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Participação do Estresse Oxidativo na Disfunção Muscular Esquelética em Ratos Diabéticos

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RESUMO

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O objetivo do estudo foi avaliar a função contrátil do músculo esquelético de ratos diabéticos, correlacionando-a com a ocorrência de estresse oxidativo. Alterações de parâmetros moleculares de potencial antioxidante, síntese e degradação proteica, miogênese, angiogênese, recaptação de cálcio e metabolismo energético também foram investigadas. Ratos Wistar machos foram mantidos diabéticos por 21 dias e tratados com o antioxidante N-acetil-L-cisteína (NAC), 300 mg/kg de peso corpóreo durante 5 dias, para investigar o envolvimento do estresse oxidativo na disfunção contrátil observada no estado diabético. A produção de força máxima, resistência à fadiga e propriedades contráteis (velocidades de contração e relaxamento) dos músculos sóleo e extensor digital longo (EDL) foram avaliadas através da estimulação elétrica *in situ* do nervo ciático. Liberação muscular de H_2O_2 foi estimada em músculo incubado com auxílio da sonda Amplex UltraRed®. O conteúdo proteico de fator induzido por hipóxia-1 alfa (HIF-1α), fator de crescimento endotelial vascular (VEGF), co-ativador do receptor gama ativado por proliferadores de peroxissomos -1alfa (PGC-1α) e citocromo c oxidase subunidade IV (COX IV) foi avaliado através de *Western Blotting*. A expressão gênica de transportador de glicose 4 (GLUT4), receptores alfa e beta ativados por proliferadores de peroxissomos (PPARα e β) e citrato sintase foi avaliada pela técnica da reação em cadeia da polimerase quantitativa em tempo real (RT-PCR). Em ratos diabéticos, ambos os músculos apresentaram estresse oxidativo, caracterizado pelo aumento no conteúdo de H_2O_2 em relação aos valores obtidos em ratos não diabéticos, o qual foi abolido pelo tratamento com NAC. O músculo sóleo de ratos diabéticos apresentou menor resistência à fadiga quando comparado ao controle. Aliado a este efeito, apresentou também menor conteúdo proteico de HIF-1α, VEGF, PGC-1α e COX IV e menor expressão gênica de PPARα, citrato sintase e GLUT4, o que pode estar associado à menor capacidade oxidativa, biogênese e conteúdo mitocondrial e angiogênese. O tratamento com NAC reduziu a produção de H_2O_2 durante contrações, retardou o desenvolvimento de fadiga e restaurou o conteúdo / expressão dos marcadores citados. O músculo EDL dos ratos diabéticos apresentou diminuição da velocidade de relaxamento. Observou-se também aumento no conteúdo proteico de PGC-1α, COX IV e na expressão gênica de PPARβ, o que estaria possivelmente associado à conversão de fibras tipo 2/glicolíticas/contração rápida para tipo 1/oxidativas/contração lenta. O tratamento com NAC restabeleceu a expressão / conteúdo desses marcadores e recuperou a velocidade de relaxamento muscular no EDL do rato diabético. Portanto, o estresse oxidativo observado no músculo esquelético durante o estado diabético está associado a alterações específicas em cada músculo avaliado. Ele participaria do desenvolvimento precoce de fadiga e comprometimento do metabolismo energético no músculo sóleo. No EDL, estaria envolvido na conversão de fibras glicolíticas/contração rápida para oxidativas/contração lenta e no comprometimento da recaptação de cálcio.

Palavras-chave: *Diabetes mellitus*. Estresse Oxidativo. Antioxidante. N-acetil-L-cisteína. Músculo Esquelético. Função contrátil.

ABSTRACT

Vitzel KF. The involvement of oxidative stress in skeletal muscle dysfunction of diabetic rats. [Ph. D. thesis (Human Physiology)]. São Paulo: Instituto de Ciências Biomédicas, Universidade de São Paulo; 2013.

The aim of the study was to evaluate the association between the contractile function alterations and oxidative stress that occurs in the skeletal muscle of diabetic rats. Alterations of molecular markers related to antioxidant capacity, protein synthesis and degradation, myogenesis, angiogenesis, calcium uptake and energy metabolism were also investigated. Male Wistar rats were kept diabetic for 21 days and then treated with the antioxidant N-acetyl-L-cysteine (NAC), 300 mg/kg b.w., for 5 days, in order to investigate the role of oxidative stress in the contractile dysfunction induced by diabetes. Electrical stimulation of the sciatic nerve *in situ* was used to evaluate the maximal force production, fatigue resistance e contractile properties (shortening and relaxation speed) of soleus and extensor digitorum lungus (EDL) muscles. Skeletal muscle incubation with Amplex UltraRed® probe was used to measure the release of H_2O_2 from muscle samples. The contents of hypoxia-inducible factor-1 alpha (HIF-1α), vascular endothelial growth factor (VEGF), peroxisome proliferator-activated receptor gamma co-activator 1alpha (PGC-1α) and cytochrome c oxidase subunit IV (COX IV) were assessed by western blotting. The expression of glucose transporter 4 (GLUT4), peroxisome proliferator-activated receptor alpha and beta (PPARα and β) and citrate synthase was evaluated using the quantitative real-time polymerase chain reaction (RT-PCR) technique. In diabetic rats, both muscles had signs of oxidative stress, as shown by the increased H_2O_2 content when compared to the control group. This effect was abolished by the NAC treatment. The soleus muscle of diabetic rats was less resistant to fatigue than control. In addition, it also presented reduced content of HIF-1α, VEGF, PGC-1α and COX IV and decreased expression of PPARα, citrate synthase and GLUT4, which can be associated to impairment of oxidative metabolism, angiogenesis and mitochondrial biogenesis. The treatment with NAC decreased soleus muscle production of H_2O_2 during contractions, delayed the onset of fatigue and restored the content / expression of the markers cited above. The EDL muscle of diabetic rats presented slowed relaxation. It also showed an increase of PGC-1α and COX IV content and PPARβ expression, which could be related to the conversion of type 2/glycolytic/fast fibers to type 1/oxidative/slow fibers. The NAC treatment reestablished the content / expression of those markers and restored the relaxation speed of the EDL muscle from diabetic rats. In summary, the oxidative stress of skeletal muscle induced by diabetes is associated with specific alterations on EDL and soleus muscles. Oxidative stress may take part in the early onset of fatigue and energy metabolism impairment of soleus muscle from diabetic rats. In the EDL muscle, it could be involved in the conversion of glycolytic/fast fibers to oxidative/slow fibers and calcium uptake impairment.

Keywords: *Diabetes mellitus*. Oxidative stress. Antioxidants. N-acetyl-L-cysteine. Skeletal muscle. Muscle contractile activity.

1 INTRODUÇÃO

O músculo esquelético produz continuamente espécies reativas de oxigênio (EROs). Por muito tempo acreditou-se que elas estivessem associadas apenas a efeitos deletérios às funções celulares. Atualmente, há evidências que suportam a proposição de que elas atuam como moléculas reguladoras de diversas funções no músculo esquelético, incluindo captação de glicose, prolongamento do transiente de cálcio, biogênese mitocondrial, proliferação de células satélites, modulação de vias de sinalização e regulação da expressão gênica. Estímulos como contração, insulina, citocinas, epinefrina e norepinefrina aumentam transitoriamente a produção de EROs no músculo.

