1. Kasting JF, Siefert JL (2002) Life and the evolution of Earth's atmosphere. Science 10:1066-1068.
2. Alberts B, Johnson A, Lewis J et al (2002) Molecular biology of the cell. New York, Garland Science.
3. Wood B, Collar M (1999) The human genus. Science 284:65-71.
4. Cerling TE (1992) Development of grasslands and savannas in East Africa during the neogene. Paleogeog Paleoclimatol Paleoecol 97:241-247.
5. Leonard WR, Robertson ML (1997) Comparative primate energetics and hominid evolution. Am J Phys Anthropol 102:265-281.
6. Ulijaszek SJ (2002) Human eating behaviour in an evolutionary ecological context. Proc Nutr Society 61:517-526.
7. Isbell LA, Pruetz JD, Lewis M, Young TP (1998) Locomotor activity differences between sympatric patas monkeys (Erytrocebus Patas) and vervet monkeys (Cercopithecus aethiops):implications for the evolution of long hindlimb length in Homo. Am J Phys Antropol 105:199-207.
8. Bramble DL, Lieberman DE (2004) Endurance running and the evolution of Homo. Nature 433:345-353.
9. Luzi L, Pizzini G (2004) Born to run: training our genes to cope with ecosystem changes in the twentieth century. Sport Sci Health 1:1-4.
10. Neel JV (1962) Diabetes mellitus: a thrifty genotype rendered detrimental by "progress. Am J Hum Genetic 14:353-362 .

Macintosh BR, Gardiner PF, McComas AJ (2006) Skeletal muscle: form and function. Human Kinetics, Leeds.

Lieber RL (2002) Skeletal muscle structure, function, and plasticity. Lippincott Williams & Wilkins, Baltimore

1. Hollán S (1996) Membrane fluidity of blood cells. Haematologia 27:109-27
2. Jacobson K, Sheets ED, Simson R (1995) Revisiting the fluid mosaic model of membranes. Science 268:1441-2
3. Singer SJ (2004) Some early history of membrane molecular biology. Annu Rev Physiol 66:1-27
4. Singer SJ, Nicolson GL (1972) The fluid mosaic model of the structure of cell membranes. Science 175:720-31

1. Terruzzi I, Senesi P, Montesano A et al (2011) Genetic polymorphisms of the enzymes involved in DNA methylation and synthesis in elite athletes. Physiol Genomics 43:965-973
2. Watson JD, Baker TA, Bell SP et al (2008) Molecular biology of the gene. Benjamin Cummings, 6th edn. New York
3. Bompa TO, Haff G (2009) Periodization: theory and methodology of training. Human Kinetics, 5th edn. Chaimpaign, IL
4. Rankinen T, Pérusse L, Rauramaa R et al (2001) The human gene map for performance and health-related fitness phenotypes. Med Sci Sports Exerc 33:855-867

1. Ziegler EE, Filer Jr LJ (1996) Present knowledge in nutrition. ILSi, Washington, DC
2. Willett W (1998) Nutritional epidemiology. Oxford University Press, NY
3. Krause MV, Maham LK (1984) Food, nutrition and diet therapy. W.B. Saunders, Philadelphia
4. Campbell NA, Williamson B, Heyden RJ (2006) Biology: exploring life. Pearson Prentice Hall, Boston, Massachusetts
5. McBride HM, Neuspiel M, Wasiak S (2006) Mitochondria: more than just a powerhouse. Curr Biol 16 (14):R551
6. Voet, D, Voet JG, Pratt CW (2006). Fundamentals of biochemistry, 2nd edn. Wiley, Hoboken NJ
7. Rich PR (2003) The molecular machinery of Keilin's respiratory chain. Biochem Soc Trans 31 (6):1095–105
8. Benardot D (2006)Advanced sports nutrition. Human Kinetics, Champaign, IL
9. Benedini S (2009) The hypothalamus and energy balance. Sport Sci Health 5(2)45-53
10. Sahu A (2003) Leptin signaling in the hypothalamus: emphasis on energy homeostasis and leptin resistance. Front Neuroendocrinol 24(4):225-53
11. Sahu A (2011) Intracellular leptin-signaling pathways in hypothalamic neurons: the emerging role of phosphatidylinositol-3 kinase-phosphodiesterase-3B-cAMP pathway. Neuroendocrinology. [Epub ahead of print]. doi: 10.1159/000326785
12. Meijer EP, Westerterp KR, Verstappen FT (1999) Effect of exercise training on total daily physical activity in elderly humans. Eur J Appl Physiol Occup Physiol 80:16–21
13. Goran MI, Poehlman ET (1992) Endurance training does not enhance total energy expenditure in healthy elderly persons. Am J Physiol263:950–957
14. Meijer G, Jannssen G, Westerterp K et al (1991) The effect of a 5-month endurance training programme on physical activity: evidence for a sex-difference in the metabolic response to exercise. Eur J Appl Physiol 62:11–17
15. Hollowell RP, Willis LH, Slentz CA et al (2009) Effects of exercise training amount on physical activity energy expenditure. Med Sci Sports Exerc 41:1640–1644
16. Slentz CA, Duscha BD, Johnson JL et al (2004) Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE—a randomized controlled study. Arch Intern Med 164:31–39
17. Zurlo F, Lillioja S, Esposito-Del Puente A et al (1990) Low ratio of fat to carbohydrate oxidation as a predictor of weight gain: study of 24 h RQ. Am J Physiol 259:650–657
18. Marra M, Scalfi L, Contaldo F, Pasanisi F (2004) Fasting respiratory quotient as a predictor of long-term weight changes in non-obese women. Ann Nutr Metab 48:189–192
19. Marra M, Scalfi L, Covino A, Esposito-Del Puente A, Contaldo F (1998) Fasting respiratory quotient as a predictor of weight changes in non-obese women. Int J Obes Relat Metab Disord 22:601-3
20. Larson D, Ferraro R, Robertson D, Ravussin E (1995) Energy metabolism in weight stable postobese individuals. Am J Clin Nutr 62:735–739
21. Kelley DE, Goodpaster B, Wing RR, Simoneau JA (1999) Skeletal muscle fatty acid metabolism in association with insulin resistance, obesity, and weight loss. Am J Physiol 277:E1130–E1141
22. Goodpaster BH, Theriault R, Watkins SC, Kelley DE. Intramuscular lipid content is increased in obesity and decreased by weight loss. Metabolism. 2000; 49(4):467-72
23. Houmard JA. Intramuscular lipid oxidation and obesity. Am J Physiol Regul Integr Comp Physiol. 2008; 294(4):1111-1116
24. Slentz CA, Houmard JA, Kraus WE (2009) Exercise, abdominal obesity, skeletal muscle, and metabolic risk: evidence for a dose response. Obesity 17 Suppl 3:27-33

1. De Graaf RA (2007) In vivo NMR spectroscopy: principles and techniques. Wiley, Chichester West Sussex UK.
2. Perseghin G, Lattuada G, Danna M, Sereni L. P, Maffi P, De Cobelli F, Battezzati A, Secchi A, Del Maschio A, and Luzi L (2003) Insulin resistance, intramyocellular lipid content, and plasma adiponectin in patients with type 1 diabetes. Am J Physiol Endocrinol Metab (6) 285:E1174-1181.
3. Hsu AC, Dawson MJ (2000) Accuracy of 1H and 31P MRS analyses of lactate in skeletal muscle. Magn Reson Med 44(3):418-26
4. Kruiskamp M.J, de Graaf RA, van Vliet G, Nicolay K (1999) Magnetic coupling of creatine/ phosphocreatine protons in rat skeletal muscle, as studied by (1)H-magnetization transfer MRS. Magn Reson Med 42(4):665-72
5. Nicolay K, Braun KP, Graaf RA, Dijkhuizen RM, Kruiskamp MJ (2001) Diffusion NMR spectroscopy, NMR Biomed, 14(2):94-111
6. Richardson RS, Duteil S, Wary C, Wray D.W, Hoff J, Carlier PG (2006) Human skeletal muscle intracellular oxygenation: the impact of ambient oxygen availability. J Physiol 571(2)Pt415 – 24.
7. Carlier PG, Bertoldi D, Baligand C, Wary C, Fromes Y (2006) Muscle blood flow and oxygenation measured by NMR imaging and spectroscopy. NMR Biomed 19(7):954-67
8. Jue T, Rothman DL, Shulman GI, Tavitian BA, DeFronzo R. A, Shulman RG (1989) Direct observation of glycogen synthesis in human muscle with 13C NMR. Proc Natl Acad Sci USA 86(12):4489-91
9. Cline GW, Vidal-Puig AJ, Dufour S, Cadman KS, Lowell BB, nd Shulman GI (2001) In vivo effects of uncoupling protein-3 gene disruption on mitochondrial energy metabolism. J Biol Chem 276(23):20240-4
10. Jucker BM, Dufour S, Ren J, Cao X, Previs SF, Underhill B, Cadman KS, Shulman GI (2000) Assessment of mitochondrial energy coupling in vivo by 13C/31P NMR. Proc Natl Acad Sci USA 97(12):6880-4
11. Hoult DI, Busby SJ, Gadian DG, Radda GK, Richards RE, Seeley PJ (1974) Observation of tissue metabolites using 31P nuclear magnetic resonance. Nature 52 (5481):285-7
12. Kemp GJ, Radda GK (1994) Quantitative interpretation of bioenergetic data from 31P and 1H magnetic resonance spectroscopic studies of skeletal muscle: an analytical review. Magn Reson Q 10(1):43-63
13. Kemp GJ, Taylor DJ, Thompson CH, Hands LJ, Rajagopalan B, Styles P, Radda GK (1993) Quantitative analysis by 31P magnetic resonance spectroscopy of abnormal mitochondrial oxidation in skeletal muscle during recovery from exercise. NMR Biomed 6(5):302-10
14. Chance B, Leigh JS, Clark BJ, Maris J, Kent J, Nioka S, Smith D (1985) Control of oxidative metabolism and oxygen delivery in human skeletal muscle: a steady-state analysis of the work/energy cost transfer function. Proc Natl Acad Sci USA 82(24):8384-8.
15. Jeneson JA, Wiseman RW, Kushmerick MJ (1997) Non-invasive quantitative 31P MRS assay of mitochondrial function in skeletal muscle in situ. Mol Cell Biochem 174(1-2):17-22
16. Lanza IR, Wigmore DM, Befroy DE, Kent-Braun JA (2006) In vivo ATP production during free-flow and ischaemic muscle contractions in humans. J Physiol 577(Pt 1):353-67
17. Drost MR, Heemskerk AM, Strijkers GJ, Dekkers EC, van Kranenburg G, Nicolay K (2003) An MR-compatible device for the in situ assessment of isometric contractile performance of mouse hind-limb ankle flexors. Pflugers Arch 447(3):371-5
18. Thompson CH, Kemp GJ, Sanderson AL, Radda GK (1995) Skeletal muscle mitochondrial function studied by kinetic analysis of postexercise phosphocreatine resynthesis. J Appl Physiol 78(6):2131-9
19. Walter G, Vandenborne K, Elliott M, Leigh JS (1999) In vivo ATP synthesis rates in single human muscles during high intensity exercise. J Physiol 519 Pt 3, 901-10
20. Conley K. E, Blei M. L, Richards T. L, Kushmerick M. J, and Jubrias S. A, 1997, Activation of glycolysis in human muscle in vivo, Am J Physiol, 273(1 Pt 1):C306-15
21. Shulman RG, Rothman DL (2001) The glycogen shunt in exercising muscle: A role for glycogen in muscle energetics and fatigue, Proc Natl Acad Sci USA 98(2):457-61
22. Codella R (2008) In vivo magnetic resonance spectroscopy studies of muscle mitochondrial function in transgenic mice. Ph.D. Thesis, University of Milan and Yale University
23. Norris DG (2001) The effects of microscopic tissue parameters on the diffusion weighted magnetic resonance imaging experiment. NMR Biomed 14:77-93

