.

Harman D (1956). Aging: A theory based on free radical and radiation chemistry. *J Gerontol* 11, 298–300.

Harrison DE, Strong R, Sharp ZD, Nelson JF, Astle CM, Flurkey K, et al. (2009). Rapamycin fed late in life extends lifespan in genetically heterogeneous mice. *Nature* 460, 392–395.

Hayflick L (1965). The limited in vitro lifetime of human diploid cell strains. *Exp Cell Res* 37, 614–636.

Herbert B, Pitts AE, Baker SI, Hamilton SE, Wright WE, Shay JW and Corey DR (1999). Inhibition of human telomerase in immortal human cells leads to progressive telomere shortening and cell death. *Proc Natl Acad Sci U S A* 96, 14276–14281.

Inoki K, Zhu T and Guan KL (2003). TSC2 mediates cellular energy response to control cell growth and survival. *Cell* 115, 577–590.

Jang YC, Lustgarten MS, Liu Y, Muller FL, Bhattacharya A, Liang H, et al. (2010). Increased superoxide in vivo accelerates age-associated muscle atrophy through mitochondrial dysfunction and neuromuscular junction degeneration. *FASEB J* 24, 1376–1390.

Jaskelioff M, Muller FL, Paik JH, Omas E, Jiang S, Adams AC, et al. (2011). Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice. *Nature* 469, 102–106.

Johnson SC, Rabinovitch PS and Kaeblerlein M (2013). mTOR is a key modulator of ageing and age-related disease. *Nature* 493, 338–345.

Kanning KC, Kaplan A and Henderson CE (2010). Motor neuron diversity in development and disease. *Annu Rev Neurosci* 33, 409–440.

- Kapahi P, Chen D, Rogers AN, Katewa SD, Li PW, thomas EL and Kockel L (2010). With TOR, less is more: a key role for the conserved nutrient-sensing TOR pathway in aging. *Cell Metab* 11, 453–465.
- Kistler PM, Sanders P, Fynn SP, Stevenson IH, Spence SJ, Vohra JK, et al. (2004). Electrophysiologic and electroanatomic changes in the human atrium associated with age. *J Am Coll Cardiol* 44, 109–116.
- Kumar V, Selby A, Rankin D, Patel R, Atherton P, Hildebrandt W, et al. (2009). Age-related differences in the dose-response relationship of muscle protein synthesis to resistance exercise in young and old men. *J Physiol* 587, 211–217.
- Lagouge M, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F, et al. (2006). Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1 α . *Cell* 127, 1109–1122.
- Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di IA, et al. (2003). Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* 95, 1851–1860.
- Lehmann M and Keul J (1986). Age-associated changes of exercise-induced plasma catecholamine responses. *Eur J Appl Physiol Occup Physiol* 55, 302–306.
- Lexell J (1997). Evidence for nervous system degeneration with advancing age. *J Nutr* 127, 1011S–1013S.
- Lexell J and Downham DY (1991). the occurrence of fibre-type grouping in healthy human muscle: a quantitative study of cross-sections of whole vastus lateralis from men between 15 and 83 years. *Acta Neuropathol (Berl)* 81, 377–381.
- Lexell J, Taylor CC and Sjoström M (1988). What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. *J Neurol Sci* 84, 275–294.
- Medvedev ZA (1990). An attempt at a rational classification of theories of ageing. *Biol Rev Camb Philos Soc* 65, 375–398.
- Mittal KR and Logmani FH (1987). Age-related reduction in 8th cervical ventral nerve root myelinated fiber diameters and numbers in man. *J Gerontol* 42, 8–10.
- Monfredi O, Dobrzynski H, Mondal T, Boyett MR and Morris GM (2010). the anatomy and physiology of the sinoatrial node – a contemporary review. *Pacing Clin Electrophysiol* 33, 1392–1406.
- Moreland JD, Richardson JA, Goldsmith CH and Clase CM (2004). Muscle weakness and falls in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 52, 1121–1129.
- Narici MV and Maffulli N (2010). Sarcopenia: characteristics, mechanisms and functional significance. *Br Med Bull* 95, 139–159.
- Pearl R (1928). the rate of living. University of London Press, London.
- Ploutz-Snyder LL, Manini T, Ploutz-Snyder RJ and Wolf DA (2002). Functionally relevant thresholds of quadriceps femoris strength. *J Gerontol A Biol Sci Med Sci* 57, B144–B152.
- Powers SK and Jackson MJ (2008). Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. *Physiol Rev* 88, 1243–1276.
- Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, et al. (1999). Midlife hand grip strength as a predictor of old age disability. *JAMA* 281, 558–560.
- Rasmussen BB, Fujita S, Wolfe RR, Mittendorfer B, Roy M, Rowe VL and Volpi E (2006). Insulin resistance of muscle protein metabolism in aging. *FASEB J* 20, 768–769.
- Ristow M, Zarse K, Oberbach A, Kloting N, Birringer M, Kiehntopf M, et al. (2009). Antioxidants prevent health-promoting effects of physical exercise in humans. *Proc Natl Acad Sci U S A* 106, 8665–8670.
- Rosen DR, Siddique T, Patterson D, Figlewicz DA, Sapp P, Hentati A, et al. (1993). Mutations in Cu/Zn superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis. *Nature* 362, 59–62.
- Rosenberg IH (1997). Sarcopenia: origins and clinical relevance. *J Nutr* 127, 990S–991S.
- Ruiz JR, Sui X, Lobelo F, Morrow JR, Jr., Jackson AW, Sjoström M, et al. (2008). Association between muscular strength and mortality in men: prospective cohort study. *BMJ* 337, a439.
- Sanz A, Pamplona R and Barja G (2006). Is the mitochondrial free radical theory of aging intact? *Antioxid Redox Signal* 8, 582–599.
- Selman C, Tullet JM, Wieser D, Irvine E, Lingard SJ, Choudhury AI, et al. (2009). Ribosomal protein S6 kinase 1 signaling regulates mammalian life span. *Science* 326, 140–144.
- Shawi M and Autexier C (2008). Telomerase, senescence and ageing. *Mech Ageing Dev* 129, 3–10.
- Shefner JM, Reaume AG, Flood DG, Scott RW, Kowall NW, Ferrante RJ, et al. (1999). Mice lacking cytosolic copper/