A depleção das EROs no músculo é realizada por sistemas antioxidantes e o balanço entre produção e detoxicação é importante para a manutenção do equilíbrio redox no tecido. O estresse oxidativo ocorre em situações crônicas de maior produção de EROs ou menor defesa antioxidante, causando lesões em estruturas celulares e comprometimento da sinalização redox. Situações patológicas, como distrofia muscular, obesidade, insuficiência cardíaca e diabetes apresentam estresse oxidativo no músculo esquelético.

9 CONCLUSÃO

O estresse oxidativo que acomete o músculo esquelético no quadro de diabetes é parte integrante do desenvolvimento ou manutenção das alterações decorrentes da doença, e que são específicas para cada tipo muscular. Tendo origem multifatorial, apenas o controle do estresse oxidativo por antioxidantes não abole completamente estas alterações, mas pode gerar um ambiente permissivo para as intervenções convencionais.

REFERÊNCIAS[1]

Adachi T, Weisbrod RM, Pimentel DR, Ying J, Sharov VS, Schöneich C, Cohen RA. S-Glutathiolation by peroxynitrite activates SERCA during arterial relaxation by nitric oxide. Nat Med. 2004 Nov;10(11):1200-7. Epub 2004 Oct 17.

Andersson U, Leighton B, Young ME, Blomstrand E, Newsholme EA. Inactivation of aconitase and oxoglutarate dehydrogenase in skeletal muscle in vitro by superoxide anions and/or nitric oxide. Biochem Biophys Res Commun. 1998 Aug 19;249(2):512-6.

Andrade FH, Reid MB, Allen DG, Westerblad H. Effect of hydrogen peroxide and dithiothreitol on contractile function of single skeletal muscle fibres from the mouse. J Physiol. 1998 Jun 1;509 (Pt 2):565-75.

Andrade FH, Reid MB, Westerblad H. Contractile response of skeletal muscle to low peroxide concentrations: myofibrillar calcium sensitivity as a likely target for redox-modulation. FASEB J. 2001 Feb;15(2):309-11. Epub 2000 Dec 8.

Aragno M, Mastrocola R, Catalano MG, Brignardello E, Danni O, Boccuzzi G. Oxidative stress impairs skeletal muscle repair in diabetic rats. Diabetes. 2004 Apr;53(4):1082-8.

Arany Z, Foo SY, Ma Y, Ruas JL, Bommi-Reddy A, Girnun G, Cooper M, Laznik D, Chinsomboon J, Rangwala SM, Baek KH, Rosenzweig A, Spiegelman BM. HIF-independent regulation of VEGF and angiogenesis by the transcriptional coactivator PGC-1alpha. Nature. 2008 Feb 21;451(7181):1008-12.

Armstrong RB, Gollnick PD, Ianuzzo CD. Histochemical properties of skeletal muscle fibers in streptozotocin-diabetic rats. Cell Tissue Res. 1975 Oct 13;162(3):387-94.

Aruoma OI, Halliwell B, Hoey BM, Butler J. The antioxidant action of N-acetylcysteine: its reaction with hydrogen peroxide, hydroxyl radical, superoxide, and hypochlorous acid. Free Radic Biol Med. 1989;6(6):593-7.

Atkinson MA. The pathogenesis and natural history of type 1 diabetes. Cold Spring Harb Perspect Med. 2012 Nov 1;2(11). pii: a007641.

Avramoglu RK, Basciano H, Adeli K. Lipid and lipoprorein dysregulation in insulin resistant states. Clin Chim Acta. 2006;368:1-19.

Baar K. Involvement of PPAR gamma co-activator-1, nuclear respiratory factors 1 and 2, and PPAR alpha in the adaptive response to endurance exercise. Proc Nutr Soc. 2004 May;63(2):269-73.

Babior BM. NADPH oxidase. Curr Opin Immunol. 2004 Feb;16(1):42-7.

[1]De acordo com:
International Committee of Medical Journal Editors. [Internet]. Uniform requirements for manuscripts submitted to Biomedical Journal: sample references. [updated 2011 Jul 15]. Available from: http://www.icmje.org.

Bakkar N, Guttridge DC. NF-kappaB signaling: a tale of two pathways in skeletal myogenesis. Physiol Rev. 2010 Apr;90(2):495-511.

Barclay JK, Hansel M. Free radicals may contribute to oxidative skeletal muscle fatigue. Can J Physiol Pharmacol. 1991 Feb;69(2):279-84.

Bassel-Duby R, Olson EN. Signaling pathways in skeletal muscle remodeling. Annu Rev Biochem. 2006;75:19-37.

Baynes JW. Role of oxidative stress in development of complications in diabetes. Diabetes. 1991 Apr;40(4):405-12.

Bejma J, Ji LL. Aging and acute exercise enhance free radical generation in rat skeletal muscle. J Appl Physiol. 1999 Jul;87(1):465-70.

Bellin C, de Wiza DH, Wiernsperger NF, Rösen P. Generation of reactive oxygen species by endothelial and smooth muscle cells: influence of hyperglycemia and metformin. Horm Metab Res. 2006 Nov;38(11):732-9.

Belviranli M, Gökbel H. Acute exercise induced oxidative stress and antioxidant changes. Eur J Gen Med. 2006;3(3):126-31.

Benders AA, Oosterhof A, Wevers RA, Veerkamp JH. Excitation-contraction coupling of cultured human skeletal muscle cells and the relation between basal cytosolic Ca2+ and excitability. Cell Calcium. 1997 Jan;21(1):81-91.

Bloch-Damti A, Bashan N. Proposed mechanisms for the induction of insulin resistance by oxidative stress. Antioxid Redox Signal. 2005 Nov-Dec;7(11-12):1553-67.

Bodine SC, Latres E, Baumhueter S, Lai VK, Nunez L, Clarke BA, Poueymirou WT, Panaro FJ, Na E, Dharmarajan K, Pan ZQ, Valenzuela DM, DeChiara TM, Stitt TN, Yancopoulos GD, Glass DJ. Identification of ubiquitin ligases required for skeletal muscle atrophy. Science. 2001 Nov 23;294(5547):1704-8. Epub 2001 Oct 25.

Bolster DR, Crozier SJ, Kimball SR, Jefferson LS. AMP-activated protein kinase suppresses protein synthesis in rat skeletal muscle through down-regulated mammalian target of rapamycin (mTOR) signaling. J Biol Chem. 2002 Jul 5;277(27):23977-80. Epub 2002 May 7.

Bonetto A, Penna F, Muscaritoli M, Minero VG, Rossi Fanelli F, Baccino FM, Costelli P. Are antioxidants useful for treating skeletal muscle atrophy? Free Radic Biol Med. 2009 Oct 1;47(7):906-16. Epub 2009 Jul 8.