24. Boesch C, Machann J, Vermathen P, and Schick F (2006) Role of proton MR for the study of muscle lipid metabolism. NMR Biomed 19:968-988
25. Petersen KF, Befroy D et al (2003) Mitochondrial dysfunction in the elderly: possible role in insulin resistance. Science 300:1140-1142
26. Forsen S, and Hoffman RA (1963) A New Method for Study of Moderately Rapid Chemical Exchange Rates Employing Nuclear Magnetic Double Resonance. Acta Chemica Scandinavica 17:1787-1788
27. Bangsbo J, Gollnick PD, et al (1990) Anaerobic energy production and O_2 deficit-debt relationship during exhaustive exercise in humans. J Physiol 422:539-559

1. Weyer C, Bogardus C, Mott DM, Pratley RE [1999] The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. J Clin Invest 104: 787-794
2. De Fronzo RA [1988] The triumvirate beta-cell, muscle, live . A collusion responsible for NIDDM. Diabetes 37: 667-687
3. McGarry JD [1992] What if Minkowski had been ageusic? An alternative angle on diabetes. Science 258: 766-770
4. McGarry JD [2002] Dysregulation of fatty acids metabolism in the etiology of type 2 diabetes. Banting Lecture 2001. Diabetes 51: 7-18
5. Reaven GM [1995] The fourth musketeer – from Alexandre Dumas to Claude Bernard. Diabetologia 38: 3-13
6. Perseghin G, Ghosh S, Gerow K, Shulman GI [1997] Metabolic defects in lean nondiabetic offspring of NIDDM parents. A cross-sectional study. Diabetes 46: 1001-1009 .
7. Roden M, Price TB, Perseghin G, et al [1996] Mechanism of free fatty acid induced insulin resistance in humans. J Clin Invest 97: 2859-286
8. Shulman GI, Rothman DL, Jue T, Stein P, DeFronzo RA, Shulman RG [1990] Quantitation of muscle glycogen synthesis in normal subjects and subjects with non-insulin-dependent diabetes by 13C nuclear magnetic resonance spectroscopy. N Engl J Med 322: 223-228
9. Perseghin G, Price TB, Petersen KF, et al [1996] Increased glucose transport/phosphorylation and muscle glycogen synthesis after exercise training in insulin resistant subjects. N Engl J Med 335: 1357-1362
10. Krssak M, Falk Petersen K, Dresner A, et al [1999] Intramyocellular lipid concentrations are correlated with insulin sensitivity in humans: a 1H NMR spectroscopy study. Diabetologia42 : 113-116
11. Perseghin G, Scifo P, De Cobelli F, et al [1999] Intramyocellular triglyceride content is a determinant of in vivo insulin resistance in humans: a 1H-13C NMR spectroscopy assessment in offspring of type 2 diabetic parents. Diabetes 48: 1600-1606
12. Jacob S, Machann J, Rett K, et al [1999] Association of increased intramyocellular lipid content with insulin resistance in lean nondiabetic offspring of type 2 diabetic subjects. Diabetes 48: 1113-1119
13. Perseghin G, Lattuada G, Danna M, et al [2003] Insulin resistance, intramyocellular lipid content and plasma adiponectin concentrations in patients with type 1 diabetes. Am J Physiol Endocrinol Metab 285: E1174-E1181
14. Greco AV, Mingrone G, Giancaterini A, et al [2002] Insulin resistance in morbid obesità. Reversal with intramyocellular fat depletion. Diabetes 51: 144-151
15. Perseghin G, Scifo P, Pagliato E, et al [2001] Gender factors affect fatty acids-induced insulin resistance in nonobese humans: effects of oral steroidal contraception. J Clin Endocrinol Metab 86: 3188-3196
16. Thamer C, Machann J, Bachmann O, et al [2003] Intramyocellular lipids: anthropometric determinants and relationships with maximal aerobic capacity and insulin sensitivity. J Clin Endocrinol Metab 88: 1785-1791

17. Perseghin G, Comola M, Scifo P, et al [2004] Postabsorptive and insulin-stimulated energy and protein metabolism in patients with Myotonic Dystrophy type 1. Am J Clin Nutr 80: 57-364
18. Szczepaniak LS, Dobbins RL, Metzger GJ, et al [2003] Myocardial triglycerides and systolic function in humans: in vivo evaluation by localized proton spectroscopy and cardiac imaging. Magn Reson Med 49:417-423
19. Reingold JS, McGavock JM, Kaka S, Tillery T, Victor RG, Szczepaniak LS [2005] Determination of triglyceride in the human myocardium using magnetic resonance spectroscopy: reproducibility and sensitivity of the method. Am J Physiol Endocrinol Metab 289:E935-939
20. McGavock JM, Victor RG, Unger RH, Szczepaniak LS [2006] Adiposity of the heart, revisited. Ann Intern Med 144:517-524
21. Kankaanpaa M, Lehto H-R, Parkka JP, et al [2006] Myocardial triglyceride content and epicardial fat mass in human obesity: relationship to left ventricular function and serum free fatty acid levels. J Clin Endocrinol Metab 91: 4689-4695
22. Sharma S, Adrogue JV, Golfman L, et al [2004] Intramyocardial lipid accumulation in the failing human heart resembles the lipotoxic rat heart. FASEB J 18:1692-700
23. Marchington JM, Mattacks CA, Pond CM [1989] Adipose tissue in the mammalian heart and pericardium: structure, foetal development and biochemical properties. Comp Biochem Physiol B 94:225–232
24. Iacobellis G, Corradi D, Sharma AM [2005] Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nat Clin Pract Cardiovasc Med 2:536–543
25. Marchesini G, Brizi M, Bianchi G, et al [2001] Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes 50: 1844-1850
26. Kelley DE, McKolanis TM, Hegazi RA, Kuller LH, Kalhan SC [2003] Fatty liver in type 2 diabetes mellitus: relation to regional adiposity, fatty acids, and insulin resistance. Am J Physiol Endocrinol Metab 285: E906-E916
27. Marchesini G, Bugianesi E, Forlani G, et al [2003] Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. Hepatology 37: 917-92
28. Petersen KF, Dufour S, Befroy D, Lehrke M, Hendler RE, Shulman GI [2005] Reversal of nonalcoholic hepatic steatosis, hepatic insulin resistance, and hyperglycaemia by moderate weight reduction in patients with type 2 diabetes. Diabetes 54: 603-608
29. Seppala-Lindroos A, Vehkavaara S, Hakkinen A-M, et al [2002] Fat accumulation in the lier is associated with defects in insulin suppression of glucose production and serum frre fatty acids independent of obesity an normal men. J Clin Endocrinol Metab 87: 3023-3028
30. Perseghin G, Bonfanti R, Magni S, et al [2006] Insulin resistance and whole body energy homeostasis in obese adolescents with fatty liver disease. Am J Physiol Endocrinol Metab 291: E697–E703
31. Brechtel K, Dahl DB, Machann J, et al [2001] Fast elevation of the intramyocellular lipid content in the presence of circulating free fatty acids and hyperinsulinemia: a dynamic 1H- MRS study. Magn Reson Med 45: 179-183
32. Bachmann OP, Dahl DB, Brechtel K, et al [2001] Effects of intravenous and dietary lipid challenge on intramyocellular lipid content and the relation with insulin sensitivity in humans. Diabetes 50: 2579-2584
33. Poynten AM, Gan SK, Kriketos AD, et al [2003] Nicotinic acid-induced insulin resistance is related to increased circulating fatty acids and fat oxidation but not muscle lipid content. Metabolism 52: 699-704
34. Belfort R, Harrison SA, Brown K, et al [2006] A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. N Engl J Med 355: 2297-307
35. Holt HB, Wild SH, Wood PJ, et al [2006] Non-esterified fatty acid concentrations are independently associated with hepatic steatosis in obese subjects. Diabetologia 49: 141-148
36. Donnelly KL, Smith CI, Schwarzberg SJ, et al [2005] Sources of fatty acids stored in liver and secreted via lipoproteins in patients with nonalcoholic fatty liver disease. J Clin Invest 115: 1343-1361

37. Diraison F, Moulin P, Beylot M [2003] Contribution of hepatic de novo lipogenesis and reesterification of plasma non esterified fatty acids to plasma triglycefide synthesis during nonalcoholic fatty liver disease. Diabet Metab 29: 478-485
38. Utzschneider KM, Kahn SE [2006] The role of insulin resistance in nonalcoholic fatty liver disease. J Clin Endocrinol Metab 91: 4753–4761
39. Coldberg SR, Simoneau JA, Thaete FL, Kelley DE [1995] Skeletal muscle utilization of free fatty acids in women with visceral obesity. J Clin Invest 95: 1846-1853
40. Kelley DE, Goodpaster B, Wing RR, Simoneau [1999] J-A Skeletal muscle fatty acid metabolism in association with insulin resistance, obesity and weight loss. Am J Physiol Endocrinol & Metab 277: E1130-E1141
41. Blaak EE, Wagenmakers AJM, Glatz JFC, et al [2000] Plasma FFA utilization and fatty acid- binding protein content are diminished in type 2 diabetic muscle. Am J Physiol Endocrinol & Metab 279: E146-E154
42. Blaak EE, Wolffenbuttel BH, Saris WH, Pelsers MM, Wagenmakers AJ [2001] Weight reduction and the impaired plasma-derived free fatty acid oxidation in type 2 diabetic subjects. J Clin Endocrinol Metab 86: 1638-1644
43. Mensink M, Blaak EE, van Baak MA, Wagenmakers AJ, Saris WH [2001] Plasma free Fatty Acid uptake and oxidation are already diminished in subjects at high risk for developing type 2 diabetes. Diabetes 50: 2548-2554
44. Luzi L, Perseghin G, Tambussi G, et al [2003] Intramyocellular lipid accumulation and reduced whole body lipid oxidation in HIV infected patients with lipodystrophy. Am J Physiol Endocrinol & Metab 284: E274-E280
45. Perseghin G, Scifo P, Danna M, et al [2002] Normal insulin sensitivity and IMCL content in overweight humans are associated with higher fasting lipid oxidation. Am J Physiol Endocrinol & Metab 283: E556-E564
46. Goodpaster BH, Katsiaras A, Kelley DE [2003] Enhanced fat oxidation through physical activity is associated with improvements in insulin sensitivity in obesity. Diabetes 52: 2191-2197
47. Gan SK, Kriketos AD, Ellis BA, Thompson CH, Kraegen EW, Chisholm DJ [2003] Changes in aerobic capacity and visceral fat but not myocyte lipid levels predict increased insulin action after exercise in overweight and obese men. Diabetes Care 26: 1706-1713
48. Lattuada G, Costantino F, Caumo A, et al [2005] Reduced whole body lipid oxidation is as- sociated with insulin resistance but not with intramyocellular lipid content in offspring of type 2 diabetic patients. Diabetologia 48: 741-747
49. Petersen KF, Dufour S, Befroy D, Garcia R, Shulman GI [2004] Impaired mitochondrial activity in the insulin-resistant offspring of patients with type 2 diabetes. N Engl J Med 350: 664-671
50. He J, Watkins S, Kelley DE [2001] Skeletal muscle lipid content and oxidative enzyme activity in relation to muscle fiber type in type 2 diabetes and obesity. Diabetes 50: 817-823
51. Gaster M, Rustan AC, Aas V, Beck-Nielsen H [2004] Reduced lipid oxidation in skeletal muscle from type 2 diabetic subjects may be of genetic origin. Evidence from cultured myotubes. Diabetes 53: 542-548
52. Kelley DE, He J, Menshikova EV, Ritov VB [2002] Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. Diabetes 51: 2944-2950
53. Petersen KF, Befroy D, Dufour S, et al [2003] Mitochondrial dysfunction in the elderly: possible role in insulin resistance. Science 300: 1140-1142
54. Schrauwen P, Hesselink MKC [2004] Oxidative capacity, lipotoxicity, and mitochondrial damage in type 2 diabetes. Diabetes 53: 1412-1417
55. Ek J, Andersen G, Urhammer SA, et al [2001] Mutation analysis of peroxisome proliferator- activated receptor-gamma coactivator-1 [PGC-1. and relationships of identified

