



Universiteit
Leiden
The Netherlands

High fat diet induced disturbances of energy metabolism

Berg, S.A.A. van den

Citation

Berg, S. A. A. van den. (2010, October 6). *High fat diet induced disturbances of energy metabolism*. Retrieved from <https://hdl.handle.net/1887/16010>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/16010>

Note: To cite this publication please use the final published version (if applicable).

References

1. Aerts JM, Ottenhoff R, Powlson AS et al. Pharmacological inhibition of glucosylceramide synthase enhances insulin sensitivity. *Diabetes* 2007;56:1341-9.
2. Ahren B, Mari A, Fyfe CL et al. Effects of conjugated linoleic acid plus n-3 polyunsaturated fatty acids on insulin secretion and estimated insulin sensitivity in men. *Eur J Clin Nutr* 2009;63:778-86.
3. Alfano CM, Klesges RC, Murray DM, Beech BM, McClanahan BS. History of sport participation in relation to obesity and related health behaviors in women. *Prev Med* 2002;34:82-9.
4. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med* 1997;14 Suppl 5:S1-85.
5. Anderson EJ, Lustig ME, Boyle KE et al. Mitochondrial H₂O₂ emission and cellular redox state link excess fat intake to insulin resistance in both rodents and humans. *J Clin Invest* 2009.
6. Arble DM, Bass J, Laposky AD, Vitaterna MH, Turek FW. Circadian timing of food intake contributes to weight gain. *Obesity (Silver Spring)* 2009;17:2100-2.
7. Arch JR. Central regulation of energy balance: inputs, outputs and leptin resistance. *Proc Nutr Soc* 2005;64:39-46.
8. Armitage JA, Ishibashi A, Balachandran AA, Jensen RI, Poston L, Taylor PD. Programmed aortic dysfunction and reduced Na⁺,K⁺-ATPase activity present in first generation offspring of lard-fed rats does not persist to the second generation. *Exp Physiol* 2007;92:583-9.
9. Baba N, Bracco EF, Hashim SA. Enhanced thermogenesis and diminished deposition of fat in response to overfeeding with diet containing medium chain triglyceride. *Am J Clin Nutr* 1982;35:678-82.
10. Bach AC, Ingenbleek Y, Frey A. The usefulness of dietary medium-chain triglycerides in body weight control: fact or fancy? *J Lipid Res* 1996;37:708-26.

11. Barzilai N, Wang J, Massilon D, Vuguin P, Hawkins M, Rossetti L. Leptin selectively decreases visceral adiposity and enhances insulin action. *J Clin Invest* 1997;100:3105-10.
12. Batterham RL, Cowley MA, Small CJ et al. Gut hormone PYY(3-36) physiologically inhibits food intake. *Nature* 2002;418:650-4.
13. Bays HE. "Sick fat," metabolic disease, and atherosclerosis. *Am J Med* 2009;122:S26-S37.
14. Bequette BJ, Sunny NE, El-Kadi SW, Owens SL. Application of stable isotopes and mass isotopomer distribution analysis to the study of intermediary metabolism of nutrients. *J Anim Sci* 2006;84:E50.
15. Berry EM, Hirsch J, Most J, McNamara DJ, Thornton J. The relationship of dietary fat to plasma lipid levels as studied by factor analysis of adipose tissue fatty acid composition in a free-living population of middle-aged American men. *Am J Clin Nutr* 1986;44:220-31.
16. Beydoun MA, Beydoun HA, Wang Y. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. *Obes Rev* 2008;9:204-18.
17. Bijl N, Sokolovic M, Vrins C et al. Modulation of glycosphingolipid metabolism significantly improves hepatic insulin sensitivity and reverses hepatic steatosis in mice. *Hepatology* 2009;50:1431-41.
18. Bijland S, van den Berg SA, Voshol PJ et al. CETP does not affect triglyceride production or clearance in APOE*3-Leiden mice. *J Lipid Res* 2010;51:97-102.
19. Bijlsma S, Bobeldijk I, Verheij ER et al. Large-scale human metabolomics studies: a strategy for data (pre-) processing and validation. *Anal Chem* 2006;78:567-74.
20. Boghossian S, Dube MG, Torto R, Kalra PS, Kalra SP. Hypothalamic clamp on insulin release by leptin-transgene expression. *Peptides* 2006;27:3245-54.
21. Bonnard C, Durand A, Peyrol S et al. Mitochondrial dysfunction results from oxidative stress in the skeletal muscle of diet-induced insulin-resistant mice. *J Clin Invest* 2008;118:789-800.
22. Bonomi AG, Plasqui G, Goris AH, Westerterp KR. Improving assessment of daily energy expenditure by identifying types of physical activity with a single accelerometer. *J Appl Physiol* 2009;107:655-61.