zinc superoxide dismutase display a distinctive motor axonopathy. *Neurology* 53, 1239–1246.

Shiraishi I, Takamatsu T, Minamikawa T, Onouchi Z and Fujita S (1992). Quantitative histological analysis of the human sinoatrial node during growth and aging. *Circulation* 85, 2176–2184.

Smith DL, Jr., Elam CF, Jr., Mattison JA, Lane MA, Roth GS, Ingram DK, et al. (2010). Metformin supplementation and life span in Fischer-344 rats. *J Gerontol A Biol Sci Med Sci* 65, 468–474.

Sohal RS and Buchan PB (1981). Relationship between physical activity and life span in the adult housefly, *Musca domestica*. *Exp Gerontol* 16, 157–162.

Speakman JR, Talbot DA, Selman C, Snart S, McLaren JS, Redman P, et al. (2004). Uncoupled and surviving: individual mice with high metabolism have greater mitochondrial uncoupling and live longer. *Aging Cell* 3, 87–95.

Tanaka H, Monahan KD and Seals DR (2001). Age-predicted maximal heart rate revisited. *J Am Coll Cardiol* 37, 153–156.

Teramoto M and Bungum TJ (2010). Mortality and longevity of elite athletes. *J Sci Med Sport* 13, 410–416.

Tomlinson BE and Irving D (1977). The numbers of limb motor neurons in the human lumbosacral cord throughout life. *J Neurol Sci* 34, 213–219.

Trappe SW, Costill DL, Fink WJ and Pearson DR (1995). Skeletal muscle characteristics among distance runners: a 20-yr follow-up study. *J Appl Physiol* 78, 823–829.