amino acid polymorphisms to Type II diabetes mellitus. Diabetologia 44: 2220-2226
56. Muller YL, Bogardus C, Beamer BA, Shuldiner AR, Baier LJ [2003] A functional variant in the peroxisome proliferator-activated receptor gamma2 promoter is associated with predictors of obesity and type 2 diabetes in Pima Indians. Diabetes 52:1864-1871
57. Mootha VK, Lindgren CM, Eriksson KF, et al [2003] PGC-1alpha-responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. Nat Genet 34: 267-273
58. Patti ME, Butte AJ, Crunkhorn 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 Nat Acad Sci USA 100: 8466-8471
59. Neubauer S [2007] Mechanisms of disease: the failing heart – an engine out of fuel. N Engl J Med 356: 1140-1151
60. Bottomley PA [1994] MR Spectroscopy or the Human Heart: The Status and the Challenges. Radiology 191: 593-612
61. Beyerbacht HP, Vliegen HV, Lamb HJ, et al [1996] Phosphorus magnetic resonance spectroscopy of the human heart: current status and clinical implications. Eur Heart J 17: 1158-66
62. Forder JR, Pohost GM [2003] Cardiovascular nuclear magnetic resonance: basic and clinical applications. J Clin Invest 111: 1630-39
63. Scheuermann-Freestone M, Madsen PL, Manners D, et al [2003] Abnormal cardiac and skeletal muscle energy metabolism in patients with type 2 diabetes. Circulation 107: 3040-3046
64. Diamant M, Lamb HJ, Groeneveld Y, et al [2003] Diastolic dysfunction is associated with altered myocardial metabolism in asymptomatic normotensive patients with well-controlled type 2 diabetes mellitus. J Am Coll Cardiol 42: 328-335
65. Perseghin G, Fiorina P, De Cobelli F, et al [2005] Cross-sectional assessment of the effect of kidney and kidney-pancreas transplantation on resting left ventricular energy metabolism in type 1 diabetic-uremic patients: a 31P-MRS study. J Am Coll Cardiol 46: 1085-1092
66. Perseghin G, Ntali G, De Cobelli F, et al [2007] Abnormal left ventricular energy metabolism in obese men with preserved systolic and diastolic functions is associated with insulin resistance. Diabetes Care 30: 1520-1527
67. Fragasso G, Perseghin G, De Cobelli F, et al [2006] Effects of metabolic modulation by trimetazidine on left ventricular function and phosphocreatine/adenosine triphosphate ratio in patients with heart failure. Eur Heart J 27: 942-948
68. Fragasso G, Montano C, Perseghin G, et al [2006] Reduction of ischemic threshold in patients with stable coronary disease after meals of different composition: effects of partial inhibition of fatty acids oxidation. Am Heart J 151: 1238.e1-1238.e8
69. Lee L, Campbell R, Scheuermann-Freestone M, et al [2005] Metabolic modulation with perhexiline in chronic heart failure. A randomized, controlled trial of short-term use of a novel treatment. Circulation 112:3280-3288
70. Tuunanen H, Engblom E, Naum A, et al [2006] Free fatty acid depletion acutely decreases cardiac work and efficiency in cardiomyopathic heart failure. Circulation 114: 2130-2137
71. Perseghin G, Lattuada G, De Cobelli F, et al [2005] Reduced intra-hepatic fat content is associated with increased whole body lipid oxidation in patients with type 1 diabetes. Diabetologia 48: 2615-2621
72. Bugianesi E, Gastaldelli A, Vanni E, et al [2005] Insulin resistance in non-diabetic patients with non-alcoholic fatty liver disease: sites and mechanisms. Diabetologia 48: 634–642
73. Perseghin G, Lattuada G, De Cobelli F, Ragogna F, Ntali G, Esposito A, Belloni E, Canu T, Terruzzi I, Scifo P, Del Maschio A, Luzi L [2007] Habitual physical activity is associated with the intra-hepatic fat content in humans. Diabetes Care 30: 683-688
74. Iozzo P, Turpeinen AK, Takala T, et al [2004] Defective liver disposal of free fatty acids in patients with impaired glucose tolerance. J Clin Endocrinol Metab 89: 3496–3502

75. Misu H, Takamura T, Matsuzawa N, et al [2007] Genes involved in oxidative phosphorylation are coordinately upregulated with fasting hyperglycaemia in livers of patients with type 2 diabetes. Diabetologia 50:268–277

1. Bergstrom J (1975) Percutaneous needle biopsy of skeletal muscle in physiological and clinical research. Scand J Clin Lab Invest 35:609-616
2. Saunders PU, Pyne DB, Telford RD, Hawley JA (2004) Factors affecting running economy in trained distance runners. Sports Med 34:465-485
3. Tessari P, Inchiostro S, Biolo G, Vincenti E, Sabadin L (1991) Effects of acute systemic hyperinsulinemia on forearm muscle proteolysis in healthy man. J Clin Invest 88:27-33
4. Nair KS, Ford GC, Ekberg K, Fernqvist-Forbes E, Wahren J (1995) Protein dynamics in whole body and in splanchnic and leg tissues in type I diabetic patients. J Clin Invest 95:2926-2937
5. Stephens FB, Constantin-Teodosiu D, Greenhaff PL (2007) New insights concerning the role of carnitine in the regulation of fuel metabolism in skeletal muscle. J Physiol 581:431-444
6. Kim YI, Lee FN, Choi WS, Lee S, Youn JH (2006) Insulin regulation of skeletal muscle PDK4 mRNA expression is impaired in acute insulin-resistant states. Diabetes 55:2311-2337
7. Winder WW, Hardie DG (1999) AMP-activated protein kinase, a metabolic master switch: possible roles in type 2 diabetes. Am J Physiol 277:E1-E10
8. Long YC, Zierath JR (2006) AMP-activated protein kinase signaling in metabolic regulation. J Clin Invest 116:1776-1783
9. Cantó C, Auwerx J (2009) PGC-1alpha, SIRT1 and AMPK, an energy sensing network that controls energy expenditure. Curr Opin Lipidol 20:98-105
10. Lagouge M, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F, Messadeq N, Milne J, Lambert P, Elliott P, Geny B, Laakso M, Puigserver P, Auwerx J (2006) Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. Cell 127:1109-1122
11. Cantó C, Jiang LQ, Deshmukh AS, Mataki C, Coste A, Lagouge M, Zierath JR, Auwerx J (2010) Interdependence of AMPK and SIRT1 for metabolic adaptation to fasting and exercise in skeletal muscle. Exercise Cell Metab 11:213-219
12. Holloszy JO (2008) Regulation by exercise of skeletal muscle content of mitochondria and GLUT4. J Physiol Pharmacol 59 Suppl 7:5-18
13. Lanza IR, Short DK, Short KR, Raghavakaimal S, Basu R, Joyner MJ, McConnell JP, Nair KS (2008) Endurance exercise as a countermeasure for aging. Diabetes 57:2933-2942
14. Wojtaszewski JF, MacDonald C, Nielsen JN (2003) Regulation of 5'AMP-activated protein kinase activity and substrate utilization in exercising human skeletal muscle. Am J Physiol Endocrinol Metab 284:E813-E822
15. Adhihetty PJ, Irrcher I, Joseph AM, Ljubicic V, Hood DA (2003) Plasticity of skeletal muscle mitochondria in response to contractile activity. Exp Physiol 88:99-107
16. Finck BN, Kelly DP (2006) PGC-1 coactivators: inducible regulators of energy metabolism in health and disease. J Clin Invest 116:615-622
17. Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, Allison DB, Cruzen C, Simmons HA, Kemnitz JW, Weindruch R (2009) Caloric restriction delays disease onset and mortality in rhesus monkeys. Science 325:201-204
18. Fontana L, Meyer TE, Klein S, Holloszy JO (2004) Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. Proc Natl Acad Sci U S A 101:6659-6663
19. Barazzoni R, Zanetti M, Bosutti A, Biolo G, Vitali-Serdoz L, Stebel M, Guarnieri G (2005) Moderate