Bonnard C, Durand A, Peyrol S, Chanseaume E, Chauvin MA, Morio B, Vidal H, Rieusset J. Mitochondrial dysfunction results from oxidative stress in the skeletal muscle of diet-induced insulin-resistant mice. J Clin Invest. 2008 Feb;118(2):789-800.

Brack AS, Rando TA. Tissue-specific stem cells: lessons from the skeletal muscle satellite cell. Cell Stem Cell. 2012 May 4;10(5):504-14.

Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem. 1976 May 7;72:248-54.

Brannon MA, Dodson MV, Wheeler BA, Mathison BD, Mathison BA. Satellite cells derived from streptozotocin-diabetic rats display altered fusion parameters in vitro. Metabolism. 1989 Apr;38(4):348-52.

Bravard A, Bonnard C, Durand A, Chauvin MA, Favier R, Vidal H, Rieusset J. Inhibition of xanthine oxidase reduces hyperglycemia-induced oxidative stress and improves mitochondrial alterations in skeletal muscle of diabetic mice. Am J Physiol Endocrinol Metab. 2011 Mar;300(3):E581-91. Epub 2011 Jan 11.

Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature. 2001; 414:813-20.

Cai D, Frantz JD, Tawa NE Jr, Melendez PA, Oh BC, Lidov HG, Hasselgren PO, Frontera WR, Lee J, Glass DJ, Shoelson SE. IKKbeta/NF-kappaB activation causes severe muscle wasting in mice. Cell. 2004 Oct 15;119(2):285-98.

Chakkalakal JV, Jones KM, Basson MA, Brack AS. The aged niche disrupts muscle stem cell quiescence. Nature. 2012 Oct 18;490(7420):355-60. Epub 2012 Sep 26.

Chao TT, Ianuzzo CD, Armstrong RB, Albright JT, Anapolle SE. Ultrastructural alterations in skeletal muscle fibers of streptozotocin-diabetic rats. Cell Tissue Res. 1976 May 6;168(2):239-46.

Chargé SB, Rudnicki MA. Cellular and molecular regulation of muscle regeneration. Physiol Rev. 2004 Jan;84(1):209-38.

Clanton TL, Zuo L, Klawitter P. Oxidants and skeletal muscle function: physiologic and pathophysiologic implications. Proc Soc Exp Biol Med. 1999 Dec;222(3):253-62.

Copray S, Liem R, Brouwer N, Greenhaff P, Habens F, Fernyhough P. Contraction-induced muscle fiber damage is increased in soleus muscle of streptozotocin-diabetic rats and is associated with elevated expression of brain-derived neurotrophic factor mRNA in muscle fibers and activated satellite cells. Exp Neurol. 2000 Feb;161(2):597-608.

Cornelison DD, Olwin BB, Rudnicki MA, Wold BJ. MyoD(-/-) satellite cells in single-fiber culture are differentiation defective and MRF4 deficient. Dev Biol. 2000 Aug 15;224(2):122-37.

Dalton TP, Chen Y, Schneider SN, Nebert DW, Shertzer HG. Genetically altered mice to evaluate glutathione homeostasis in health and disease. Free Radic Biol Med. 2004 Nov 15;37(10):1511-26.

Davies KJ, Quintanilha AT, Brooks GA, Packer L. Free radicals and tissue damage produced by exercise. Biochem Biophys Res Commun. 1982 Aug 31;107(4):1198-205.

De Angelis K, Senna S, Irigoyen MC, Cestari IA. Diabetes-induced alterations in latissimus dorsi muscle properties impair effectiveness of dynamic cardiomyoplasty in rats. Artif Organs. 2004 Apr;28(4):326-31.

De Angelis KL, Cestari IA, Barp J, Dall'Ago P, Fernandes TG, de Bittencourt PI, Belló-Klein A, Belló AA, Llesuy S, Irigoyen MC. Oxidative stress in the latissimus dorsi muscle of diabetic rats. Braz J Med Biol Res. 2000 Nov;33(11):1363-8.

Demasi M, Silva GM, Netto LE. 20 S proteasome from Saccharomyces cerevisiae is responsive to redox modifications and is S-glutathionylated. J Biol Chem. 2003 Jan 3;278(1):679-85. Epub 2002 Oct 29.

Drowley L, Okada M, Beckman S, Vella J, Keller B, Tobita K, Huard J. Cellular antioxidant levels influence muscle stem cell therapy. Mol Ther. 2010 Oct;18(10):1865-73. Epub 2010 Jul 27.

Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005; 365:1415-28.

Eibschutz B, Lopaschuk GD, McNeill JH, Katz S. Ca2+-transport in skeletal muscle sarcoplasmic reticulum of the chronically diabetic rat. Res Commun Chem Pathol Pharmacol. 1984 Aug;45(2):301-4.

El Midaoui A, Chiasson JL, Tancrède G, Nadeau A. Physical training reverses the increased activity of the hepatic ketone body synthesis pathway in chronically diabetic rats. Am J Physiol Endocrinol Metab. 2006 Feb;290(2):E207-12.

Emanueli C, Salis MB, Pinna A, Stacca T, Milia AF, Spano A, Chao J, Chao L, Sciola L, Madeddu P. Prevention of diabetes-induced microangiopathy by human tissue kallikrein gene transfer. Circulation. 2002 Aug 20;106(8):993-9.

Fan X, Hussien R, Brooks GA. H2O2-induced mitochondrial fragmentation in C2C12 myocytes. Free Radic Biol Med. 2010 Dec 1;49(11):1646-54. Epub 2010 Aug 27.

Fariss MW, Chan CB, Patel M, Van Houten B, Orrenius S. Role of mitochondria in toxic oxidative stress. Mol Interv. 2005 Apr;5(2):94-111.

Favero TG, Zable AC, Abramson JJ. Hydrogen peroxide stimulates the Ca2+ release channel from skeletal muscle sarcoplasmic reticulum. J Biol Chem. 1995 Oct 27;270(43):25557-63.

Ferreira LD, Bräu L, Nikolovski S, Raja G, Palmer TN, Fournier PA. Effect of streptozotocin-induced diabetes on glycogen resynthesis in fasted rats post-high-intensity exercise. Am J Physiol Endocrinol Metab. 2001 Jan;280(1):E83-91.

Ferreira LF, Reid MB. Muscle-derived ROS and thiol regulation in muscle fatigue. J Appl Physiol. 2008 Mar;104(3):853-60. Epub 2007 Nov 15.

Fewell JG, Moerland TS. Responses of mouse fast and slow skeletal muscle to streptozotocin diabetes: myosin isoenzymes and phosphorous metabolites. Mol Cell Biochem. 1995 Jul 19;148(2):147-54.

Gale EA. Type 1 diabetes in the young: the harvest of sorrow goes on. Diabetologia. 2005 Aug;48(8):1435-8.

Gayraud-Morel B, Chrétien F, Flamant P, Gomès D, Zammit PS, Tajbakhsh S. A role for the myogenic determination gene Myf5 in adult regenerative myogenesis. Dev Biol. 2007 Dec 1;312(1):13-28. Epub 2007 Sep 11.