23. Bosselaar M, Boon H, van Loon LJ, van den Broek PH, Smits P, Tack CJ. Intra-arterial AICA-riboside administration induces NO-dependent vasodilation in vivo in human skeletal muscle. *Am J Physiol Endocrinol Metab* 2009;297:E759-E766.
24. Boulange A, Planche E, de Gasquet P. Onset of genetic obesity in the absence of hyperphagia during the first week of life in the Zucker rat (fa/fa). *J Lipid Res* 1979;20:857-64.
25. Bray GA, Popkin BM. Dietary fat intake does affect obesity! *Am J Clin Nutr* 1998;68:1157-73.
26. Brown WJ, Miller YD, Miller R. Sitting time and work patterns as indicators of overweight and obesity in Australian adults. *Int J Obes Relat Metab Disord* 2003;27:1340-6.
27. Buettner R. Defining high-fat-diet rat models: metabolic and molecular effects of different fat types. 2006.
28. Buettner R, Scholmerich J, Bollheimer LC. High-fat diets: modeling the metabolic disorders of human obesity in rodents. *Obesity (Silver Spring)* 2007;15:798-808.
29. Burcelin R, Crivelli V, Dacosta A, Roy-Tirelli A, Thorens B. Heterogeneous metabolic adaptation of C57BL/6J mice to high-fat diet. *Am J Physiol Endocrinol Metab* 2002;282:E834-E842.
30. Buscemi S, Verga S, Caimi G, Cerasola G. Low relative resting metabolic rate and body weight gain in adult Caucasian Italians. *Int J Obes (Lond)* 2005;29:287-91.
31. Butler AA, Kozak LP. A recurring problem with the analysis of energy expenditure in genetic models expressing lean and obese phenotypes. *Diabetes* 2010;59:323-9.
32. Butte NF, Cai G, Cole SA et al. Metabolic and behavioral predictors of weight gain in Hispanic children: the Viva la Familia Study. *Am J Clin Nutr* 2007;85:1478-85.
33. Cai D. Local and systemic insulin resistance resulting from hepatic activation of IKK-beta and NF-kappaB. 2005.
34. Cai D, Yuan M, Frantz DF et al. Local and systemic insulin resistance resulting from hepatic activation of IKK-beta and NF-kappaB. *Nat Med* 2005;11:183-90.

35. Cairns CB, Walther J, Harken AH, Banerjee A. Mitochondrial oxidative phosphorylation thermodynamic efficiencies reflect physiological organ roles. *Am J Physiol* 1998;274:R1376-R1383.
36. Carpentier YA, Portois L, Malaisse WJ. n-3 fatty acids and the metabolic syndrome. *Am J Clin Nutr* 2006;83:1499S-504S.
37. Catenacci VA, Wyatt HR. The role of physical activity in producing and maintaining weight loss. *Nat Clin Pract Endocrinol Metab* 2007;3:518-29.
38. Chan CB. Uncoupling proteins: role in insulin resistance and insulin insufficiency. 2006.
39. Chavez JA, Knotts TA, Wang LP et al. A role for ceramide, but not diacylglycerol, in the antagonism of insulin signal transduction by saturated fatty acids. *J Biol Chem* 2003;278:10297-303.
40. Chavez JA, Summers SA. Lipid oversupply, selective insulin resistance, and lipotoxicity: Molecular mechanisms. *Biochim Biophys Acta* 2009.
41. Chavez JA, Summers SA. Characterizing the effects of saturated fatty acids on insulin signaling and ceramide and diacylglycerol accumulation in 3T3-L1 adipocytes and C2C12 myotubes. *Archives of Biochemistry and Biophysics* 2003;419:101-9.
42. Chen C, Shah YM, Morimura K et al. Metabolomics reveals that hepatic stearoyl-CoA desaturase 1 downregulation exacerbates inflammation and acute colitis. *Cell Metab* 2008;7:135-47.
43. Christiansen E, Garby L, Sorensen TI. Quantitative analysis of the energy requirements for development of obesity. *J Theor Biol* 2005;234:99-106.
44. Cleary MP, Vasselli JR, Greenwood MR. Development of obesity in Zucker obese (fa/fa) rat in absence of hyperphagia. *Am J Physiol* 1980;238:E284-E292.
45. Cline GW, Vidal-Puig AJ, Dufour S, Cadman KS, Lowell BB, Shulman GI. In Vivo Effects of Uncoupling Protein-3 Gene Disruption on Mitochondrial Energy Metabolism. *J Biol Chem* 2001;276:20240-4.
46. Cooper JA, Watras AC, Adams AK, Schoeller DA. Effects of dietary fatty acid composition on 24-h energy expenditure and chronic disease risk factors in men. *Am J Clin Nutr* 2009;89:1350-6.