caloric restriction, but not physiological hyperleptinemia per se, enhances mitochondrial oxidative capacity in rat liver and skeletal muscle--tissue-specific impact on tissue triglyceride content and AKT activation. Endocrinology 146:2098-2106
20. Nisoli E, Tonello C, Cardile A, Cozzi V, Bracale R, Tedesco L, Falcone S, Valerio A, Cantoni O, Clementi E, Moncada S, Carruba MO (2005) Calorie restriction promotes mitochondrial biogenesis by inducing the expression of eNOS. Science 310:314-317
21. Zangarelli A, Chanseaume E, Morio B, Brugère C, Mosoni L, Rousset P, Giraudet C, Patrac V, Gachon P, Boirie Y, Walrand S (2006) Synergistic effects of caloric restriction with maintained protein intake on skeletal muscle performance in 21-month-old rats: a mitochondria-mediated pathway. FASEB J 20:2439-2450
22. Harman D (1981) The aging process. Proc Natl Acad Sci 78:7124-7128
23. Sinclair DA (2005) Toward a unified theory of caloric restriction and longevity regulation. Mech Ageing Dev 126:987-1002
24. Rachek LI, Musiyenko SI, LeDoux SP, Wilson GL (2007) Palmitate induced mitochondrial deoxyribonucleic acid damage and apoptosis in l6 rat skeletal muscle cells. Endocrinology 148:293-299
25. Pimenta AS, Gaidhu MP, Habib S, So M, Fediuc S, Mirpourian M, Musheev M, Curi R, Ceddia RB (2008) Prolonged exposure to palmitate impairs fatty acid oxidation despite activation of AMP-activated protein kinase in skeletal muscle cells. J Cell Physiol 217:478-485
26. Hirabara SM, Curi R, Maechler P (2010) Saturated fatty acid-induced insulin resistance is associated with mitochondrial dysfunction in skeletal muscle cells. J Cell Physiol 222:187-194
27. Yuzefovych L, Wilson G, Rachek L (2010) Different effects of oleate vs. palmitate on mitochondrial function, apoptosis, and insulin signaling in L6 skeletal muscle cells: role of oxidative stress. Am J Physiol Endocrinol Metab 299:E1096-E105
28. Brandt JM, Djouadi F, Kelly DP (1998) Fatty acids activate transcription of the muscle carnitine palmitoyltransferase I gene in cardiac myocytes via the peroxisome proliferator-activated receptor alpha. J Biol Chem 273:23786-23792
29. Iossa S, Lionetti L, Mollica MP, Crescenzo R, Botta M, Barletta A, Liverini G (2003) Effect of high-fat feeding on metabolic efficiency and mitochondrial oxidative capacity in adult rats. Br J Nutr 90:953-960
30. Sparks LM, Xie H, Koza RA, Mynatt R, Hulver MW, Bray GA, Smith SR (2005) A high-fat diet coordinately downregulates genes required for mitochondrial oxidative phosphorylation in skeletal muscle. Diabetes 54:1926-1933
31. Turner N, Bruce CR, Beale SM, Hoehn KL, So T, Rolph MS, Cooney GJ (2007) Excess lipid availability increases mitochondrial fatty acid oxidative capacity in muscle: evidence against a role for reduced fatty acid oxidation in lipid-induced insulin resistance in rodents. Diabetes 56:2085-2092
32. Garcia-Roves P, Huss JM, Han DH, Hancock CR, Iglesias-Gutierrez E, Chen M, Holloszy JO (2007) Raising plasma fatty acid concentration induces increased biogenesis of mitochondria in skeletal muscle. Proc Natl Acad Sci U S A 104:10709-10713
33. Bigrigg JK, Heigenhauser GJ, Inglis JG, LeBlanc PJ, Peters SJ (2009) Carbohydrate refeeding after a high-fat diet rapidly reverses the adaptive increase in human skeletal muscle PDH kinase activity. Am J Physiol Regul Integr Comp Physiol 297:R885-R891
34. Medikayala S, Piteo B, Zhao X, Edwards JG (2011) Chronically elevated glucose compromises myocardial mitochondrial DNA integrity by alteration of mitochondrial topoisomerase function. Am J Physiol Cell Physiol 300:C338-C348
35. Aas V, Hessvik NP, Wettergreen M, Hvammen AW, Hallén S, Thoresen GH, Rustan AC (2011) Chronic hyperglycemia reduces substrate oxidation and impairs metabolic switching of human myotubes. Biochim Biophys Acta 1812:94-105
36. Liu HY, Cao SY, Hong T, Han J, Liu Z, Cao W (2009) Insulin is a stronger inducer of insulin resistance than hyperglycemia in mice with type 1 diabetes mellitus (T1DM). J Biol Chem 284:27090-27100

37. Ragheb R, Shanab GM, Medhat AM, Seoudi DM, Adeli K, Fantus IG (2009) Free fatty acid-induced muscle insulin resistance and glucose uptake dysfunction: evidence for PKC activation and oxidative stress-activated signaling pathways. Biochem Biophys Res Commun 389:211-216
38. Bonnard C, Durand A, Peyrol S, Chanseaume E, Chauvin MA, Morio B, Vidal H, Rieusset J (2008) Mitochondrial dysfunction results from oxidative stress in the skeletal muscle of dietinduced insulin-resistant mice. J Clin Invest 118:789-800
39. Anderson EJ, Lustig ME, Boyle KE, (2009) Mitochondrial H2O2 emission and cellular redox state link excess fat intake to insulin resistance in both rodents and humans. J Clin Invest 119:573–581
40. Nishikawa T, Edelstein D, Du XL, Yamagishi S, Matsumura T, Kaneda Y, Yorek MA, Beebe D, Oates PJ, Hammes HP, Giardino I, Brownlee M (2000) Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. Nature 404:787–790
41. Shoelson SE, Lee J, Goldfine AB (2006) Inflammation and insulin resistance. J Clin Invest 116:1793-1801
42. Supinski GS, Callahan LA (2007) Free radical-mediated skeletal muscle dysfunction in inflammatory conditions. J Appl Physiol 102:2056-2063
43. Wei Y, Sowers JR, Clark SE, Li W, Ferrario CM, Stump CS (2008) Angiotensin II-induced skeletal muscle insulin resistance mediated by NF-kappaB activation via NADPH oxidase. Am J Physiol Endocrinol Metab 294:E345-E351
44. Green CJ, Macrae K, Fogarty S, Hardie DG, Sakamoto K, Hundal HS (2011) Counter modulation of fatty acid-induced proinflammatory NFkB signalling in rat skeletal muscle cells by AMPK. Biochem J 435:463-474
45. Kim JK, Kim YJ, Fillmore JJ, Chen Y, Moore I, Lee J, Yuan M, Li ZW, Karin M, Perret P, Shoelson SE, Shulman GI (2001) Prevention of fat-induced insulin resistance by salicylate. J Clin Invest 108:437-446
46. Valerio A, Cardile A, Cozzi V, Bracale R, Tedesco L, Pisconti A, Palomba L, Cantoni O, Clementi E, Moncada S, Carruba MO, Nisoli E (2006) TNF-alpha downregulates eNOS expression and mitochondrial biogenesis in fat and muscle of obese rodents. J Clin Invest 116:2791-2798
47. Spriet LL, Heigenhauser GJ (2002) Regulation of pyruvate dehydrogenase (PDH) activity in human skeletal muscle during exercise. Exerc Sport Sci Rev 30:91-95
48. Pilegaard H, Saltin B, Neufer PD (2003) Exercise induces transient transcriptional activation of the PGC-1alpha gene in human skeletal muscle. J Physiol 546:851-858
50. Gibala MJ, McGee SL, Garnham AP, Howlett KF, Snow RJ, Hargreaves M (2009) Brief intense interval exercise activates AMPK and p38 MAPK signaling and increases the expression of PGC-1alpha in human skeletal muscle. J Appl Physiol 106:929-934
51. Little JP, Safdar A, Cermak N, Tarnopolsky MA, Gibala MJ (2010) Acute endurance exercise increases the nuclear abundance of PGC-1alpha in trained human skeletal muscle. Am J Physiol Regul Integr Comp Physiol 298:R912-R917
52. Schrauwen P, Hesselink MK (2004) Oxidative capacity, lipotoxicity, and mitochondrial damage in type 2 diabetes. Diabetes 53:1412-1417
53. Summers SA (2010) Sphingolipids and insulin resistance: the five Ws. Curr Opin Lipidol 21:128-135
54. Muoio DM (2010) Intramuscular triacylglycerol and insulin resistance: guilty as charged or wrongly accused? Biochim Biophys Acta 1801:281-288
55. Morino K, Petersen KF, Shulman GI (2006) Molecular mechanisms of insulin resistance in humans and their potential links with mitochondrial dysfunction. Diabetes 55 Suppl 2:S9-S15
56. Kelley DE, He J, Menshikova EV, Ritov VB (2002) Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. Diabetes 51:2944-2950
57. Ritov VB, Menshikova EV, He J, Ferrell RE, Goodpaster BH, Kelley DE (2005) Deficiency of subsarcolemmal mitochondria in obesity and type 2 diabetes. Diabetes 54:8-14
58. Morino K, Petersen KF, Dufour S, Befroy D, Frattini J, Shatzkes N, Neschen S, White MF, Bilz S,

Sono S, Pypaert M, Shulman GI (2005) Reduced mitochondrial density and increased IRS-1 serine phosphorylation in muscle of insulin-resistant offspring of type 2 diabetic parents. J Clin Invest 115:3587-3593
59. Mogensen M, Sahlin K, Fernström M, Glintborg D, Vind BF, Beck-Nielsen H, Højlund K (2007) Mitochondrial respiration is decreased in skeletal muscle of patients with type 2 diabetes. Diabetes 56:1592-1599
60. Heilbronn LK, Gan SK, Turner N, Campbell LV, Chisholm DJ (2007) Markers of mitochondrial biogenesis and metabolism are lower in overweight and obese insulin-resistant subjects. J Clin Endocrinol Metab 92:1467-1473
61. Boushel R, Gnaiger E, Schjerling P, Skovbro M, Kraunsøe R, Dela F (2007) Patients with type 2 diabetes have normal mitochondrial function in skeletal muscle. Diabetologia 50:790-796
62. Ritov VB, Menshikova EV, Azuma K, Wood R, Toledo FG, Goodpaster BH, Ruderman NB, Kelley DE (2010) Deficiency of electron transport chain in human skeletal muscle mitochondria in type 2 diabetes mellitus and obesity. Am J Physiol Endocrinol Metab 298:E49-E58
63. Mootha VK, Lindgren CM, Eriksson KF, Subramanian A, Sihag S, Lehar J, Puigserver P, Carlsson E, Ridderstråle M, Laurila E, Houstis N, Daly MJ, Patterson N, Mesirov JP, Golub TR, Tamayo P, Spiegelman B, Lander ES, Hirschhorn JN, Altshuler D, Groop LC (2003) PGC-1 alpha-responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. Nat Genet 34:267-273
64. Richardson DK, Kashyap S, Bajaj M, Cusi K, Mandarino SJ, Finlayson J, DeFronzo RA, Jenkinson CP, Mandarino LJ (2005) Lipid infusion decreases the expression of nuclear encoded mitochondrial genes and increases the expression of extracellular matrix genes in human skeletal muscle. J Biol Chem 280:10290-10297
65. Bajaj M, Medina-Navarro R, Suraamornkul S, Meyer C, DeFronzo RA, Mandarino LJ (2007) Paradoxical changes in muscle gene expression in insulin-resistant subjects after sustained reduction in plasma free fatty acid concentration. Diabetes 56:743-752
66. Chavez AO, Kamath S, Jani R, Sharma LK, Monroy A, Abdul-Ghani MA, Centonze VE, Sathyanarayana P, Coletta DK, Jenkinson CP, Bai Y, Folli F, DeFronzo RA, Tripathy D (2010) Effect of short-term free fatty acids elevation on mitochondrial function in skeletal muscle of healthy individuals. J Clin Endocrinol Metab 95:422–429
67. Rabøl R, Højberg PM, Almdal T, Boushel R, Haugaard SB, Madsbad S, Dela F (2009) Effect of hyperglycemia on mitochondrial respiration in type 2 diabetes. J Clin Endocrinol Metab 94:1372-1378
68. Toledo FG, Menshikova EV, Azuma K, Radiková Z, Kelley CA, Ritov VB, Kelley DE (2008) Mitochondrial capacity in skeletal muscle is not stimulated by weight loss despite increases in insulin action and decreases in intramyocellular lipid content. Diabetes 57:987-994
69. Phielix E, Meex R, Moonen-Kornips E, Hesselink MK, Schrauwen P (2010) Exercise training increases mitochondrial content and ex vivo mitochondrial function similarly in patients with type 2 diabetes and in control individuals. Diabetologia 53:1714-1721
70. Bruce CR, Thrush AB, Mertz VA, Bezaire V, Chabowski A, Heigenhauser GJ, Dyck DJ (2006) Endurance training in obese humans improves glucose tolerance and mitochondrial fatty acid oxidation and alters muscle lipid content. Am J Physiol Endocrinol Metab 291:E99-E107
71. Bordenave S, Metz L, Flavier S, Lambert K, Ghanassia E, Dupuy AM, Michel F, Puech-Cathala AM, Raynaud E, Brun JF, Mercier J (2008) Training-induced improvement in lipid oxidation in type 2 diabetes mellitus is related to alterations in muscle mitochondrial activity. Effect of endurance training in type 2 diabetes. Diabetes Metab 34:162-168
72. Short KR, Vittone JL, Bigelow ML, Proctor DN, Rizza RA, Coenen-Schimke JM, Nair KS (2003) Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. Diabetes 52:1888-1896