Tyner SD, Venkatachalam S, Choi J, Jones S, Ghebranious N, Igelmann H, et al. (2002). p53 mutant mice that display early ageing-associated phenotypes. *Nature* 415, 45–53.

von Zglinicki T (2002). Oxidative stress shortens telomeres. *Trends Biochem Sci* 27, 339–344.

Weismann A (1892). *Über Leben und Tod*. Gustav Fischer, Jena.

Wolfe RR (2006). The underappreciated role of muscle in health and disease. *Am J Clin Nutr* 84, 475–482.

Wu Y, Gao Z, Chen B, Koval OM, Singh MV, Guan X, et al. (2009). Calmodulin kinase II is required for fight or flight sinoatrial node physiology. *Proc Natl Acad Sci U S A* 106, 5972–5977.

■ جهت مطالعه بیشتر

Costa-Mattioli M, Sossin WS, Klann E and Sonenberg N (2009). Translational control of long-lasting synaptic plasticity and memory. *Neuron* 61, 10–211.

Kandel ER, Schwartz JH, Jessell TM and Hudspeth AJ (2012). *Principles of neural science*, 5th edn. McGraw-Hill, New York.

Kanning KC, Kaplan A and Henderson CE (2010). Motor neuron diversity in development and disease. *Annu Rev Neurosci* 33, 409–440.

Kim SJ and Linden DJ (2007). Ubiquitous plasticity and memory storage. *Neuron* 56, 582–592.

Lomo T (2003). The discovery of long-term potentiation. *Philos Trans R Soc Lond B Biol Sci* 358, 617–620.

Mendell LM (2005). The size principle: a rule describing the recruitment of motoneurons. *J Neurophysiol* 93, 3024–3026.

■ منابع

Alvarez VA and Sabatini BL (2007). Anatomical and physiological plasticity of dendritic spines. *Annu Rev Neurosci* 30, 79–97.

Andrechek ER, Hardy WR, Girgis-Gabardo AA, Perry RL, Butler R, Graham FL, et al. (2002). ErbB2 is required for muscle spindle and myoblast cell survival. *Mol Cell Biol* 22, 4714–4722.

Arellano JI, Benavides-Piccione R, Defelipe J and Yuste R (2007). Ultrastructure of dendritic spines: correlation between synaptic and spine morphologies. *Front Neurosci* 1, 131–143.

Bliss TV and Lomo T (1973). Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *J Physiol* 232, 331–356.

Boecker H, Sprenger T, Spilker ME, Henriksen G, Koppenhoefer M, Wagner KJ, et al. (2008). The runner's high: opioidergic mechanisms in the human brain. *Cereb Cortex* 18, 2523–2531.

Burke RE, Levine DN, Tsairis P and Zajac FE, III (1973). Physiological types and histochemical profiles in motor units