Gilbert HF. Biological disulfides: the third messenger? Modulation of phosphofructokinase activity by thiol/disulfide exchange. J Biol Chem. 1982 Oct 25;257(20):12086-91.

Gilde AJ, Van Bilsen M. Peroxisome proliferator-activated receptors (PPARS): regulators of gene expression in heart and skeletal muscle. Acta Physiol Scand. 2003 Aug;178(4):425-34.

Glass DJ. Skeletal muscle hypertrophy and atrophy signaling pathways. Int J Biochem Cell Biol. 2005 Oct;37(10):1974-84.

Goldberg AL, Goodman HM. Relationship between cortisone and muscle work in determining muscle size. J Physiol. 1969 Feb;200(3):667-75.

Gomes MD, Lecker SH, Jagoe RT, Navon A, Goldberg AL. Atrogin-1, a muscle-specific F-box protein highly expressed during muscle atrophy. Proc Natl Acad Sci U S A. 2001 Dec 4;98(25):14440-5. Epub 2001 Nov 20.

Gomez-Cabrera MC, Borrás C, Pallardó FV, Sastre J, Ji LL, Viña J. Decreasing xanthine oxidase-mediated oxidative stress prevents useful cellular adaptations to exercise in rats. J Physiol. 2005 Aug 15;567(Pt 1):113-20. Epub 2005 Jun 2.

Goodyear LJ, Hirshman MF, Horton ES. Exercise-induced translocation of skeletal muscle glucose transporters. Am J Physiol. 1991 Dec;261(6 Pt 1):E795-9.

Gumieniczek A, Hopkała H, Wójtowicz Z, Nieradko M. Differences in antioxidant status in skeletal muscle tissue in experimental diabetes. Clin Chim Acta. 2001 Dec;314(1-2):39-45.

Guttridge DC, Mayo MW, Madrid LV, Wang CY, Baldwin AS Jr. NF-kappaB-induced loss of MyoD messenger RNA: possible role in muscle decay and cachexia. Science. 2000 Sep 29;289(5488):2363-6.

Halvatsiotis P, Short KR, Bigelow M, Nair KS. Synthesis rate of muscle proteins, muscle functions, and amino acid kinetics in type 2 diabetes. Diabetes. 2002 Aug;51(8):2395-404.

Handschin C, Spiegelman BM. Peroxisome proliferator-activated receptor gamma coactivator 1 coactivators, energy homeostasis, and metabolism. Endocr Rev. 2006 Dec;27(7):728-35. Epub 2006 Oct 3.

Harris ED. Regulation of antioxidant enzymes. FASEB J. 1992 Jun;6(9):2675-83.

Hebert SL, Nair KS. Protein and energy metabolism in type 1 diabetes. Clin Nutr. 2010 Feb;29(1):13-7. Epub 2009 Sep 27.

Hegarty PV, Rosholt MN. Effects of streptozotocin-induced diabetes on the number and diameter of fibres in different skeletal muscles of the rat. J Anat. 1981 Sep;133(Pt 2):205-11.

Hidalgo C, Sánchez G, Barrientos G, Aracena-Parks P. A transverse tubule NADPH oxidase activity stimulates calcium release from isolated triads via ryanodine receptor type 1 S -glutathionylation. J Biol Chem. 2006 Sep 8;281(36):26473-82. Epub 2006 Jun 8.

Hirabara SM, Silveira LR, Abdulkader F, Carvalho CRO, Procopio J, Curi R. Time-dependent effects of fatty acids on skeletal muscle metabolism. J of cell physiol. 2007; 210:7-15.

Howarth FC, Glover L, Culligan K, Qureshi MA, Ohlendieck K. Calsequestrin expression and calcium binding is increased in streptozotocin-induced diabetic rat skeletal muscle though not in cardiac muscle. Pflugers Arch. 2002 May;444(1-2):52-8. Epub 2002 Feb 7.

Hyldahl RD, Schwartz LM, Clarkson PM. NF-KB activity functions in primary pericytes in a cell- and non-cell-autonomous manner to affect myotube formation. Muscle Nerve. 2013 Apr;47(4):522-31. Epub 2013 Jan 31.

Jackson MJ, Edwards RH, Symons MC. Electron spin resonance studies of intact mammalian skeletal muscle. Biochim Biophys Acta. 1985 Nov 20;847(2):185-90.

Jellinger PS. Metabolic consequences of hyperglycemia and insulin resistance. Clin Cornerstone. 2007;8 Suppl 7:S30-42.

Ji LL. Antioxidant signaling in skeletal muscle: a brief review. Exp Gerontol. 2007 Jul;42(7):582-93. Epub 2007 Mar 21.

Ji LL. Modulation of skeletal muscle antioxidant defense by exercise: Role of redox signaling. Free Radic Biol Med. 2008 Jan 15;44(2):142-52. Epub 2007 Mar 12.

Johansen JS, Harris AK, Rychly DJ, Ergul A. Oxidative stress and the use of antioxidants in diabetes: linking basic science to clinical practice. Cardiovasc Diabetol. 2005 Apr 29;4(1):5.

Johnson SE, Allen RE. Proliferating cell nuclear antigen (PCNA) is expressed in activated rat skeletal muscle satellite cells. J Cell Physiol. 1993 Jan;154(1):39-43.
Juel C. Muscle fatigue and reactive oxygen species. J Physiol. 2006 Oct 1;576(Pt 1):1. Epub 2006 Aug 10.

Kang C, O'Moore KM, Dickman JR, Ji LL. Exercise activation of muscle peroxisome proliferator-activated receptor-gamma coactivator-1alpha signaling is redox sensitive. Free Radic Biol Med. 2009 Nov 15;47(10):1394-400. Epub 2009 Aug 14.

Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J. Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. Diabetes Care. 2000 Oct;23(10):1516-26.

Kelleher AR, Fairchild TJ, Keslacy S. STZ-induced skeletal muscle atrophy is associated with increased p65 content and downregulation of insulin pathway without NF-κB canonical cascade activation. Acta Diabetol. 2010 Dec;47(4):315-23. Epub 2010 Jul 17.

Keppler, D. and Decker, K. Glycogen determination with amyloglucosidase. In: Bergmeyer HU, editor. Methods of enzymatic analysis. New York: Academic Press; 1974. vol. 3. p. 1127-31.

Kivelä R, Silvennoinen M, Touvra AM, Lehti TM, Kainulainen H, Vihko V. Effects of experimental type 1 diabetes and exercise training on angiogenic gene expression and capillarization in skeletal muscle. FASEB J. 2006 Jul;20(9):1570-2.

Klip A, Pâquet MR. Glucose transport and glucose transporters in muscle and their metabolic regulation. Diabetes Care. 1990 Mar;13(3):228-43.

Klueber KM, Feczko JD. Ultrastructural, histochemical, and morphometric analysis of skeletal muscle in a murine model of type I diabetes. Anat Rec. 1994 May;239(1):18-34.

Knapp JR, Davie JK, Myer A, Meadows E, Olson EN, Klein WH. Loss of myogenin in postnatal life leads to normal skeletal muscle but reduced body size. Development. 2006 Feb;133(4):601-10. Epub 2006 Jan 11.