47. Corpeleijn E, Saris WH, Blaak EE. Metabolic flexibility in the development of insulin resistance and type 2 diabetes: effects of lifestyle. *Obes Rev* 2009;10:178-93.
48. Dallal GE, Roberts SB. DLW: a computer program for the calculation of total energy expenditure in doubly labeled water ($^{2\text{H}}\text{H}^{18}\text{O}$) studies. *Comput Biomed Res* 1991;24:143-51.
49. Darvall KA, Sam RC, Silverman SH, Bradbury AW, Adam DJ. Obesity and thrombosis. *Eur J Vasc Endovasc Surg* 2007;33:223-33.
50. Davidson MH. Mechanisms for the hypotriglyceridemic effect of marine omega-3 fatty acids. *Am J Cardiol* 2006;98:27i-33i.
51. de Lange P, Lanni A, Beneduce L et al. Uncoupling Protein-3 Is a Molecular Determinant for the Regulation of Resting Metabolic Rate by Thyroid Hormone. *Endocrinology* 2001;142:3414-20.
52. de Wilde J, Mohren R, van den Berg S et al. Short-term high fat-feeding results in morphological and metabolic adaptations in the skeletal muscle of C57BL/6J mice. *Physiol Genomics* 2008;32:360-9.
53. de JL, Nguyen T, Smith SR, Zachwieja JJ, Roy HJ, Bray GA. Prediction of energy expenditure in a whole body indirect calorimeter at both low and high levels of physical activity. *Int J Obes Relat Metab Disord* 2001;25:929-34.
54. DeFronzo RA, Jacot E, Jequier E, Maeder E, Wahren J, Felber JP. The effect of insulin on the disposal of intravenous glucose. Results from indirect calorimetry and hepatic and femoral venous catheterization. *Diabetes* 1981;30:1000-7.
55. DeFronzo RA, Sherwin RS, Kraemer N. Effect of physical training on insulin action in obesity. *Diabetes* 1987;36:1379-85.
56. DeLany JP, Windhauser MM, Champagne CM, Bray GA. Differential oxidation of individual dietary fatty acids in humans. *Am J Clin Nutr* 2000;72:905-11.
57. den Boer MA, Voshol PJ, Kuipers F, Romijn JA, Havekes LM. Hepatic glucose production is more sensitive to insulin-mediated inhibition than hepatic VLDL-triglyceride production. *Am J Physiol Endocrinol Metab* 2006;291:E1360-E1364.
58. den HM, Westerterp-Plantenga MS, Bouwman FG, Mariman EC, Westerterp KR. Postprandial responses in hunger and satiety are

- associated with the rs9939609 single nucleotide polymorphism in FTO. Am J Clin Nutr 2009;90:1426-32.
59. Devaraj S, Singh U, Jialal I. Human C-reactive protein and the metabolic syndrome. Curr Opin Lipidol 2009;20:182-9.
 60. Douketis JD, Feightner JW, Attia J, Feldman WF. Periodic health examination, 1999 update: 1. Detection, prevention and treatment of obesity. Canadian Task Force on Preventive Health Care. CMAJ 1999;160:513-25.
 61. Dourmashkin JT, Chang GQ, Hill JO, Gayles EC, Fried SK, Leibowitz SF. Model for predicting and phenotyping at normal weight the long-term propensity for obesity in Sprague-Dawley rats. Physiol Behav 2006;87:666-78.
 62. Draisma HH, Reijmers TH, Bobeldijk-Pastorova I et al. Similarities and differences in lipidomics profiles among healthy monozygotic twin pairs. OMICS 2008;12:17-31.
 63. Duivenvoorden I. Apolipoprotein C3 deficiency results in diet-induced obesity and aggravated insulin resistance in mice. 2005.
 64. Duivenvoorden I, Teusink B, Rensen PC et al. Acute inhibition of hepatic beta-oxidation in APOE*3Leiden mice does not affect hepatic VLDL secretion or insulin sensitivity. J Lipid Res 2005;46:988-93.
 65. Dumas JF, Simard G, Roussel D et al. Mitochondrial energy metabolism in a model of undernutrition induced by dexamethasone. Br J Nutr 2003;90:969-77.
 66. Echtaray KS. Mitochondrial uncoupling proteins--what is their physiological role? 2007.
 67. Elia M. Organ and tissue contribution to metabolic rate. In: Kinney JM TH, ed. Energy metabolism. Tissue determinants and cellular corollaries. New York: Raven Press 1992:61-77.
 68. Esposito K, Marfella R, Ciotola M et al. Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA 2004;292:1440-6.
 69. Even PC, Nicolaïdis S. Adaptive changes in energy expenditure during mild and severe feed restriction in the rat. Br J Nutr 1993;70:421-31.