73. Sartorio A, Fontana P, Trecate L, Lafortuna CL (2003) Short-term changes of fatigability and muscle performance in severe obese patients after an integrated body mass reduction program. Diabetes Nutr Metab 16:88-93
74. Sartorio A, Narici MV, Fumagalli E, Faglia G, Lafortuna CL (2001) Aerobic and anaerobic performance before and after a short-term body mass reduction program in obese subjects. Diabetes Nutr Metab 14:51-57
75. Stump CS, Short KR, Bigelow ML, Schimke JM, Nair KS (2003) Effect of insulin on human skeletal muscle mitochondrial ATP production, protein synthesis, and mRNA transcripts. Proc Natl Acad Sci U S A 100:7996-8001
76. Asmann YW, Stump CS, Short KR, Coenen-Schimke JM, Guo Z, Bigelow ML, Nair KS (2006) Skeletal muscle mitochondrial functions, mitochondrial DNA copy numbers, and gene transcript profiles in type 2 diabetic and nondiabetic subjects at equal levels of low or high insulin and euglycemia. Diabetes 55:3309-3319
77. Hoeks J, van Herpen NA, Mensink M, Moonen-Kornips E, van Beurden D, Hesselink MK, Schrauwen P (2010) Prolonged fasting identifies skeletal muscle mitochondrial dysfunction as consequence rather than cause of human insulin resistance. Diabetes 59:2117-2125
78. Østergård T, Andersen JL, Nyholm B, Lund S, Nair KS, Saltin B, Schmitz O (2006) Impact of exercise training on insulin sensitivity, physical fitness, and muscle oxidative capacity in first-degree relatives of type 2 diabetic patients. Am J Physiol Endocrinol Metab 290:E998-E1005
79. Nair KS, Bigelow ML, Asmann YW, Chow LS, Coenen-Schimke JM, Klaus KA, Guo ZK, Sreekumar R, Irving BA (2008) Asian Indians have enhanced skeletal muscle mitochondrial capacity to produce ATP in association with severe insulin resistance. Diabetes 57:1166-1175
80. Choi CS, Befroy DE, Codella R, Kim S, Reznick RM, Hwang YJ, Liu ZX, Lee HY, Distefano A, Samuel VT, Zhang D, Cline GW, Handschin C, Lin J, Petersen KF, Spiegelman BM, Shulman GI (2008) Paradoxical effects of increased expression of PGC-1alpha on muscle mitochondrial function and insulin-stimulated muscle glucose metabolism. Proc Natl Acad Sci U S A 105:19926-19931
81. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, Nakayama O, Makishima M, Matsuda M, Shimomura I (2004) Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest 114:1752-1761
82. Kern PA, Saghizadeh M, Ong JM, Bosch RJ, Deem R, Simsolo RB (1995) The expression of tumor necrosis factor in human adipose tissue. Regulation by obesity, weight loss, and relationship to lipoprotein lipase. J Clin Invest 95:2111-2119
83. Melov S, Shoffner JM, Kaufman A, Wallace DC (1995) Marked increase in the number and variety of mitochondrial DNA rearrangements in aging human skeletal muscle. Nucleic Acids Res 23:4122-4126
84. Rooyackers OE, Adey DB, Ades PA, Nair KS (1996) Effect of age on in vivo rates of mitochondrial protein synthesis in human skeletal muscle. Proc Natl Acad Sci U S A 93:15364-15369
85. Short KR, Bigelow ML, Kahl J, Singh R, Coenen-Schimke J, Raghavakaimal S, Nair KS (2005) Decline in skeletal muscle mitochondrial function with aging in humans. Proc Natl Acad Sci U S A 102:5618-5623
86. Kouidi E, Albani M, Natsis K, Megalopoulos A, Gigis P, Guiba-Tziampiri O, Tourkantonis A, Deligiannis A (1998) The effects of exercise training on muscle atrophy in haemodialysis patients. Nephrol Dial Transplant 13:685-699
87. Gosker HR, Schrauwen P, Broekhuizen R, Hesselink MK, Moonen-Kornips E, Ward KA, Franssen FM, Wouters EF, Schols AM (2006) Exercise training restores uncoupling protein-3 content in limb muscles of patients with chronic obstructive pulmonary disease. Am J Physiol Endocrinol Metab 290:E976-E981
88. Tyni-Lenné R, Gordon A, Jansson E, Bermann G, Sylvén C (1997) Skeletal muscle endurance training improves peripheral oxidative capacity, exercise tolerance, and health-related quality of life in women with chronic congestive heart failure secondary to either ischemic cardiomyopathy or idiopathic dilated

cardiomyopathy. Am J Cardiol 80:1025-1029
89. Gielen S, Adams V, Linke A, Erbs S, Möbius-Winkler S, Schubert A, Schuler G, Hambrecht R (2005) Exercise training in chronic heart failure: correlation between reduced local inflammation and improved oxidative capacity in the skeletal muscle. Eur J Cardiovasc Prev Rehabil 12:393-400
90. Fredriksson K, Tjäder I, Keller P, Petrovic N, Ahlman B, Schéele C, Wernerman J, Timmons JA, Rooyackers O (2008) Dysregulation of mitochondrial dynamics and the muscle transcriptome in ICU patients suffering from sepsis induced multiple organ failure. PLoS One 3:e3686
91. Adey D, Kumar R, McCarthy JT, Nair KS (2000) Reduced synthesis of muscle proteins in chronic renal failure. Am J Physiol Endocrinol Metab 278:E219-E225

1. Jacquez JA (1992) Theory of production rate calculations in steady and non-steady states and its applications to glucose metabolism. Am J Physiol 262:E779-E790.
2. Cobelli C, Caumo A (1998) Using what is accessible to measure that which is not: necessity of model of system. Metabolism 47:1009-1035.
3. Zierler K (1999) Whole body glucose metabolism. Am J Physiol 276:E409-E426.
4. Carson and Cobelli (2001) Modeling methodology for physiology and medicine. Academic Press, San Diego.

1. The Action to Control Cardiovascular Risk in Diabetes Study G [2008] Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 358:2545-2559
2. Abdul-Ghani MA, DeFronzo RA [2009] plasma glucose concentration and prediction of future risk of type 2 diabetes. Diabetes Care 32:S194-S198
3. DeFronzo RA [2010] Overview of newer agents: where treatment is going. Am J Med 123: S38-S48
4. Nathan DM [1993] Long-Term complications of diabetes mellitus. N Engl J Med 328:1676-1685 5. Pickup JC, Crook MA [1998] Is type II diabetes mellitus a disease of the innate immune system? Diabetologia 41:1241-1248
6. Pickup JC, Mattock MB, Chusney GD, Burt D [1997] NIDDM as a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome X. Diabetologia 40:1286-1292
7. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM [2001] C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 286:327-334
8. Spranger J, Kroke A, Mohlig M, et al [2003] Inflammatory cytokines and the risk to develop type 2 diabetes: results of the prospective population-based European Prospective Investigation into Cancer and Nutrition [EPIC]-Potsdam Study. Diabetes 52:812-817
9. Schenk S, Saberi M, Olefsky JM [2008] Insulin sensitivity: modulation by nutrients and inflammation. J Clin Invest 118:2992-3002
10. Hotamisligil GS, Shargill NS, Spiegelman BM [1993] Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science 259:87-91
11. Pickup JC [2004] Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes Care 27:813-823
12. Tanaka T, Itoh H, Doi K, et al [1999] Down regulation of peroxisome proliferator-activated receptor gamma expression by inflammatory cytokines and its reversal by thiazolidinediones. Diabetologia 42:702-710
13. Shoelson SE, Lee J, Goldfine AB [2006] Inflammation and insulin resistance. The Journal of Clinical Investigation 116:1793-1801
14. Tilg H, Moschen AR [2008] Inflammatory mechanisms in the regulation of insulin resistance. Mol Med 14:222-231
15. Karin M, Takahashi T, Kapahi P, et al [2001] Oxidative stress and gene expression: the AP-1 and NF-