- of the cat gastrocnemius. *J Physiol* 234, 723–748.
- Cajal R (1894). The Croonian lecture: la fine structure des centres nerveux. *Proc R Soc Lond B Biol Sci* 55, 444–468.
- Chen HH, Hippenmeyer S, Arber S and Frank E (2003). Development of the monosynaptic stretch reflex circuit. *Curr Opin Neurobiol* 13, 96–102.
- Collingridge GL, Kehl SJ and McLennan H (1983). The antagonism of amino acid-induced excitations of rat hippocampal CA1 neurons in vitro. *J Physiol* 334, 19–31.
- Costa-Mattioli M, Gobert D, Stern E, Gamache K, Colina R, Cuello C, et al. (2007). eIF2 α phosphorylation bidirectionally regulates the switch from short- to long-term synaptic plasticity and memory. *Cell* 129, 195–206.
- Costa-Mattioli M, Sossin WS, Klann E and Sonenberg N (2009). Translational control of long-lasting synaptic plasticity and memory. *Neuron* 61, 10–26.
- Courtine G, Bunge MB, Fawcett JW, Grossman RG, Kaas JH, Lemon R, et al. (2007). Can experiments in nonhuman primates expedite the translation of treatments for spinal cord injury in humans? *Nat Med* 13, 561–566.
- Dalla Torre di Sanguinetto S, Dasen JS and Arber S (2008). Transcriptional mechanisms controlling motor neuron diversity and connectivity. *Curr Opin Neurobiol* 18, 36–43.
- Flavell SW and Greenberg ME (2008). Signaling mechanisms linking neuronal activity to gene expression and plasticity of the nervous system. *Annu Rev Neurosci* 31, 563–590.
- Foley TE and Fleshner M (2008). Neuroplasticity of dopamine circuits after exercise: implications for central fatigue. *Neuromolecular Med* 10, 67–80.
- Fox PW, Hershberger SL and Bouchard TJ, Jr. (1996). Genetic and environmental contributions to the acquisition of a motor skill. *Nature* 384, 356–358.
- Garcia-Campmany L, Stam FJ and Goulding M (2010). From circuits to behaviour: motor networks in vertebrates. *Curr Opin Neurobiol* 20, 116–125.
- Gollnick PD, Piehl K and Saltin B (1974). Selective glycogen depletion pattern in human muscle fibres after exercise of varying intensity and at varying pedalling rates. *J Physiol* 241, 45–57.
- Goulding M (2009). Circuits controlling vertebrate locomotion: moving in a new direction. *Nat Rev Neurosci* 10, 507–518.
- Hagglund M, Borgius L, Dougherty KJ and Kiehn O (2010). Activation of groups of excitatory neurons in the mammalian spinal cord or hindbrain evokes locomotion. *Nat Neurosci* 13, 246–252.
- Hebb DO (1949). *Organization of behaviour: a neuropsychological theory*. John Wiley, New York.
- Jungblut S (2009). The correct interpretation of the size principle and its practical application to resistance training. *Medicina Sportiva* 13, 203–209.
- Kanning KC, Kaplan A and Henderson CE (2010). Motor neuron diversity in development and disease. *Annu Rev Neurosci* 33, 409–440.
- Karni A, Meyer G, Jezzard P, Adams MM, Turner R and Ungerleider LG (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature* 377, 155–158.
- Kiehn O (2006). Locomotor circuits in the mammalian spinal cord. *Annu Rev Neurosci* 29, 279–306.
- Kiehn O (2010). Development and functional organization of spinal locomotor circuits. *Curr Opin Neurobiol* 21, 100–109.
- Kim SJ and Linden DJ (2007). Ubiquitous plasticity and memory storage. *Neuron* 56, 582–592.
- Kullander K, Butt SJ, Le Bret JM, Lundfald L, Restrepo CE, Rydstrom A, et al. (2003). Role of EphA4 and EphrinB3 in local neuronal circuits that control walking. *Science* 299, 1889–1892.
- Lanuza GM, Gosgnach S, Pierani A, Jessell TM and Goulding M (2004). Genetic identification of spinal interneurons that coordinate left-right locomotor activity necessary for walking movements. *Neuron* 42, 375–386.
- Lee SJ, Escobedo-Lozoya Y, Sztamari EM and Yasuda R (2009). Activation of CaMKII in single dendritic spines during long-term potentiation. *Nature* 458, 299–304.
- Lemon RN (2008). Descending pathways in motor control. *Annu Rev Neurosci* 31, 195–218.
- Lisman J, Schulman H and Cline H (2002). The molecular basis of CaMKII function in synaptic and behavioural memory. *Nat Rev Neurosci* 3, 175–190.
- Lomo T (1966). Frequency potentiation of excitatory synaptic activity in the dentate area of the hippocampal formation. *Acta Physiol Scand* 68, 128.
- Lomo T (2003). The discovery of long-term potentiation. *Philos Trans R Soc Lond B Biol Sci* 358, 617–620.
- London M and Hausser M (2005). Dendritic computation. *Annu Rev Neurosci* 28, 503–532.