70. Faeh D, Minehira K, Schwarz JM, Periasamy R, Park S, Tappy L. Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. *Diabetes* 2005;54:1907-13.
71. Farley C, Cook JA, Spar BD, Austin TM, Kowalski TJ. Meal pattern analysis of diet-induced obesity in susceptible and resistant rats. *Obes Res* 2003;11:845-51.
72. Feige JN, Lagouge M, Auwerx J. Dietary manipulation of mouse metabolism. *Curr Protoc Mol Biol* 2008;Chapter 29:Unit.
73. Feinman RD, Fine EJ. Nonequilibrium thermodynamics and energy efficiency in weight loss diets. *Theor Biol Med Model* 2007;4:27.
74. Fischer J, Koch L, Emmerling C et al. Inactivation of the Fto gene protects from obesity. *Nature* 2009;458:894-8.
75. Flatt JP. The difference in the storage capacities for carbohydrate and for fat, and its implications in the regulation of body weight. *Ann N Y Acad Sci* 1987;499:104-23.
76. Flatt JP. Carbohydrate-fat interactions and obesity examined by a two-compartment computer model. *Obes Res* 2004;12:2013-22.
77. Flowers JB, Rabaglia ME, Schueler KL et al. Loss of stearoyl-CoA desaturase-1 improves insulin sensitivity in lean mice but worsens diabetes in leptin-deficient obese mice. *Diabetes* 2007;56:1228-39.
78. Fogli-Cawley JJ, Dwyer JT, Saltzman E et al. The 2005 Dietary Guidelines for Americans and risk of the metabolic syndrome. *Am J Clin Nutr* 2007;86:1193-201.
79. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002;287:356-9.
80. Foster GD, Wadden TA, Swain RM, Anderson DA, Vogt RA. Changes in resting energy expenditure after weight loss in obese African American and white women. *Am J Clin Nutr* 1999;69:13-7.
81. Fredriksson R, Hagglund M, Olszewski PK et al. The obesity gene, FTO, is of ancient origin, up-regulated during food deprivation and expressed in neurons of feeding-related nuclei of the brain. *Endocrinology* 2008;149:2062-71.

82. Friedman MI. Fuel partitioning and food intake. *Am J Clin Nutr* 1998;67:513S-8S.
83. Friedman MI, Harris RB, Ji H, Ramirez I, Tordoff MG. Fatty acid oxidation affects food intake by altering hepatic energy status. *Am J Physiol* 1999;276:R1046-R1053.
84. Funari SS. Effects of oleic acid and its congeners, elaidic and stearic acids, on the structural properties of phosphatidylethanolamine membranes. 2003.
85. Funato H, Tsai AL, Willie JT et al. Enhanced orexin receptor-2 signaling prevents diet-induced obesity and improves leptin sensitivity. *Cell Metab* 2009;9:64-76.
86. Gaillard D, Laugerette F, Darcel N et al. The gustatory pathway is involved in CD36-mediated orosensory perception of long-chain fatty acids in the mouse. *FASEB J* 2008;22:1458-68.
87. Gautron L, Lee C, Funahashi H, Friedman J, Lee S, Elmquist J. Melanocortin-4 receptor expression in a vago-vagal circuitry involved in postprandial functions. *J Comp Neurol* 2010;518:6-24.
88. Goudriaan JR. CD36 deficiency increases insulin sensitivity in muscle, but induces insulin resistance in the liver in mice. 2003.
89. Goudriaan JR, Dahlmans VE, Teusink B et al. CD36 deficiency increases insulin sensitivity in muscle, but induces insulin resistance in the liver in mice. *J Lipid Res* 2003;44:2270-7.
90. Groener JE, Poorthuis BJ, Kuiper S, Helmond MT, Hollak CE, Aerts JM. HPLC for simultaneous quantification of total ceramide, glucosylceramide, and ceramide trihexoside concentrations in plasma. *Clin Chem* 2007;53:742-7.
91. Guo J, Hall KD. Estimating the continuous-time dynamics of energy and fat metabolism in mice. *PLoS Comput Biol* 2009;5:e1000511.
92. Hac-Wydro K. The influence of fatty acids on model cholesterol/phospholipid membranes. 2007.
93. Hanley AJ, Bowden D, Wagenknecht LE et al. Associations of adiponectin with body fat distribution and insulin sensitivity in nondiabetic Hispanics and African-Americans. *J Clin Endocrinol Metab* 2007;92:2665-71.