Kraegen EW, Cooney GJ. Free fatty acids and skeletal muscle insulin resistance. Curr Opin Lipidol. 2008; 19:235–41.

Kramer HF, Goodyear LJ. Exercise, MAPK, and NF-kappaB signaling in skeletal muscle. J Appl Physiol. 2007 Jul;103(1):388-95. Epub 2007 Feb 15.

Krause MP, Riddell MC, Gordon CS, Imam SA, Cafarelli E, Hawke TJ. Diabetic myopathy differs between Ins2Akita+/- and streptozotocin-induced Type 1 diabetic models. J Appl Physiol. 2009 May;106(5):1650-9. Epub 2009 Feb 26.

Krause MP, Riddell MC, Hawke TJ. Effects of type 1 diabetes mellitus on skeletal muscle: clinical observations and physiological mechanisms. Pediatr Diabetes. 2011 Jun;12(4 Pt 1):345-64. Epub 2010 Sep 22

Krishnamurthy N, Balakumar B, Thombre DP. Acute effects of experimental diabetes on skeletal muscle contractile functions. Clin Physiol Biochem. 1992;9(4):119-23.

Kuwahara H, Horie T, Ishikawa S, Tsuda C, Kawakami S, Noda Y, Kaneko T, Tahara S, Tachibana T, Okabe M, Melki J, Takano R, Toda T, Morikawa D, Nojiri H, Kurosawa H, Shirasawa T, Shimizu T. Oxidative stress in skeletal muscle causes severe disturbance of exercise activity without muscle atrophy. Free Radic Biol Med. 2010 May 1;48(9):1252-62. Epub 2010 Feb 13.

Le Grand F, Rudnicki MA. Skeletal muscle satellite cells and adult myogenesis. Curr Opin Cell Biol. 2007 Dec;19(6):628-33. Epub 2007 Nov 8.

Lecarpentier Y, Krokidis X, Martin P, Pineau T, Hébert JL, Quillard J, Cortes-Morichetti M, Coirault C. Increased entropy production in diaphragm muscle of PPAR alpha knockout mice. J Theor Biol. 2008 Jan 7;250(1):92-102. Epub 2007 Sep 21.

Lecker SH, Jagoe RT, Gilbert A, Gomes M, Baracos V, Bailey J, Price SR, Mitch WE, Goldberg AL. Multiple types of skeletal muscle atrophy involve a common program of changes in gene expression. FASEB J. 2004 Jan;18(1):39-51.

Lecker SH, Salomon V, Price SR, Kwon YT, Mitch WE, Goldberg AL. Ubiquitin conjugation by the N-end rule pathway and mRNAs for its components increase in muscles of diabetic rats. J Clin Invest. 1999; 104:1411–20.

Lee SJ, McPherron AC. Regulation of myostatin activity and muscle growth. Proc Natl Acad Sci U S A. 2001 Jul 31;98(16):9306-11. Epub 2001 Jul 17.

Leone TC, Weinheimer CJ, Kelly DP. A critical role for the peroxisome proliferator-activated receptor alpha (PPARalpha) in the cellular fasting response: the PPARalpha-null mouse as a model of fatty acid oxidation disorders. Proc Natl Acad Sci U S A. 1999 Jun 22;96(13):7473-8.

Lesniewski LA, Miller TA, Armstrong RB. Mechanisms of force loss in diabetic mouse skeletal muscle. Muscle Nerve. 2003 Oct;28(4):493-500.

Li YP, Schwartz RJ, Waddell ID, Holloway BR, Reid MB. Skeletal muscle myocytes undergo protein loss and reactive oxygen-mediated NF-kappaB activation in response to tumor necrosis factor alpha. FASEB J. 1998 Jul;12(10):871-80.

Lin J, Puigserver P, Donovan J, Tarr P, Spiegelman BM. Peroxisome proliferator-activated receptor gamma coactivator 1beta (PGC-1beta), a novel PGC-1-related transcription coactivator associated with host cell factor. J Biol Chem. 2002 Jan 18;277(3):1645-8. Epub 2001 Nov 30.

Liu D, Black BL, Derynck R. TGF-beta inhibits muscle differentiation through functional repression of myogenic transcription factors by Smad3. Genes Dev. 2001 Nov 15;15(22):2950-66.

Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods. 2001 Dec;25(4):402-8.

Ljubisavljevic M, Qureshi A, Nagelkerke N. The effects of neuropeptide Y on skeletal muscle contractile properties in streptozotocin diabetic rats. Mol Cell Biochem. 2010 Jan;333(1-2):27-32. Epub 2009 Jul 19.

Loh K, Deng H, Fukushima A, Cai X, Boivin B, Galic S, Bruce C, Shields BJ, Skiba B, Ooms LM, Stepto N, Wu B, Mitchell CA, Tonks NK, Watt MJ, Febbraio MA, Crack PJ, Andrikopoulos S, Tiganis T. Reactive oxygen species enhance insulin sensitivity. Cell Metab. 2009 Oct;10(4):260-72.

Lokireddy S, McFarlane C, Ge X, Zhang H, Sze SK, Sharma M, Kambadur R. Myostatin induces degradation of sarcomeric proteins through a Smad3 signaling mechanism during skeletal muscle wasting. Mol Endocrinol. 2011 Nov;25(11):1936-49. Epub 2011 Sep 29.

Long YC, Zierath JR. AMP-activated protein kinase signaling in metabolic regulation. J Clin Invest. 2006 Jul;116(7):1776-83.

Luquet S, Lopez-Soriano J, Holst D, Fredenrich A, Melki J, Rassoulzadegan M, Grimaldi PA. Peroxisome proliferator-activated receptor delta controls muscle development and oxidative capability. FASEB J. 2003 Dec;17(15):2299-301. Epub 2003 Oct 2.

Maccarrone M, Ullrich V. Redox regulation in disease and ageing. Cell Death Differ. 2004 Aug;11(8):949-51.

Mair SD, Seaber AV, Glisson RR, Garrett WE Jr. The role of fatigue in susceptibility to acute muscle strain injury. Am J Sports Med. 1996 Mar-Apr;24(2):137-43.

Maritim AC, Sanders RA, Watkins JB 3rd. Diabetes, oxidative stress, and antioxidants: a review. J Biochem Mol Toxicol. 2003;17(1):24-38.

Masaoka T, Suzuki H, Hosoda H, Ota T, Minegishi Y, Nagata H, Kangawa K, Ishii H. Enhanced plasma ghrelin levels in rats with streptozotocin-induced diabetes. FEBS Lett. 2003 Apr 24;541(1-3):64-8.

Mastrocola R, Reffo P, Penna F, Tomasinelli CE, Boccuzzi G, Baccino FM, Aragno M, Costelli P. Muscle wasting in diabetic and in tumor-bearing rats: role of oxidative stress. Free Radic Biol Med. 2008 Feb 15;44(4):584-93. Epub 2007 Nov 1.