- Lynch GS, Dunwiddie T and Gribkoff V (1977). Heterosynaptic depression: a postsynaptic correlate of long-term potentiation. *Nature* 266, 737–739.
- Lynch G, Larson J, Kelso S, Barrionuevo G, and Schottler F (1983). Intracellular injections of EGTA block induction of hippocampal long-term potentiation. *Nature* 305, 719–721.
- Lynch MA (2004). Long-term potentiation and memory. *Physiol Rev* 84, 87–136.
- Ma DK, Bonaguidi MA, Ming GL and Song H (2009). Adult neural stem cells in the mammalian central nervous system. *Cell Res* 19, 672–682.
- Mendell LM (2005). The size principle: a rule describing the recruitment of motoneurons. *J Neurophysiol* 93, 3024–3026.
- Missitzi J, Geladas N and Klissouras V (2004). Heritability in neuromuscular coordination: implications for motor control strategies. *Med Sci Sports Exerc* 36, 233–240.
- Pereira AC, Huddleston DE, Brickman AM, Sosunov AA, Hen R, McKhann GM, et al. (2007). An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proc Natl Acad Sci U S A* 104, 5638–5643.
- Porter RS and Kaplan LS (2010). *The Merck Manual*, 19 edn. Merck Sharp & Dohme Corp., White house Station, New Jersey.
- Rioutl-Pedotti MS, Friedman D and Donoghue JP (2000). Learning-induced LTP in neocortex. *Science* 290, 533–536.
- Sacktor TC (2011). How does PKMzeta maintain long-term memory? *Nat Rev Neurosci* 12, 9–15.
- Schwartzkroin PA and Wester K (1975). Long-lasting facilitation of a synaptic potential following tetanization in the in vitro hippocampal slice. *Brain Res* 89, 107–119.
- Shors TJ, Anderson ML, Curlik DM and Nokia MS (2011). Use it or lose it: How neurogenesis keeps the brain fit for learning. *Behav Brain Res* 227, 450–458.
- Silva AJ, Stevens CF, Tonegawa S and Wang Y (1992). Deficient hippocampal long-term potentiation in alpha-calmodulin kinase II mutant mice. *Science* 257, 201–206.
- Tang SJ, Reis G, Kang H, Gingras AC, Sonenberg N and Schuman EM (2002). A rapamycin-sensitive signaling pathway contributes to long-term synaptic plasticity in the hippocampus. *Proc Natl Acad Sci U S A* 99, 467–472.
- Thompson AK, Chen XY and Wolpaw JR (2009). Acquisition of a simple motor skill: task-dependent adaptation plus long-term change in the human soleus H-reflex. *J Neurosci* 29, 5784–5792.
- Tischmeyer W, Schicknick H, Kraus M, Seidenbecher CI, Staak S, Scheich H, et al. (2003). Rapamycin-sensitive signalling in long-term consolidation of auditory cortex-dependent memory. *Eur J Neurosci* 18, 942–950.
- van Praag H (2009). Exercise and the brain: something to chew on. *Trends Neurosci* 32, 283–290.
- von Kraus LM, Sacktor TC and Francis JT (2010). Erasing sensorimotor memories via PKMzeta inhibition. *PLoS ONE* 5, e11125.
- Walmsley B, Hodgson JA and Burke RE (1978). Forces produced by medial gastrocnemius and soleus muscles during locomotion in freely moving cats. *J Neurophysiol* 41, 1203–1216.
- Williams RW and Herrup K (1988). The control of neuron number. *Annu Rev Neurosci* 11, 423–453.
- Xu T, Yu X, Perlik AJ, Tobin WF, Zweig JA, Tennant K, et al. (2009). Rapid formation and selective stabilization of synapses for enduring motor memories. *Nature* 462, 915–919.
- Yu X and Zuo Y (2011). Spine plasticity in the motor cortex. *Curr Opin Neurobiol* 21, 169–174.
- Zhang CL, Zou Y, He W, Gage FH and Evans RM (2008). A role for adult TLX-positive neural stem cells in learning and behaviour. *Nature* 451, 1004–1007.