kappaB connections. Biofactors 15:87-89
16. Hosogai N, Fukuhara A, Oshima K, et al [2007] Adipose tissue hypoxia in obesity and its impact on adipocytokine dysregulation. Diabetes 56:901-911
17. de Luca C, Olefsky JM [2008] Inflammation and insulin resistance. FEBS Lett 582: 97-105
18. K, Sergeev P, Ris F, et al [2002] Glucose-induced beta cell production of IL-1beta contributes to glucotoxicity in human pancreatic islets. J Clin Invest 110: 851-860
19. Prentki M, Nolan CJ [2006] Islet beta cell failure in type 2 diabetes. J Clin Invest 116: 802- 1812
20. Lovis P, Roggli E, Laybutt DR, et al [2008] Alterations in microRNA expression contribute to fatty acid-induced pancreatic beta-cell dysfunction. Diabetes 57: 2728-2736
21. Newsholme P, Keane D, Welters HJ, Morgan NG [2007] Life and death decisions of the pancreatic beta-cell: the role of fatty acids. Clin Sci [Lond] 112: 27-42
22. K, Oberholzer J, Bucher P, Spinas GA, Donath MY [2003] Monounsaturated fatty acids prvent the deleterious effects of palmitate and high glucose on human pancreatic beta-cell turnover and function. Diabetes 52: 726-733
23. K, Spinas GA, Dyntar D, Moritz W, Kaiser N, Donath MY [2001] Distinct effects of saturated and monounsaturated fatty acids on beta-cell turnover and function. Diabetes 50: 69-76
24. Donath MY, Ehses JA, K, et al [2005] Mechanisms of beta-cell death in type 2 diabetes. Diabetes 54 Suppl 2: S108-113
25. Solinas G, Vilcu C, Neels JG, et al [2007] JNK1 in hematopoietically derived cells contributes to diet-induced inflammation and insulin resistance without affecting obesity. Cell Metab6: 386-397
26. Arkan MC, Hevener AL, Greten FR, et al [2005] IKK-beta links inflammation to obesity-induced insulin resistance. Nat Med 11: 191-198
27. Larsen CM, Faulenbach M, Vaag A, et al [2007] Interleukin-1-Receptor Antagonist in Type 2 Diabetes Mellitus. N Engl J Med 356: 1517-1526
28. Woods JA, Vieira VJ, Keylock KT [2009] Exercise, Inflammation, and Innate Immunity. Immunology and Allergy Clinics of North America 29: 381-393
29. Kohut ML, Sim YJ, Yu S, Yoon KJ, Loiacono CM [2009] Chronic Exercise Reduces Illness Severity, Decreases Viral Load, and Results in Greater Anti-Inflammatory Effects than Acute Exercise during Influenza Infection. The Journal of Infectious Diseases 200: 1434-1442
30. Mathur N, Pedersen BK [2008] Exercise as a Mean to Control Low-Grade Systemic Inflammation. Mediators of Inflammation 2008: 6
31. Si-Young K, Tae-Won J, Young-Soo L, Hye-Kyung N, Young-Joon S, Wook S [2009] Effects of Exercise on Cyclooxygenase-2 Expression and Nuclear Factor-κB DNA Binding in Human Peripheral Blood Mononuclear Cells. Annals of the New York Academy of Sciences 1171: 464-471
32. Starkie R, Ostrowski SR, Jauffred S, Febbraio M, Pedersen BK [2003] Exercise and IL-6 in-fusion inhibit endotoxin-induced TNF-α; production in humans. FASEB J17:887-889
33.Ramos DS, Olivo CR, Quirino Santos Lopes FDTR, et al [2009] Low-Intensity Swimming Training Partially Inhibits Lipopolysaccharide-Induced Acute Lung Injury. Medicine & Science in Sports & Exercise 42: 113-119
34. Jankord R, Jemiolo B [2004] Influence of Physical Activity on Serum IL-6 and IL-10 Levels in Healthy Older Men. Medicine & Science in Sports & Exercise 36: 960-964
35. Pischon T, Hankinson SE, Hotamisligil GS, Rifai N, Rimm EB [2003] Leisure-Time Physical Activity and Reduced Plasma Levels of Obesity-Related Inflammatory Markers. Obesity 11: 1055-1064
36. Verdaet D, Dendale P, De Bacquer D, Delanghe J, Block P, De Backer G [2004] Association between leisure time physical activity and markers of chronic inflammation related to coronary heart disease. Atherosclerosis 176: 303-310
37. Albert MA, Glynn RJ, Ridker PM [2004] Effect of physical activity on serum C-reactive protein. The American Journal of Cardiology 93: 221-225
38. Kim Y, Shin Y, Bae J, et al [2008] Beneficial effects of cardiac rehabilitation and exercise after percutaneous coronary intervention on hsCRP and inflammatory cytokines in CAD patients Pflügers Archiv European Journal of Physiology 455:1081-1088
39. Niessner A, Richter B, Penka M, et al [2006] Endurance training reduces circulating inflammatory

markers in persons at risk of coronary events: Impact on plaque stabilization? Atherosclerosis 186: 160-165
40. Balagopal P, George D, Patton N, et al [2005] Lifestyle-only intervention attenuates the inflammatory state associated with obesity: A randomized controlled study in adolescents. The Journal of Pediatrics 146: 342-348
41. Kelly AS, Wetzsteon RJ, Kaiser DR, Steinberger J, Bank AJ, Dengel DR [2004] Inflammation, insulin, and endothelial function in overweight children and adolescents: The role of exercise. The Journal of Pediatrics 145: 731-736
42. Okita K, Nishijima H, Murakami T, et al [2004] Can Exercise Training With Weight Loss Lower Serum C-Reactive Protein Levels? Arterioscler Thromb Vasc Biol 24: 1868-1873
43. Marcell TJ, McAuley KA, Traustadóttir T, Reaven PD [2005] Exercise training is not associated with improved levels of C-reactive protein or adiponectin. Metabolism 54: 533-541
44. Smith JK, Dykes R, Douglas JE, Krishnaswamy G, Berk S [1999] Long-term Exercise and Atherogenic Activity of Blood Mononuclear Cells in Persons at Risk of Developing Ischemic Heart Disease. JAMA 281: 1722-1727
45. Goldhammer E, Tanchilevitch A, Maor I, Beniamini Y, Rosenschein U, Sagiv M [2005] Exercise training modulates cytokines activity in coronary heart disease patients. International Journal of Cardiology 100: 93-99
46. Fantuzzi G [2005] Adipose tissue, adipokines, and inflammation. Journal of Allergy and Clinical Immunology 115: 911-919
47. Wang B, Wood I, Trayhurn P [2007] Dysregulation of the expression and secretion of inflammation-related adipokines by hypoxia in human adipocytes. Pflügers Archiv European Journal of Physiology 455:479-492
48. Fargnoli J, Sun Q, Olenczuk D, et al [2010] Resistin is associated with biomarkers of inflammation while total and high-molecular weight adiponectin are associated with biomarkers of inflammation, insulin resistance, and endothelial function. European Journal of Endocrinology 162: 281-288
49. Carrel A, McVean J, Clark R, Peterson S, Eickhoff J, Allen D [2009] School-based Exercise Improves Fitness, Body Composition, Insulin Sensitivity, and Markers of Inflammation in Non-Obese Children. Journal of Pediatric Endocrinology & Metabolism 22: 409-415
50. Weisberg S, McCann D, Desai M, Rosenbaum M, Leibel R, Ferrante Jr. A [2003] Obesity is associated with macrophage accumulation in adipose tissue. J. Clin. Invest. 112: 1796-1808
51. Xu H, Barnes G, Yang Q, et al [2003] Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J. Clin. Invest. 112: 1821-1830
52. Bouloumie A, Curat C, Sengene C, Lolme K, Miranvillea A, Bussea R [2005] Role of macrophage tissue infiltration in metabolic diseases. Curr Opin Clin Nutr Metab Care 8: 347-354
53. Christiansen T, Richelsen B, Bruun J [2005] Monocyte chemoattractant protein-1 is produced in isolated adipocytes, associated with adiposity and reduced after weight loss in morbid obese subjects. International Journal of Obesity 29:146-150
54. Pedersen B, Akerstrom T, Nielsen A, Fischer C [2007] Role of myokines in exercise and metabolism. J Appl Physiol 103: 1093-1098
55. Esposito K, Pontillo A, Di Palo C, et al [2003] Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. JAMA 289:1799-1804
56. Petersen E, Carey A, Sacchetti M [2005] Acute IL-6 treatment increases fatty acid turnover in elderly humans in vivo and in tissue culture in vitro. American Journal of Physiology 288: 155-161
57. Esposito K, Nappo F, Marfella R, et al [2002] Inflammatory Cytokine Concentrations Are Acutely Increased by Hyperglycemia in Humans: Role of Oxidative Stress. Circulation 106: 2067-2072
58. Sigal RJ, Kenny GP, Boule NG, et al [2007] Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med 147: 357-369
59. Krutzfeldt J, Kuwajima S, Braich R, et al [2007] Specificity, duplex degradation and subcellular localization of antagomirs. Nucleic Acids Res 35: 2885-2892
60. Bevilaqua MP, Pober JS, Wheeler ME, Cotran RS, Gimbrone Jr MA [1985] Interleukin 1 acts on cultured human vascular endothelium to increase the adhesion of polymorphonuclear leukocytes,

monocytes, and related leukocyte cell lines. J Clin Invest 76:2003-2011
61. Liu L, Zhang Y, Chen N, Shi X, Tsang B, Yu YH [2007] Upregulation of myocellular DGAT1 augments triglyceride synthesis in skeletal muscle and protects against fat-induced insulin resistance. J Clin Invest 117: 1679-1689
62. Ikeda S, Miyazaki H, Nakatani T, et al [2002] Up-regulation of SREBP-1c and lipogenic genes in skeletal muscles after exercise training. Biochem Biophys Res Commun 296: 395-400
63. Bradley RL, Jeon JY, Liu FF, Maratos-Flier E [2008] Voluntary exercise improves insulin sensitivity and adipose tissue inflammation in diet-induced obese mice. Am J Physiol Endocrinol Metab 295: E586-594
64. Rockl KS, Hirshman MF, Brandauer J, Fujii N, Witters LA, Goodyear LJ [2007] Skeletal muscle adaptation to exercise training: AMP-activated protein kinase mediates muscle fiber type shift. Diabetes 56: 2062-2069
65. Zierath JR, Hawley JA [2004] Skeletal muscle fiber type: influence on contractile and metabolic properties. PLoS Biol 2: e348
66. Kivelä R, Silvennoinen M, Lehti M, Jalava S, Vihko V, Kainulainen H [2008] Exercise-induced expression of angiogenic growth factors in skeletal muscle and in capillaries of healthy and diabetic mice. Cardiovasc Diabetol 7: 13
67. Drummond MJ, McCarthy JJ, Fry CS, Esser KA, Rasmussen BB [2008] Aging differentially affects human skeletal muscle microRNA expression at rest and following resistance exercise and essential amino acid ingestion. Am J Physiol Endocrinol Metab:
68. Nader GA, Lundberg IE [2009] Exercise as an anti-inflammatory intervention to combat inflammatory diseases of muscle. Curr Opin Rheumatol 21: 599-603 510.1097/BOR. 1090b1013e3283319d3283353
69. Nathan DM, Buse JB, Davidson MB, et al [2009] Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy. Diabetes Care 32: 193-203
70. Beavers KM, Brinkley TE, Nicklas BJ [2010] Effect of exercise training on chronic inflammation. Clinica Chimica Acta 411:785-793

1. Ezrin C, Kovacs K, Horvath E]1978] A functional anatomy of the endocrine hypothalamus and hypophysis. Med Clin North Am 62]2]: 229-33
2. Frohman LA, Felig PA [eds] 2001[] Endocrinology and Metabolism 4th ed.: McGrow-Hill
3. Lightman SL, Windle RJ, Ma XM, Harbuz MS, Shanks NM, Julian MD, Wood SA, Kershaw YM, Ingram CD 2002[] Hypothalamic-pituitary-adrenal function. Arch Physiol Biochem 110]1-2]: 90-3
4. Seasholtz AF, Valverde RA, Denver RJ]2002] Corticotropin-releasing hormone-binding protein: biochemistry and function from fishes to mammals. J Endocrinol 175]1]: 89-97
5. Bristow AF, Gleed C, Fauchère JL, Schwyzer R, Schulster D 1980[] Effects of ACTH [corticotropin] analogues on steroidogenesis and cyclic AMP in rat adrenocortical cells. Evidence for two different steroidogenically responsive receptors. Biochem J 186]2]: 599-603
6. Bell ME, Bhatnagar S, Akana SF, Choi S, Dallman SF 2000[] Disruption of arcuate/paraventricular nucleus connections changes body energy balance and response to acute stress. J Neurosci 20]17]: 6707-13
7. Nieuwenhuizen AG, Rutters F 2008[] The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. Physiol Behav 94]2]: 169-77
8. De Vos P, Lefebvre AM, Shrivo I, Fruchart JC, Auwerx J 1998[] Glucocorticoids induce the expression of the leptin gene through a non-classical mechanism of transcriptional activation. Eur J Biochem 253]3]: 619-26
9. Bornstein SR, Uhlmann K, Haidan A, Ehrhart-Bornstein M, Scherbaum WA]1997] Evidence for a novel peripheral action of leptin as a metabolic signal to the adrenal gland: leptin inhibits cortisol release directly. Diabetes 46]7]: 1235-8
10. Woods SC, Seeley RJ, Porte D Jr, Schwartz MW 1998[] Signals that regulate food intake and energy