Matsunami T, Sato Y, Sato T, Ariga S, Shimomura T, Yukawa M. Oxidative stress and gene expression of antioxidant enzymes in the streptozotocin-induced diabetic rats under hyperbaric oxygen exposure. Int J Clin Exp Pathol. 2009 Nov 30;3(2):177-88.

Matkovics B, Sasvári M, Kotormán M, Varga IS, Hai DQ, Varga C. Further prove on oxidative stress in alloxan diabetic rat tissues. Acta Physiol Hung. 1997-1998;85(3):183-92.

Mayr B, Montminy M. Transcriptional regulation by the phosphorylation-dependent factor CREB. Nat Rev Mol Cell Biol. 2001 Aug;2(8):599-609.

McArdle A, Pattwell D, Vasilaki A, Griffiths RD, Jackson MJ. Contractile activity-induced oxidative stress: cellular origin and adaptive responses. Am J Physiol Cell Physiol. 2001 Mar;280(3):C621-7.

McGuire M, MacDermott M. The influence of streptozotocin diabetes and metformin on erythrocyte volume and on the membrane potential and the contractile characteristics of the extensor digitorum longus and soleus muscles in rats. Exp Physiol. 1999 Nov;84(6):1051-8.

McGuire M, MacDermott M. The influence of streptozotocin-induced diabetes and the antihyperglycaemic agent metformin on the contractile characteristics and the membrane potential of the rat diaphragm. Exp Physiol. 1998 Jul;83(4):481-7.

McKenna MJ, Medved I, Goodman CA, Brown MJ, Bjorksten AR, Murphy KT, Petersen AC, Sostaric S, Gong X. N-acetylcysteine attenuates the decline in muscle Na+,K+-pump activity and delays fatigue during prolonged exercise in humans. J Physiol. 2006 Oct 1;576(Pt 1):279-88. Epub 2006 Jul 13.

McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. Nature. 1997 May 1;387(6628):83-90.

Medved I, Brown MJ, Bjorksten AR, Murphy KT, Petersen AC, Sostaric S, Gong X, McKenna MJ. N-acetylcysteine enhances muscle cysteine and glutathione availability and attenuates fatigue during prolonged exercise in endurance-trained individuals. J Appl Physiol. 2004 Oct;97(4):1477-85. Epub 2004 Jun 11.

Moopanar TR, Allen DG. Reactive oxygen species reduce myofibrillar Ca2+ sensitivity in fatiguing mouse skeletal muscle at 37 degrees C. J Physiol. 2005 Apr 1;564(Pt 1):189-99. Epub 2005 Feb 17.

Moore RD, Munford JW, Pillsworth TJ Jr. Effects of streptozotocin diabetes and fasting on intracellular sodium and adenosine triphosphate in rat soleus muscle. J Physiol. 1983 May;338:277-94.

Muoio DM, MacLean PS, Lang DB, Li S, Houmard JA, Way JM, Winegar DA, Corton JC, Dohm GL, Kraus WE. Fatty acid homeostasis and induction of lipid regulatory genes in skeletal muscles of peroxisome proliferator-activated receptor (PPAR) alpha knock-out mice. Evidence for compensatory regulation by PPAR delta. J Biol Chem. 2002 Jul 19;277(29):26089-97. Epub 2002 May 6.

Murphy RM, Dutka TL, Lamb GD. Hydroxyl radical and glutathione interactions alter calcium sensitivity and maximum force of the contractile apparatus in rat skeletal muscle fibres. J Physiol. 2008 Apr 15;586(8):2203-16. Epub 2008 Feb 28.

Nakagawa M, Kobayashi S, Kimura I, Kimura M. Diabetic state-induced modification of Ca, Mg, Fe and Zn content of skeletal, cardiac and smooth muscles. Endocrinol Jpn. 1989 Dec;36(6):795-807.

Novelli GP, Bracciotti G, Falsini S. Spin-trappers and vitamin E prolong endurance to muscle fatigue in mice. Free Radic Biol Med. 1990;8(1):9-13.

Oktyabrsky ON, Smirnova GV. Redox regulation of cellular functions. Biochemistry (Mosc). 2007 Feb;72(2):132-45.

Ortiz-Caro J, González C, Jolin T. Diurnal variations of plasma growth hormone, thyrotropin, thyroxine, and triiodothyronine in streptozotocin-diabetic and food-restricted rats. Endocrinology. 1984 Dec;115(6):2227-32.

Packer L, Cadenas E, Davies KJ. Free radicals and exercise: an introduction. Free Radic Biol Med. 2008 Jan 15;44(2):123-5. Epub 2007 Jun 6.

Palsamy P, Subramanian S. Ameliorative potential of resveratrol on proinflammatory cytokines, hyperglycemia mediated oxidative stress, and pancreatic beta-cell dysfunction in streptozotocin-nicotinamide-induced diabetic rats. J Cell Physiol. 2010 Aug;224(2):423-32.

Pepato MT, Migliorini RH, Goldberg AL, Kettelhut IC. Role of different proteolytic pathways in degradation of muscle protein from streptozotocin-diabetic rats. Am J Physiol. 1996 Aug;271(2 Pt 1):E340-7.

Pinheiro CH, Silveira LR, Nachbar RT, Vitzel KF, Curi R. Regulation of glycolysis and expression of glucose metabolism-related genes by reactive oxygen species in contracting skeletal muscle cells. Free Radic Biol Med. 2010 Apr 1;48(7):953-60. Epub 2010 Jan 18.

Pinheiro CH, Vitzel KF, Curi R. Effect of N-acetylcysteine on markers of skeletal muscle injury after fatiguing contractile activity. Scand J Med Sci Sports. 2012 Feb;22(1):24-33. Epub 2010 Jul 29.

Plant DR, Lynch GS, Williams DA. Hydrogen peroxide modulates Ca2+-activation of single permeabilized fibres from fast- and slow-twitch skeletal muscles of rats. J Muscle Res Cell Motil. 2000;21(8):747-52.

Posterino GS, Cellini MA, Lamb GD. Effects of oxidation and cytosolic redox conditions on excitation-contraction coupling in rat skeletal muscle. J Physiol. 2003 Mar 15;547(Pt 3):807-23. Epub 2003 Jan 31.

Powers SK, Jackson MJ. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. Physiol Rev. 2008 Oct;88(4):1243-76.

Powers SK, Kavazis AN, McClung JM. Oxidative stress and disuse muscle atrophy. J Appl Physiol. 2007 Jun;102(6):2389-97. Epub 2007 Feb 8.

Powers SK, Lennon SL. Analysis of cellular responses to free radicals: focus on exercise and skeletal muscle. Proc Nutr Soc. 1999 Nov;58(4):1025-33.

Pownall ME, Gustafsson MK, Emerson CP Jr. Myogenic regulatory factors and the specification of muscle progenitors in vertebrate embryos. Annu Rev Cell Dev Biol. 2002;18:747-83. Epub 2002 Apr 2.

Price N, Proud C. The guanine nucleotide-exchange factor, eIF-2B. Biochimie. 1994;76(8):748-60.