- Adam S, van Hall G, Osada T, Sacchetti M, Saltin B and Pedersen BK (2000). Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *J Physiol* 529, 237–242.
- Baum M, Muller-Steinhardt M, Liesen H and Kirchner H (1997). Moderate and exhaustive endurance exercise influences the interferon-gamma levels in whole-blood culture supernatants. *Eur J Appl Physiol Occup Physiol* 76, 165–169.
- Beals KA and Manore MM (1994). The prevalence and consequences of subclinical eating disorders in female athletes.

- Int J Sport Nutr 4, 175–195.
- Bishop NC, Walker GJ, Gleeson M, Wallace FA and Hewitt CR (2009). Human T lymphocyte migration towards the supernatants of human rhinovirus infected airway epithelial cells: influence of exercise and carbohydrate intake. *Exerc Immunol Rev* 15, 127–144.
- Boxer LA, Allen JM and Baehner RL (1980). Diminished polymorphonuclear leukocyte adherence. Function dependent on release of cyclic AMP by endothelial cells after stimulation of beta-receptors by epinephrine. *J Clin Invest* 66, 268–274.
- Cai D, Frantz JD, Tawa NE, Jr, Melendez PA, Oh BC, Lidov HG, et al. (2004). IKKbeta/NF-kappaB activation causes severe muscle wasting in mice. *Cell* 119, 285–298.
- Calder PC, Yaqoob P, Thies F, Wallace FA and Miles EA (2002). Fatty acids and lymphocyte functions. *Br J Nutr* 87 Suppl 1, S31–S48.
- Carey AL, Steinberg GR, Macaulay SL, Thomas WG, Holmes AG, Ramm G, et al. (2006). Interleukin-6 increases insulin-stimulated glucose disposal in humans and glucose uptake and fatty acid oxidation in vitro via AMP-activated protein kinase. *Diabetes* 55, 2688–2697.
- Chandra RK (1997). Nutrition and the immune system: an introduction. *Am J Clin Nutr* 66, 460S–463S.
- Chinda D, Nakaji S, Umeda T, Shimoyama T, Kurakake S, Okamura N, et al. (2003). A competitive marathon race decreases neutrophil functions in athletes. *Luminescence* 18, 324–329.
- Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, et al. (2005). Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. *FASEB J* 19, 422–424.
- de Craen AJ, Posthuma D, Remarque EJ, van den Biggelaar AH, Westendorp RG and Boomsma DI (2005). Heritability estimates of innate immunity: an extended twin study. *Genes Immun* 6, 167–170.
- Doyle A, Zhang G, Abdel Fattah EA, Tony Eissa N and Li YP (2011). Toll-like receptor 4 mediates lipopolysaccharide-induced muscle catabolism via coordinate activation of ubiquitin-proteasome and autophagy-lysosome pathways. *FASEB J* 25, 99–110.
- Dumke BR and Lees SJ (2011). Age-related impairment of T cell-induced skeletal muscle precursor cell function. *Am J Physiol Cell Physiol* 300, C1226–C1233.
- Febbraio MA, Hiscock N, Sacchetti M, Fischer CP and Pedersen BK (2004). Interleukin-6 is a novel factor mediating glucose homeostasis during skeletal muscle contraction. *Diabetes* 53, 1643–1648.
- Gleeson M, Bishop NC, Oliveira M and Tauler P (2011). Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *Int J Sport Nutr Exerc Metab* 21, 55–64.
- Gray P, Gabriel B, Thies F and Gray SR (2012). Fish oil supplementation augments post-exercise immune function in young males. *Brain Behav Immun* 26, 1265–1272.
- Heath GW, Ford ES, Craven TE, Macera CA, Jackson KL and Pate RR (1991). Exercise and the incidence of upper respiratory tract infections. *Med Sci Sports Exerc* 23, 152–157.
- Heinz SA, Henson DA, Austin MD, Jin F and Nieman DC (2010). Quercetin supplementation and upper respiratory tract infection: A randomized community clinical trial. *Pharmacol Res* 62, 237–242.
- Kappel M, Tvede N, Galbo H, Haahr PM, Kjaer M, Linstow M, et al. (1991). Evidence that the effect of physical exercise on NK cell activity is mediated by epinephrine. *J Appl Physiol* 70, 2530–2534.
- Lancaster GI, Khan Q, Drysdale PT, Wallace F, Jeukendrup AE, Drayson MT, et al. (2005). Effect of prolonged exercise and carbohydrate ingestion on type 1 and type 2 T lymphocyte distribution and intracellular cytokine production in humans. *J Appl Physiol* 98, 565–571.
- Li YP, Schwartz RJ, Waddell ID, Holloway BR and Reid MB (1998). Skeletal muscle myocytes undergo protein loss and reactive oxygen-mediated NF- κ B activation in response to tumor necrosis factor D. *FASEB J* 12, 871–880.
- Mitchell JB, Pizza FX, Paquet A, Davis BJ, Forrest MB and Braun WA (1998). Influence of carbohydrate status on immune responses before and after endurance exercise. *J Appl Physiol* 84, 1917–1925.
- Moreira A, Delgado LS, Moreira P and Haahtela T (2009). Does exercise increase the risk of upper respiratory tract infections? *Br Med Bull* 90, 111–131.
- Mourkioti F, Kratsios P, Luedde T, Song YH, Delafontaine P, Adami R, et al. (2006). Targeted ablation of IKK2 improves skeletal muscle strength, maintains mass, and promotes regeneration. *J Clin Invest* 116, 2945–2954.
- Newsholme P, Curi R, Pithon Curi TC, Murphy CJ, Garcia C and Pires de Melo M (1999). Glutamine metabolism by lymphocytes, macrophages, and neutrophils: its importance in health and disease. *J Nutr Biochem* 10, 316–324.