94. Hardy R, Wills AK, Wong A et al. Life course variations in the associations between FTO and MC4R gene variants and body size. *Hum Mol Genet* 2009.
95. Harney D, Patijn J. Meralgia paresthetica: diagnosis and management strategies. *Pain Med* 2007;8:669-77.
96. Haslam DW, James WP. Obesity. *Lancet* 2005;366:1197-209.
97. Hatunic M, Burns N, Finucane F, Mannion C, Nolan JJ. Contrasting clinical and cardiovascular risk status between early and later onset type 2 diabetes. *Diabetes and Vascular Disease Research* 2005;2:73-5.
98. Hesselink MK. Human uncoupling protein-3 and obesity: an update. 2003.
99. Hida K, Wada J, Eguchi J et al. Visceral adipose tissue-derived serine protease inhibitor: a unique insulin-sensitizing adipocytokine in obesity. *Proc Natl Acad Sci U S A* 2005;102:10610-5.
100. Himms-Hagen J. On raising energy expenditure in ob/ob mice. *Science* 1997;276:1132-3.
101. Hoeks J, Briede JJ, de VJ et al. Mitochondrial function, content and ROS production in rat skeletal muscle: effect of high-fat feeding. *FEBS Lett* 2008;582:510-6.
102. Hoeks J, Hesselink MK, van BM et al. Differential response of UCP3 to medium versus long chain triacylglycerols; manifestation of a functional adaptation. *FEBS Lett* 2003;555:631-7.
103. Holland WL, Brozinick JT, Wang LP et al. Inhibition of ceramide synthesis ameliorates glucocorticoid-, saturated-fat-, and obesity-induced insulin resistance. *Cell Metab* 2007;5:167-79.
104. Holland WL, Knotts TA, Chavez JA, Wang LP, Hoehn KL, Summers SA. Lipid mediators of insulin resistance. *Nutr Rev* 2007;65:S39-S46.
105. Holland WL, Summers SA. Sphingolipids, insulin resistance, and metabolic disease: new insights from in vivo manipulation of sphingolipid metabolism. *Endocr Rev* 2008;29:381-402.
106. Holland WL, Brozinick JT, Wang LP et al. Inhibition of Ceramide Synthesis Ameliorates Glucocorticoid-, Saturated-Fat-, and Obesity-Induced Insulin Resistance. *Cell Metabolism* 2007;5:167-79.