Proud CG. eIF2 and the control of cell physiology. Semin Cell Dev Biol. 2005 Feb;16(1):3-12. Epub 2004 Dec 10.

Py G, Eydoux N, Perez-Martin A, Raynaud E, Brun JF, Préfaut C, Mercier J. Streptozotocin-induced diabetes decreases rat sarcolemmal lactate transport. Metabolism. 2001 Apr;50(4):418-24.

Radák Z, Pucsok J, Mecseki S, Csont T, Ferdinandy P. Muscle soreness-induced reduction in force generation is accompanied by increased nitric oxide content and DNA damage in human skeletal muscle. Free Radic Biol Med. 1999 Apr;26(7-8):1059-63.

Ramakrishna V, Jailkhani R. Oxidative stress in non-insulin-dependent diabetes mellitus (NIDDM) patients. Acta Diabetol. 2008 Mar;45(1):41-6. Epub 2007 Oct 9.

Randle PJ, Garland PB, Hales CN, Newsholme EA. The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. Lancet. 1963; 1:785–789.

Randle PJ. Regulatory interactions between lipids and carbohydrates: The glucose fatty acid cycle after 35 years. Diabetes Metab Rev. 1998;14(4):263–83.

Rauramaa R, Harri M, Puhakainen E, Kuusela P, Hänninen O. Metabolic adaptation in muscle and brown adipose tissues to insulin deficiency in streptozotocin treated rats. Comp Biochem Physiol B. 1980;66(3):391-5.

Regensteiner JG, Sippel J, McFarling ET, Wolfel EE, Hiatt WR. Effects of non-insulin-dependent diabetes on oxygen consumption during treadmill exercise. Med Sci Sports Exerc. 1995 May;27(5):661-7.

Reid MB, Khawli FA, Moody MR. Reactive oxygen in skeletal muscle. III. Contractility of unfatigued muscle. J Appl Physiol. 1993 Sep;75(3):1081-7.

Reid MB, Stokić DS, Koch SM, Khawli FA, Leis AA. N-acetylcysteine inhibits muscle fatigue in humans. J Clin Invest. 1994 Dec;94(6):2468-74.

Reid MB. Nitric oxide, reactive oxygen species, and skeletal muscle contraction. Med Sci Sports Exerc. 2001 Mar;33(3):371-6.

Rhee SG, Chang TS, Jeong W, Kang D. Methods for detection and measurement of hydrogen peroxide inside and outside of cells. Mol Cells. 2010 Jun;29(6):539-49. Epub 2010 Jun 4.

Rhees RW, Wilson CT, Heninger RW. Influence of streptozotocin diabetes and insulin therapy on plasma corticosterone levels in male rats. Horm Metab Res. 1983 Jul;15(7):353-4.

Ristow M, Zarse K, Oberbach A, Klöting N, Birringer M, Kiehntopf M, Stumvoll M, Kahn CR, Blüher M. Antioxidants prevent health-promoting effects of physical exercise in humans. Proc Natl Acad Sci U S A. 2009 May 26;106(21):8665-70. Epub 2009 May 11.

Roberts-Wilson TK, Reddy RN, Bailey JL, Zheng B, Ordas R, Gooch JL, Price SR. Calcineurin signaling and PGC-1alpha expression are suppressed during muscle atrophy due to diabetes. Biochim Biophys Acta. 2010 Aug;1803(8):960-7. Epub 2010 Mar 29.

Roy D, Marette A. Exercise induces the translocation of GLUT4 to transverse tubules from an intracellular pool in rat skeletal muscle. Biochem Biophys Res Commun. 1996 Jun 5;223(1):147-52.

Roy M, Collier B, Roy A. Hypothalamic-pituitary-adrenal axis dysregulation among diabetic outpatients. Psychiatry Res. 1990 Jan;31(1):31-7.

Rutschmann M, Dahlmann B, Reinauer H. Loss of fast-twitch isomyosins in skeletal muscles of the diabetic rat. Biochem J. 1984 Aug 1;221(3):645-50.

Sabourin LA, Girgis-Gabardo A, Seale P, Asakura A, Rudnicki MA. Reduced differentiation potential of primary MyoD-/- myogenic cells derived from adult skeletal muscle. J Cell Biol. 1999 Feb 22;144(4):631-43.

Salvi N, Guellich A, Michelet P, Demoule A, Le Guen M, Renou L, Bonne G, Riou B, Langeron O, Coirault C. Upregulation of PPARbeta/delta is associated with structural and functional changes in the type I diabetes rat diaphragm. PLoS One. 2010 Jul 8;5(7):e11494.

Sandri M. Signaling in muscle atrophy and hypertrophy. Physiology (Bethesda). 2008 Jun;23:160-70.

Sartori R, Milan G, Patron M, Mammucari C, Blaauw B, Abraham R, Sandri M. Smad2 and 3 transcription factors control muscle mass in adulthood. Am J Physiol Cell Physiol. 2009 Jun;296(6):C1248-57. Epub 2009 Apr 8.

Scherer NM, Deamer DW. Oxidative stress impairs the function of sarcoplasmic reticulum by oxidation of sulfhydryl groups in the Ca2+-ATPase. Arch Biochem Biophys. 1986 May 1;246(2):589-601.

Sen CK, Packer L. Thiol homeostasis and supplements in physical exercise. Am J Clin Nutr. 2000 Aug;72(2 Suppl):653S-69S.

Shapiro AL, Vinuela E, Maizel JV Jr. Molecular weight estimation of polypeptide chains by electrophoresis in SDS polyacrylamide gels. Biochem Biophys Res Commun. 1967;28(5):815–20.

Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010 Jan;87(1):4-14. Epub 2009 Nov 6.

Silveira L, Hirabara SM, Alberici LC, Lambertucci RH, Peres CM, Takahashi HK, Pettri A, Alba-Loureiro T, Luchessi AD, Cury-Boaventura MF, Vercesi AE, Curi R. Effect of lipid infusion on metabolism and force of rat skeletal muscles during intense contractions. Cell Physiol Biochem. 2007;20(1-4):213-26.

Silveira LR, Fiamoncini J, Hirabara SM, Procópio J, Cambiaghi TD, Pinheiro CHJ, Lopes LR, Curi R. Updating the effects of fatty acids on skeletal muscle. J Cell Physiol. 2008; 217(1):1-12.

Simonides WS, Thelen MH, van der Linden CG, Muller A, van Hardeveld C. Mechanism of thyroid-hormone regulated expression of the SERCA genes in skeletal muscle: implications for thermogenesis. Biosci Rep. 2001 Apr;21(2):139-54.

Skapek SX, Rhee J, Spicer DB, Lassar AB. Inhibition of myogenic differentiation in proliferating myoblasts by cyclin D1-dependent kinase. Science. 1995 Feb 17;267(5200):1022-4.

Smith OL, Wong CY, Gelfand RA. Skeletal muscle proteolysis in rats with acute streptozotocin-induced diabetes. Diabetes. 1989;38:1117–22.

Soukup T, Zacharová G, Smerdu V. Fibre type composition of soleus and extensor digitorum longus muscles in normal female inbred Lewis rats. Acta Histochem. 2002;104(4):399-405.