homeostasis. Science 280]5368]: 1378-83
11. Strack AM, Sebastian RJ, Schwartz MW, Dallman MF 1995[] Glucocorticoids and insulin: reciprocal signals for energy balance. Am J Physiol 268]1 Pt 2]: R142-9
12. Smith SR, de Jonge L, Pellymounter M, Nguyen T, Harris R, York D, Redmann S, Rood J, Bray GA 2001[] Peripheral administration of human corticotropinin-releasing hormone: a novel method to increase energy expenditure and fat oxidation in man. J Clin Endocrinol Metab 86]5]: 1991-8
13. Ruzzin, J, Wagman AS, Jensen J 2005[] Glucocorticoid-induced insulin resistance in skeletal muscles: defects in insulin signalling and the effects of a selective glycogen synthase kinase-3 inhibitor. Diabetologia 48]10]: 2119-30
14. Schakman O, Gilson H, Thissen JP 2008[] Mechanisms of glucocorticoid-induced myopathy. J Endocrinol 197]1]: 1-10
15. Randle PJ, Garland PB, Hales CN, Newsholme EA 1963[] The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. Lancet 1]7285]: 785-9
16. Park E, Chan O, Li Q, Kirali M, Matthews SG, Riddell MC 2005[] Changes in basal hypothalamo-pituitary-adrenal activity during exercise training are centrally mediated. Am J Physiol Regul Integr Comp Physiol 289]5]: R1360-71
17. Kelso TB, Herbert WG, Gwazdauskas FC, Goss FL, Hess JL 1984[] Exercise-thermoregulatory stress and increased plasma beta-endorphin/beta-lipotropin in humans. J Appl Physiol 57]2]: 444-9
18. Luger A, Deuster PA, Kyle SB, Gallucci WT, Montgomery LC, Gold PW, Loriaux DL, Chrousos GP 1987[] Acute hypothalamic-pituitary-adrenal responses to the stress of treadmill exercise. Physiologic adaptations to physical training. N Engl J Med 316]21]:1309-15
19. Duclos M, Corcuff JB, Rashedi M, Fougère V, Manier G 1997[] Trained versus untrained men: different immediate post-exercise responses of pituitary adrenal axis. A preliminary study. Eur J Appl Physiol Occup Physiol 75]4]: 343-50
20. Duclos M, Guinot M, Le Bouc Y 2007[] Cortisol and GH: odd and controversial ideas. Appl Physiol Nutr Metab 32]5]: 895-903

1. Popkin BM [2005] Using research on the obesity pandemic as a guide to a unified vision of nutrition. Public Health Nutrition 8:724–729
2. Schoeller DA [2008] Insights into energy balance from doubly labeled water. Int J Obes 32 Suppl 7:S72-5
3. Westerterp KR, Speakman JR [2008] Physical activity energy expenditure has not declined since the 1980s and matches energy expenditures of wild mammals. Int J Obes 32:1256-63
4. Dugas LR, Harders R, Merrill Set at [2011] Energy expenditure in adults living in developing compared with industrialized countries: a meta-analysis of doubly labeled water studies. Am J Clin Nutr 93:427-41
5. Prentice AM, Black AE, Coward WA et al [1986] High levels of energy expenditure in obese women. Br Med J 292: 983–987
6. Bandini LG, Schoeller DA, Dietz WH [1990] Energy expenditure in obese and nonobese adolescents. Pediatr Res 27:198–203
7. Ekelund U, Aman J, Yngve A et al [2002] Physical activity but not energy expenditure is reduced in obese adolescents: a case-control study. Am J Clin Nutr 76:935-41
8. Westerterp KR [2010] Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies. Nutr Rev 68:148-54
9. American Psychiatry Association [2000] Diagnostic and statistical manual of mental disorders. 4th text revision Washington [DC].
10. Davis C, Katzman DK, Kirsh C [1999] Compulsive physical activity in adolescents with anorexia nervosa: a psychobehavioral spiral of pathology. J Nerv Ment Dis 187:336-42

11. Shroff H, Reba L, Thornton LM et al [2006] Features associated with excessive exercise in women with eating disorders. Int J Eat Disord 39:454-61
12. Eisler I, Le Grange D [1990] Excessive exercise and anorexia nervosa. Int J Eat Disord 9: 377-86
12. Dixon DP, Ackert AM, Eckel LA [2003] Development of, and recovery from, activity-based anorexia in female rats. Physiol Behav 80:273-9
13. Hillebrand JJ, Kas MJ, van Elburg AA et al [2008] Leptin's effect on hyperactivity: potential downstream effector mechanisms. Physiol Behav 94:689-95
14. Nogueira JP, Maraninchi M, Lorec AM et al [2010] Specific adipocytokines profiles in patients with hyperactive and/or binge/purge form of anorexia nervosa. Eur J Clin Nutr 64:840-4
15. Klein DA, Mayer LE, Schebendach JE et al [2007] Physical activity and cortisol in anorexia nervosa. Psychoneuroendocrinology 32:539-47
16. Steinhausen HC, Grigoroiu-Serbanescu M, Boyadjieva S et al [2008] Course and predictors of rehospitalization in adolescent anorexia nervosa in a multisite study. Int J Eat Disord 41:29-36
17. Davies S, Parekh K, Etelapaa K et al [2008] The inpatient management of physical activity in young people with anorexia nervosa. Eur Eat Disord Rev.6:334-40

1. Garber C, Blissmer B, Deschenes M et al (2011) American College of Sports Medicine posi-tion 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 43:1334-59
2. U.S. Department of Health and Human Services. The Surgeon General's Vision for a Healthy and Fit Nation. Rockville, MD: U.S. Department of Health and Human Services, Office of the Surgeon General, January 2010
3. Painter P (2005) Exercise following organ transplantation: a critical part of the routine post transplant care. Ann Transplant 10: 28-30
4. Kjzr M, Beyer N, Secher N (1999) Exercise and organ transplantation. Scand J Med Sci Sports 9: 1-14
5. Drummond M, Fry C, Glynn E et al (2009) Rapamycin administration in humans blocks the contraction-induced increase in skeletal muscle protein synthesis J Physiol 587: 1535-1546
6. Painter P, Topp K, Krasnoff J et al (2003) Health-related fitness and quality of life following steroid withdrawal in renal transplant recipients. Kidney Int 63: 2309-2316
7. Vitro A, Krasnoff J, Painter P (2002) Roles of nutrition and physical activity in musculoskeletal complications before and after liver transplantation. AACN Clin Issues 13: 333-347
8. Pina I, Apstein C, Balady G et al (2003) Exercise and heart failure a statement from the American heart association committee on exercise, rehabilitation and prevention. Circulation 107:1210-25
9. Ward H (2009) Nutritional and Metabolic Issues in Solid Organ Transplantation: Targets for Future Research. J Ren Nutr 19: 111–122
10. Armstrong K, Rakhit D, Jeffriess L et al (2006) Cardiorespiratory fitness is related to physical inactivity, metabolic risk factors and atherosclerotic burden in glucose-intollerant renal transplant recipients. Clin J Am Soc Nephrol 1: 1275–1283
11. Sharif A (2010) Metabolic Syndrome and Solid-Organ Transplantation. Am J Transplant 10 (1): 12–17
12. Poggioli R, Enfield G, Messinger S et al (2008) Nutritional status and behavior in subjects with type 1 diabetes, before and after islet transplantation. Transplantation 85: 501-506
13. Nabipour I, Vahdat K, Jafari S et al (2006) The association of metabolic syndrome and Chlamydia pneumoniae, Helicobacter pylori , cytomegalovirus, and herpes simplex virus type 1: The Persian Gulf Healthy Heart Study. Cardiovasc Diabetol 5: 25–30
14. De Vries A, Bakker S, van Son W et al (2004) Metabolic syndrome is associated with impaired long-term renal allograft function; not all component criteria contribute equally. Am J Transplant 4: 1675–

1683
15. Surgit O, Ersoz G, Gursel Y, Ersol S (2001) Effects of exercise training on specific immune parameters in transplant recipients. Transplant Proc 33: 3298
16. Luzi L, Codella R, Lauriola V et al (2011) Immunomodulatory Effects of Exercise in Type 1 Diabetes Mellitus (being published)
17. Schulman L, Estenne M (2003) Effect of transplantation on lung and exercise physiology. Eur Respir Mon 26: 220–242
18. Bartels M, Armstrong H, Gerardo R et al (2011) Evaluation of pulmonary function and exercise performance by cardiopulmonary exercise testing before and after lung transplantation. Chest prepublished online june 16
19. Wickerson L, Mathur S, Brooks D (2010) Exercise training after lung transplantation: a systematic rewiew. J Heart Lung Transplant 29: 497-503
20. Galant L, Ferrari R, Forgiarini L et al (2010) Relationship Between MELD severity score and the distance walked and respiratory muscle strength in candidates for liver transplantation. Transplant Proc 42: 1729–1730
21. Pagadala M, dasarathy S, Eghtesad B, McCullough AJ (2009) Posttransplant metabolic syndrome: an epidemic waiting to happen. Liver Transpl 15:1662-1670
22. ADA (2011) Executive summary: standards of medical care in diabetes-2011 Diabetes Care 34: S4-10
23. Codella R, Delmonte V, La Torre A, Luzi L (2011) Exercise in an Islet-transplanted non-promarathon-runner: Effects on Training, Autoimmunity and Metabolic Profile (in press)

1. Carlsson HE, Schapiro SJ, Farah I, Hau J (2004) Use of primates in research: a global overview. Am J Primatol 63(4):225-37
2. .Chavez AO, Lopez-Alvarenga JC, Tejero ME, Triplitt C, Bastarrachea RA, Sriwijitkamol A, et al (2008) Physiological and molecular determinants of insulin action in the baboon. Diabetes57(4899-908:(
3. Comuzzie AG, Cole SA, Martin L, Carey KD, Mahaney MC, Blangero J, et al (2003) The baboon as a nonhuman primate model for the study of the genetics of obesity. Obes Res11(1):75-80
4. VandeBerg JL, Williams-Blangero S, Tardif SD (2009) The baboon in biomedical research. Springer, New York
5. Garcia C, Rosetta L, Ancel A, Lee PC, Caloin M (2004)Kinetics of stable isotope and body composition in olive baboons (Papio anubis) estimated by deuterium dilution space: a pilot study. J Med Primatol 33(3):146-51
6. Chavez AO, Gastaldelli A, Guardado-Mendoza R, Lopez-Alvarenga JC, Leland MM, Tejero ME, et al (2009)Predictive models of insulin resistance derived from simple morphometric and biochemical indices related to obesity and the metabolic syndrome in baboons. Cardiovasc Diabetol 8:22
7. Rogers J, Hixson JE (1997) Baboons as an animal model for genetic studies of common human disease. Am J Hum Genet 61(3):489-9
8. Aufdemorte TB, Fox WC, Miller D, Buffum K, Holt GR, Carey KD.(1993) A non-human primate model for the study of osteoporosis and oral bone loss. Bone14(3):581-6
9. 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 10:325(5937201-4:(
10. Barnett A, Allsworth J, Jameson K, Mann R (2007) A review of the effects of antihyperglycaemic agents on body weight: the potential of incretin targeted therapies. Curr Med Res Opin 23(7):1493-507.
11. Sriwijitkamol A, Coletta DK, Wajcberg E, Balbontin GB, Reyna SM, Barrientes J, et al (2007) Effect of acute exercise on AMPK signaling in skeletal muscle of subjects with type 2 diabetes: a time-course and dose-response study. Diabetes 56(3):836-48