107. HOLLIFIELD G, PARSON W. Metabolic adaptations to a "stuff and starve" feeding program. I. Studies of adipose tissue and liver glycogen in rats limited to a short daily feeding period. *J Clin Invest* 1962;41:245-9.
108. Hommelberg PP, Plat J, Langen RC, Schols AM, Mensink RP. Fatty acid-induced NF-kappaB activation and insulin resistance in skeletal muscle are chain length dependent. *Am J Physiol Endocrinol Metab* 2009;296:E114-E120.
109. Horton TJ, Drougas H, Brache A, Reed GW, Peters JC, Hill JO. Fat and carbohydrate overfeeding in humans: different effects on energy storage. *Am J Clin Nutr* 1995;62:19-29.
110. Hotamisligil GS, Erbay E. Nutrient sensing and inflammation in metabolic diseases. *Nat Rev Immunol* 2008;8:923-34.
111. Hotta K, Funahashi T, Bodkin NL et al. Circulating concentrations of the adipocyte protein adiponectin are decreased in parallel with reduced insulin sensitivity during the progression to type 2 diabetes in rhesus monkeys. *Diabetes* 2001;50:1126-33.
112. Hu E, Liang P, Spiegelman BM. AdipoQ is a novel adipose-specific gene dysregulated in obesity. *J Biol Chem* 1996;271:10697-703.
113. Hu FB, Li TY, Colditz GA, Willett WC, Manson JE. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 2003;289:1785-91.
114. Huang LS, Kim MR, Jeong TS, Sok DE. Linoleoyl lysophosphatidic acid and linoleoyl lysophosphatidylcholine are efficient substrates for mammalian lipoxygenases. *Biochim Biophys Acta* 2007;1770:1062-70.
115. Iossa S, Mollica MP, Lionetti L, Crescenzo R, Tasso R, Liverini G. A Possible Link Between Skeletal Muscle Mitochondrial Efficiency and Age-Induced Insulin Resistance. *Diabetes* 2004;53:2861-6.
116. Jackson JE. A user's guide to principal components. New York: Wiley Interscience, 1991.
117. Jambor de Sousa UL, Arnold M, Langhans W, Geary N, Leonhardt M. Caprylic acid infusion acts in the liver to decrease food intake in rats. *Physiol Behav* 2006;87:388-95.
118. Jansen JJ, Hoefsloot HCJ, van der Greef J, Timmerman ME, Westerhuis JA, Smilde AK. ASCA: Analysis of multivariate data obtained from an experimental design. *Journal of Chemometrics* 2005;19:469-81.

119. Jen KL. Differential effects of fatty acids and exercise on body weight regulation and metabolism in female Wistar rats. 2003.
120. Jequier E, Schutz Y. Energy expenditure in obesity and diabetes. *Diabetes Metab Rev* 1988;4:583-93.
121. Jones PJ, Schoeller DA. Polyunsaturated:saturated ratio of diet fat influences energy substrate utilization in the human. *Metabolism* 1988;37:145-51.
122. Judge MK, Zhang J, Turner N, Carter C, Daniels MJ, Scarpase PJ. Prolonged hyperphagia with high-fat feeding contributes to exacerbated weight gain in rats with adult-onset obesity. *Am J Physiol Regul Integr Comp Physiol* 2008;295:R773-R780.
123. Jula A, Marniemi J, Huupponen R, Virtanen A, Rastas M, Ronnemaa T. Effects of diet and simvastatin on serum lipids, insulin, and antioxidants in hypercholesterolemic men: a randomized controlled trial. *JAMA* 2002;287:598-605.
124. Kabayama K, Sato T, Saito K et al. Dissociation of the insulin receptor and caveolin-1 complex by ganglioside GM3 in the state of insulin resistance. *Proc Natl Acad Sci U S A* 2007;104:13678-83.
125. Karra E, Chandarana K, Batterham RL. The role of peptide YY in appetite regulation and obesity. *J Physiol* 2009;587:19-25.
126. Kelley D, Mokan M, Veneman T. Impaired postprandial glucose utilization in non-insulin-dependent diabetes mellitus. *Metabolism* 1994;43:1549-57.
127. Kelley DE, Mandarino LJ. Hyperglycemia normalizes insulin-stimulated skeletal muscle glucose oxidation and storage in noninsulin-dependent diabetes mellitus. *J Clin Invest* 1990;86:1999-2007.
128. Kerner A, Avizohar O, Sella R et al. Association between elevated liver enzymes and C-reactive protein: possible hepatic contribution to systemic inflammation in the metabolic syndrome. *Arterioscler Thromb Vasc Biol* 2005;25:193-7.
129. Kien CL, Bunn JY. Effects of palmitate and oleate on the respiratory quotient during acute feeding. *Obesity (Silver Spring)* 2007;15:1640-2.
130. Kien CL, Bunn JY, Ugrasbul F. Increasing dietary palmitic acid decreases fat oxidation and daily energy expenditure. *Am J Clin Nutr* 2005;82:320-6.