- Nieman DC, Nehlsen-Cannarella SL, Markoff PA, Balk-Lamberton AJ, Yang H, Chritton DB, et al. (1990). The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections. *Int J Sports Med* 11, 467–473.
- Nieman DC, Miller AR, Henson DA, Warren BJ, Gusewitch G, Johnson RL, et al. (1994). Effect of high- versus moderate-intensity exercise on lymphocyte subpopulations and proliferative response. *Int J Sports Med* 15, 199–206.
- Nieman DC, Buckley KS, Henson DA, Warren BJ, Suttles J, Ahle JC, et al. (1995). Immune function in marathon runners versus sedentary controls. *Med Sci Sports Exerc* 27, 986–992.
- Nieman DC, Henson DA, Fagoaga OR, Utter AC, Vinci DM, Davis JM, et al. (2002). Change in salivary IgA following a competitive marathon race. *Int J Sports Med* 23, 69–75.
- Nieman DC, Henson DA, McAnulty SR, Jin F and Maxwell KR (2009). n-3 polyunsaturated fatty acids do not alter immune and inflammation measures in endurance athletes. *Int J Sport Nutr Exerc Metab* 19, 536–546.
- Northoff H and Berg A (1991). Immunologic mediators as parameters of the reaction to strenuous exercise. *Int J Sports Med* 12 Suppl 1, S9–15.
- Oliveira M and Gleeson M (2010). The influence of prolonged cycling on monocyte Toll-like receptor 2 and 4 expression in healthy men. *Eur J Appl Physiol* 109, 251–257.
- Ostrowski K, Hermann C, Bangash A, Schjerling P, Nielsen JN and Pedersen BK (1998). A trauma-like elevation of plasma cytokines in humans in response to treadmill running. *J Physiol* 513, 889–894.
- Parry-Billings M, Budgett R, Koutedakis Y, Blomstrand E, Brooks S, Williams C, et al. (1992). Plasma amino acid concentrations in the overtraining syndrome: possible effects on the immune system. *Med Sci Sports Exerc* 24, 1353–1358.
- Pedersen BK, Tvede N, Klarlund K, Christensen LD, Hansen FR, Galbo H, et al. (1990). Indomethacin in vitro and in vivo abolishes post-exercise suppression of natural killer cell activity in peripheral blood. *Int J Sports Med* 11, 127–131.
- Pedersen BK, Helge JW, Richter EA, Rohde T and Kiens B (2000). Training and natural immunity: effects of diets rich in fat or carbohydrate. *Eur J Appl Physiol* 82, 98–102.
- Peters EM and Bateman ED (1983). Ultramarathon running and upper respiratory tract infections. An epidemiological survey. *S Afr Med J* 64, 582–584.
- Quinn LS, Anderson BG, Strait-Bodey L, Stroud AM and Argiles JM (2009). Oversecretion of interleukin-15 from skeletal muscle reduces adiposity. *Am J Physiol* 296, E191–202.
- Robson PJ, Blannin AK, Walsh NP, Castell LM and Gleeson M (1999). Effects of exercise intensity, duration and recovery on in vitro neutrophil function in male athletes. *Int J Sports Med* 20, 128–135.