Stephenson GM, O'Callaghan A, Stephenson DG. Single-fiber study of contractile and biochemical properties of skeletal muscles in streptozotocin-induced diabetic rats. Diabetes. 1994 May;43(5):622-8.

St-Pierre J, Drori S, Uldry M, Silvaggi JM, Rhee J, Jäger S, Handschin C, Zheng K, Lin J, Yang W, Simon DK, Bachoo R, Spiegelman BM. Suppression of reactive oxygen species and neurodegeneration by the PGC-1 transcriptional coactivators. Cell. 2006 Oct 20;127(2):397-408.

Sun Z, Liu L, Liu N, Liu Y. Muscular response and adaptation to diabetes mellitus. Front Biosci. 2008 May 1;13:4765-94.

Surh YJ, Kundu JK, Na HK. Nrf2 as a master redox switch in turning on the cellular signaling involved in the induction of cytoprotective genes by some chemopreventive phytochemicals. Planta Med. 2008 Oct;74(13):1526-39. Epub 2008 Oct 20.

Towbin H, Staehelin T, Gordon J. Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. Proc Natl Acad Sci USA. 1979; 76(9):4350–4.

Toyoda T, Hayashi T, Miyamoto L, Yonemitsu S, Nakano M, Tanaka S, Ebihara K, Masuzaki H, Hosoda K, Inoue G, Otaka A, Sato K, Fushiki T, Nakao K. Possible involvement of the alpha1 isoform of 5'AMP-activated protein kinase in oxidative stress-stimulated glucose transport in skeletal muscle. Am J Physiol Endocrinol Metab. 2004 Jul;287(1):E166-73. Epub 2004 Mar 16.

Trendelenburg AU, Meyer A, Rohner D, Boyle J, Hatakeyama S, Glass DJ. Myostatin reduces Akt/TORC1/p70S6K signaling, inhibiting myoblast differentiation and myotube size. Am J Physiol Cell Physiol. 2009 Jun;296(6):C1258-70. Epub 2009 Apr 8.

Tretter L, Adam-Vizi V. Alpha-ketoglutarate dehydrogenase: a target and generator of oxidative stress. Philos Trans R Soc Lond B Biol Sci. 2005 Dec 29;360(1464):2335-45.

Turrens JF. Mitochondrial formation of reactive oxygen species. J Physiol. 2003 Oct 15;552(Pt 2):335-44.

Unsworth BR, Witzmann FA, Fitts RH. A comparison of rat myosin from fast and slow skeletal muscle and the effect of disuse. J Biol Chem. 1982 Dec 25;257(24):15129-36.

Ustanina S, Carvajal J, Rigby P, Braun T. The myogenic factor Myf5 supports efficient skeletal muscle regeneration by enabling transient myoblast amplification. Stem Cells. 2007 Aug;25(8):2006-16. Epub 2007 May 10.

van der Laan L, Oyen WJ, Verhofstad AA, Tan EC, ter Laak HJ, Gabreels-Festen A, Hendriks T, Goris RJ. Soft tissue repair capacity after oxygen-derived free radical-induced damage in one hindlimb of the rat. J Surg Res. 1997 Sep;72(1):60-9.

van Loon LJ, Goodpaster BH. Increased intramuscular lipid storage in the insulin resistant and endurance-trained state. Pflugers Arch. 2006; 451:606-16.

van Montfort RL, Congreve M, Tisi D, Carr R, Jhoti H. Oxidation state of the active-site cysteine in protein tyrosine phosphatase 1B. Nature. 2003 Jun 12;423(6941):773-7.

Vignaud A, Ramond F, Hourdé C, Keller A, Butler-Browne G, Ferry A. Diabetes provides an unfavorable environment for muscle mass and function after muscle injury in mice. Pathobiology. 2007;74(5):291-300.

Vitzel KF, Bikopoulos G, Hung S, Pistor KE, Patterson JD, Curi R, Ceddia RB. Chronic Treatment with the AMP-Kinase Activator AICAR Increases Glycogen Storage and Fatty Acid Oxidation in Skeletal Muscles but Does Not Reduce Hyperglucagonemia and Hyperglycemia in Insulin Deficient Rats. PLoS One. 2013 Apr 19;8(4):e62190.

Wang H, Hertlein E, Bakkar N, Sun H, Acharyya S, Wang J, Carathers M, Davuluri R, Guttridge DC. NF-kappaB regulation of YY1 inhibits skeletal myogenesis through transcriptional silencing of myofibrillar genes. Mol Cell Biol. 2007 Jun;27(12):4374-87. Epub 2007 Apr 16.

Wang YX, Zhang CL, Yu RT, Cho HK, Nelson MC, Bayuga-Ocampo CR, Ham J, Kang H, Evans RM. Regulation of muscle fiber type and running endurance by PPARdelta. PLoS Biol. 2004 Oct;2(10):e294. Epub 2004 Aug 24.

Westerblad H, Allen DG. Changes of myoplasmic calcium concentration during fatigue in single mouse muscle fibers. J Gen Physiol. 1991 Sep;98(3):615-35.

Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004 May;27(5):1047-53.

Winbanks CE, Weeks KL, Thomson RE, Sepulveda PV, Beyer C, Qian H, Chen JL, Allen JM, Lancaster GI, Febbraio MA, Harrison CA, McMullen JR, Chamberlain JS, Gregorevic P. Follistatin-mediated skeletal muscle hypertrophy is regulated by Smad3 and mTOR independently of myostatin. J Cell Biol. 2012 Jun 25;197(7):997-1008. Epub 2012 Jun 18.

Witczak CA, Sharoff CG, Goodyear LJ. AMP-activated protein kinase in skeletal muscle: from structure and localization to its role as a master regulator of cellular metabolism. Cell Mol Life Sci. 2008 Nov;65(23):3737-55.

Wojtaszewski JF, Hansen BF, Ursø B, Richter EA. Wortmannin inhibits both insulin- and contraction-stimulated glucose uptake and transport in rat skeletal muscle. J Appl Physiol. 1996 Oct;81(4):1501-9.

Yin H, Price F, Rudnicki MA. Satellite cells and the muscle stem cell niche. Physiol Rev. 2013 Jan;93(1):23-67.

Zhou M, Diwu Z, Panchuk-Voloshina N, Haugland RP. A stable nonfluorescent derivative of resorufin for the fluorometric determination of trace hydrogen peroxide: applications in detecting the activity of phagocyte NADPH oxidase and other oxidases. Anal Biochem. 1997;253(2):162-8.

Zhu H, Itoh K, Yamamoto M, Zweier JL, Li Y. Role of Nrf2 signaling in regulation of antioxidants and phase 2 enzymes in cardiac fibroblasts: protection against reactive oxygen and nitrogen species-induced cell injury. FEBS Lett. 2005 Jun 6;579(14):3029-36.

Zissimopoulos S, Lai FA. Redox regulation of the ryanodine receptor/calcium release channel. Biochem Soc Trans. 2006 Nov;34(Pt 5):919-21.