12. Hunnell NA, Rockcastle NJ, McCormick KN, Sinko LK, Sullivan EL, Cameron JL (2007) Physical activity of adult female rhesus monkeys (Macaca mulatta) across the menstrual cycle. Am J Physiol Endocrinol Metab 292(6):E1520-5
13. Papailiou A, Sullivan E, Cameron JL (2008) Behaviors in rhesus monkeys (Macaca mulatta) associated with activity counts measured by accelerometer. Am J Primatol 70(2):185-90
14. Cefalu WT (2006) Animal models of type 2 diabetes: clinical presentation and pathophysiological relevance to the human condition. ILAR J 47(3):186-98
15. Wagner JE, Kavanagh K, Ward GM, Auerbach BJ, Harwood HJ, Jr., Kaplan JR (2006) Old world nonhuman primate models of type 2 diabetes mellitus. ILAR J 47(3):259-71
16. Kaplan JR, Wagner JD (2006) Type 2 diabetes-an introduction to the development and use of animal models. ILAR J 47(3):181-5
17. Kahn CR, Folli F (1993) Molecular determinants of insulin action. Horm Res 39 Suppl 3:93-101
18. Biddinger SB, Kahn CR (2006) From mice to men: insights into the insulin resistance syndromes. Annu Rev Physiol 68:123-58
19. Guardado-Mendoza R, Davalli AM, Chavez AO, Hubbard GB, Dick EJ, Majluf-Cruz A, et al(2009) Pancreatic islet amyloidosis, beta-cell apoptosis, and alpha-cell proliferation are determinants of islet remodeling in type-2 diabetic baboons. Proc Natl Acad Sci USA 7-139(33) 106;18
20. Guardado-Mendoza R, Dick EJ, Jr., Jimenez-Ceja LM, Davalli A, Chavez AO, Folli F, et al (2009) Spontaneous pathology of the baboon endocrine system. J Med Primatol 38(6):383-9
21. Hubbard GB, Steele KE, Davis KJ, 3rd, Leland MM (2002) Spontaneous pancreatic islet amyloidosis in 40 baboons. J Med Primatol 31(2):84-90
22. Cole SA, Martin LJ, Peebles KW, Leland MM, Rice K, VandeBerg JL, et al (2003) Genetics of leptin expression in baboons. Int J Obes Relat Metab Disord 27(7):778-83
23. Hull RL, Westermark GT, Westermark P, Kahn SE (2004) Islet amyloid: a critical entity in the pathogenesis of type 2 diabetes. J Clin Endocrinol Metab 89(8):3629-43
24. Ortmeyer HK, Sajan MP, Miura A, Kanoh Y, Rivas J, Li Y, et al (2011) Insulin signaling and insulin sensitizing in muscle and liver of obese monkeys: PPARgamma agonist improves defective activation of atypical protein kinase C. Antioxid Redox Signal 14(2):207-19
25. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK (2009) American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc 41(2):459-71
26. American Diabetes Association (2009) Standards of medical care in diabetes 2009. Diabetes Care 32 Suppl 1:S13-61
27. Mann TM, Williams KE, Pearce PC, Scott EA.(2005) A novel method for activity monitoring in small non-human primates. Lab Anim 39(2):169-77
28. Sullivan EL, Koegler FH, Cameron JL (2006) Individual differences in physical activity are closely associated with changes in body weight in adult female rhesus monkeys (Macaca mulatta). Am J Physiol Regul Integr Comp Physiol 291(3):R633-42
29. Talan MI, Engel BT (1986) Learned control of heart rate during dynamic exercise in nonhuman primates. J Appl Physiol 61(2):545-53
30. Hohimer AR, Hales JR, Rowell LB, Smith OA (1983) Regional distribution of blood flow during mild dynamic leg exercise in the baboon. J Appl Physiol 55(4):1173-7
31. Hohimer AR, Smith OA (1979) Decreased renal blood flow in the baboon during mild dynamic leg exercise. Am J Physiol 236(1):H141-50
32. Dempsey DT, Crosby LO, Mullen JL (1986) Indirect calorimetry in chair-adapted primates JPEN J Parenter Enteral Nutr 10(3):324-7
33. 33 .Williams NI (2003) Lessons from experimental disruptions of the menstrual cycle in humans and monkeys. Med Sci Sports Exerc 35(9):1564-72

34. Rising R, Signaevsky M, Rosenblum LA, Kral JG, Lifshitz F (2008) Energy expenditure in chow-fed female non-human primates of various weights. Nutr Metab (Lond). 5:32
35. Edgerton VR, Barnard RJ, Peter JB, Gillespie CA, Simpson DR (1972) Overloaded skeletal muscles of a nonhuman primate (Galago senegalensis). Exp Neurol 37(2):322-39
36. Rhyu IJ, Bytheway JA, Kohler SJ, Lange H, Lee KJ, Boklewski J, et al (2010) Effects of aerobic exercise training on cognitive function and cortical vascularity in monkeys. Neuroscience 167(41239-:(48
37. Ivy JL, Coelho AM, Jr., Easley SP, Carley KD, Rogers WR, Shade RE (1994)Training adaptations of baboons to light and moderate treadmill exercise. J Med Primatol 23(8):442-9
38. Bourrin S, Zerath E, Vico L, Milhaud C, Alexandre C (1992) Bone mass and bone cellular variations after five months of physical training in rhesus monkeys: histomorphometric study. Calcif Tissue Int 50(5):404-10
39. Zerath E, Milhaud C, Nogues C (1993) The effects of a 5-month physical training on iliac bone morphology in monkeys. Eur J Appl Physiol Occup Physiol 67(1):1-6
40. Ingram DK (2000) Age-related decline in physical activity: generalization to nonhumans. Med Sci Sports Exerc 32(9):1623-9
41. Sallis JF (2000) Age-related decline in physical activity: a synthesis of human and animal studies. Med Sci Sports Exerc 32(9):1598-600
42. Hales JR, Rowell LB, King RB.(1979) Regional distribution of blood flow in awake heat-stressed baboons. Am J Physiol 237(6):H705-12
43. Vatner SF (1978) Effects of exercise and excitement on mesenteric and renal dynamics in conscious, unrestrained baboons. Am J Physiol 234(2):H210-4
44. Malavolti M, Pietrobelli A, Dugoni M, Poli M, Romagnoli E, De Cristofaro P, et al (2007) A new device for measuring resting energy expenditure (REE) in healthy subjects. Nutr Metab Cardiovasc Dis 17(5):338-43
45. Berntsen S, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen KH, et al (2008) Validity of physical activity monitors in adults participating in free-living activities. Br J Sports Med 44:657-664
46. St-Onge M, Mignault D, Allison DB, Rabasa-Lhoret R (2007) Evaluation of a portable device to measure daily energy expenditure in free-living adults. Am J Clin Nutr 85(3):742-9
47. Fruin ML, Rankin JW (2004) Validity of a multi-sensor armband in estimating rest and exercise energy expenditure. Med Sci Sports Exerc 36(6):1063-9
48. Jakicic JM, Marcus M, Gallagher KI, Randall C, Thomas E, Goss FL, et al (2004) Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. Med Sci Sports Exerc 36(5):897-904
49. King GA, Torres N, Potter C, Brooks TJ, Coleman KJ (2004) Comparison of activity monitors to estimate energy cost of treadmill exercise. Med Sci Sports Exerc 36(7):1244-51
50. Bertoli S, Posata A, Battezzati A, Spadafranca A, Testolin G, Bedogni G (2008) Poor between a portable armband and indirect calorimetry in the assessment of resting energy expenditure. Clin Nutr 27(2):307-10
51. Calabro MA, Welk GJ, Eisenmann JC (2009) Validation of the SenseWear Pro Armband algorithms in children. Med Sci Sports Exerc 41(9):1714-20
52. Arvidsson D, Slinde F, Hulthen L (2009) Free-living energy expenditure in children using multi-sensor activity monitors. Clin Nutr 28(3):305-12
53. Arvidsson D, Slinde F, Larsson S, Hulthen L (2007) Energy cost of physical activities in children: validation of SenseWear Armband. Med Sci Sports Exerc 39(11):2076-84
54. Arvidsson D, Slinde F, Larsson S, Hulthen L (2009)Energy cost in children assessed by multisensory activity monitors. Med Sci Sports Exerc 41(3):603-11
55. Ridley K, Olds TS (2008) Assigning energy costs to activities in children: a review and synthesis. Med

Sci Sports Exerc 40(8):1439-46
56. Dorminy CA, Choi L, Akohoue SA, Chen KY, Buchowski MS (2008) Validity of a multisensory armband in estimating 24-h energy expenditure in children. Med Sci Sports Exerc 40(4699-706:(
57. Papazoglou D, Augello G, Tagliaferri M, Savia G, Marzullo P, Maltezos E, et al (2006) Evaluation of a multisensor armband in estimating energy expenditure in obese individuals. Obesity 14(12):2217-23
58. Cereda E, Pezzoli G, Barichella M (2009) Role of an electronic armband in motor function monitoring in patients with Parkinson's disease. Nutrition 26(2):240-2
59. Cereda E, Turrini M, Ciapanna D, Marbello L, Pietrobelli A, Corradi E (2007) Assessing energy expenditure in cancer patients: a pilot validation of a new wearable device. J Parenter Enteral Nutr 31(6):502-7
60. Dwyer TJ, Alison JA, McKeough ZJ, Elkins MR, Bye PT (2009) Evaluation of the SenseWear activity monitor during exercise in cystic fibrosis and in health. Respir Med 103(101511-7:(
61. Mafra D, Deleaval P, Teta D, Cleaud C, Perrot MJ, Rognon S, et al (2009) New measurements of energy expenditure and physical activity in chronic kidney disease. J Ren Nutr 19(1):16-9
62. Coelho AM, Jr., Carey KD (1990) A social tethering system for nonhuman primates used in laboratory research. Lab Anim Sci 40(4):388-94
63. Gleeson M, McFarlin B, Flynn M.(2006) Exercise and Toll-like receptors. Exerc Immunol Rev 12:34-53
64. Tsukumo DM, Carvalho-Filho MA, Carvalheira JB, Prada PO, Hirabara SM, Schenka AA, et al (2007) Loss-of-function mutation in Toll-like receptor 4 prevents diet-induced obesity and insulin resistance. Diabetes 56(8):1986-98
65. Prada PO, Ropelle ER, Mourao RH, de Souza CT, Pauli JR, Cintra DE, et al (2009) EGFR tyrosine kinase inhibitor (PD153035) improves glucose tolerance and insulin action in high-fat diet-fed mice. Diabetes 258(12):2910-9
66. Lambert CP, Wright NR, Finck BN, Villareal DT (2008) Exercise but not diet-induced weight loss decreases skeletal muscle inflammatory gene expression in frail obese elderly persons. J Appl Physiol 105(2):473-8