- Rohde T, Asp S, MacLean DA and Pedersen BK (1998). Competitive sustained exercise in humans, lymphokine activated killer cell activity, and glutamine: an intervention study. *Eur J Appl Physiol Occup Physiol* 78, 448–453.
- Rotter V, Nagaev I and Smith U (2003). Interleukin-6 (IL-6) induces insulin resistance in 3T3-L1 adipocytes and is, like IL-8 and tumor necrosis factor-alpha, overexpressed in human fat cells from insulin-resistant subjects. *J Biol Chem* 278, 45777–45784.
- Scharhag J, Meyer T, Gabriel HH, Auracher M and Kindermann W (2002). Mobilization and oxidative burst of neutrophils are influenced by carbohydrate supplementation during prolonged cycling in humans. *Eur J Appl Physiol* 87, 584–587.
- Simpson R, Florida-James G, Whyte G and Guy K (2006). The effects of intensive, moderate and downhill treadmill running on human blood lymphocytes expressing the adhesion/activation molecules CD54 (ICAM-1), CD18 (E2 integrin) and CD53. *Eur J Appl Physiol* 97, 109–121.
- Simpson RJ, Florida-James GD, Whyte GP, Black JR, Ross JA, et al. (2007). Apoptosis does not contribute to the blood lymphocytopenia observed after intensive and downhill treadmill running in humans. *Res Sports Med* 15, 157–174.
- Smith JA and Pyne DB (1997). Exercise, training, and neutrophil function. *Exerc Immunol Rev* 3, 96–116.
- Starkie RL, Rolland J, Angus DJ, Anderson MJ and Febbraio MA (2001). Circulating monocytes are not the source of elevations in plasma IL-6 and TNF-alpha levels after prolonged running. *Am J Physiol* 280, C769–C774.
- Steensberg A, Keller C, Starkie RL, Osada T, Febbraio MA and Pedersen BK (2002). IL-6 and TNF-alpha expression in, and release from, contracting human skeletal muscle. *Am J Physiol* 283, E1272–E1278.
- Tabata I, Atomi Y and Miyashita M (1984). Blood glucose concentration dependent ACTH and cortisol responses to prolonged exercise. *Clin Physiol* 4, 299–307.

- Tidball JG and Villalta SA (2010). Regulatory interactions between muscle and the immune system during muscle regeneration. *Am J Physiol* 298, R1173–R1187.
- Toft AD, thorn M, Ostrowski K, Asp S, Moller K, Iversen S, et al. (2000). N-3 polyunsaturated fatty acids do not affect cytokine response to strenuous exercise. *J Appl Physiol* 89, 2401–2406.
- Wallenius V, Wallenius K, Ahren B, Rudling M, Carlsten H, Dickson SL, et al. (2002). Interleukin- 6-deficient mice develop mature-onset obesity. *Nat Med* 8, 75–79.
- Weidner TG, Cranston T, Schurr T and Kaminsky LA (1998). the effect of exercise training on the severity and duration of a viral upper respiratory illness. *Med Sci Sports Exerc* 30, 1578–1583.
- West TE, Chierakul W, Chantratita N, Limmathurotsakul D, Wuthiekanun V, Emond MJ, et al. (2012). Toll-like receptor 4 region genetic variants are associated with susceptibility to melioidosis. *Genes Immun* 13, 38–46.