131. Kim Y, Lee S. Physical activity and abdominal obesity in youth. *Appl Physiol Nutr Metab* 2009;34:571-81.
132. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998;21:1414-31.
133. Koh KK, Han SH, Quon MJ. Inflammatory markers and the metabolic syndrome: insights from therapeutic interventions. *J Am Coll Cardiol* 2005;46:1978-85.
134. Koopman R, Schaart G, Hesselink MK. Optimisation of oil red O staining permits combination with immunofluorescence and automated quantification of lipids. *Histochem Cell Biol* 2001;116:63-8.
135. Korsheninnikova E. Sustained activation of the mammalian target of rapamycin nutrient sensing pathway is associated with hepatic insulin resistance, but not with steatosis, in mice. 2006.
136. Kotronen A, Westerbacka J, Bergholm R, Pietilainen KH, Yki-Jarvinen H. Liver fat in the metabolic syndrome. *J Clin Endocrinol Metab* 2007;92:3490-7.
137. Kovacs TR, Ussher JR, Noland RC et al. Mitochondrial overload and incomplete fatty acid oxidation contribute to skeletal muscle insulin resistance. *Cell Metab* 2008;7:45-56.
138. Kraegen EW, Clark PW, Jenkins AB, Daley EA, Chisholm DJ, Storlien LH. Development of muscle insulin resistance after liver insulin resistance in high-fat-fed rats. *Diabetes* 1991;40:1397-403.
139. Kraus WE, Houmard JA, Duscha BD et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med* 2002;347:1483-92.
140. Kubota N, Yano W, Kubota T et al. Adiponectin stimulates AMP-activated protein kinase in the hypothalamus and increases food intake. *Cell Metab* 2007;6:55-68.
141. Kumahara H, Schutz Y, Ayabe M et al. The use of uniaxial accelerometry for the assessment of physical-activity-related energy expenditure: a validation study against whole-body indirect calorimetry. *Br J Nutr* 2004;91:235-43.
142. Langeveld M, Aerts JM. Glycosphingolipids and insulin resistance. *Prog Lipid Res* 2009;48:196-205.

143. Leigh RM, Davies PS. Energy cost of activity assessed by indirect calorimetry and a $^{13}\text{CO}_2$ breath test. *Med Sci Sports Exerc* 2001;33:834-8.
144. Leyton J, Drury PJ, Crawford MA. Differential oxidation of saturated and unsaturated fatty acids in vivo in the rat. *Br J Nutr* 1987;57:383-93.
145. Lichtenstein AH, Schwab US. Relationship of dietary fat to glucose metabolism. *Atherosclerosis* 2000;150:227-43.
146. Lin S, Storlien LH, Huang XF. Leptin receptor, NPY, POMC mRNA expression in the diet-induced obese mouse brain. *Brain Res* 2000;875:89-95.
147. Lissner L, Heitmann BL. Dietary fat and obesity: evidence from epidemiology. *Eur J Clin Nutr* 1995;49:79-90.
148. Livingstone MB. Childhood obesity in Europe: a growing concern. *Public Health Nutr* 2001;4:109-16.
149. Look AHEAD Research Group. Reduction in Weight and Cardiovascular Disease Risk Factors in Individuals With Type 2 Diabetes. *Diabetes Care* 2007;30:1374-83.
150. Loos RJ. Recent progress in the genetics of common obesity. *Br J Clin Pharmacol* 2009;68:811-29.
151. Loos RJ, Lindgren CM, Li S et al. Common variants near MC4R are associated with fat mass, weight and risk of obesity. *Nat Genet* 2008;40:768-75.
152. Lopez S, Bermudez B, Abia R, Muriana FJ. The influence of major dietary fatty acids on insulin secretion and action. *Curr Opin Lipidol* 2009.
153. Luke A, Durazo-Arvizu R, Cao G, Adeyemo A, Tayo B, Cooper R. Positive association between resting energy expenditure and weight gain in a lean adult population. *Am J Clin Nutr* 2006;83:1076-81.
154. Madsen L, Guerre-Millo M, Flindt EN et al. Tetradecylthioacetic acid prevents high fat diet induced adiposity and insulin resistance. *J Lipid Res* 2002;43:742-50.
155. Maeda N, Shimomura I, Kishida K et al. Diet-induced insulin resistance in mice lacking adiponectin/ACRP30. *Nat Med* 2002;8:731-7.

156. Marcinek DJ, Schenkman KA, Ciesielski WA, Lee D, Conley KE. Reduced mitochondrial coupling in vivo alters cellular energetics in aged mouse skeletal muscle. *J Physiol* 2005;569:467-73.
157. Matsuzaka T. Crucial role of a long-chain fatty acid elongase, Elovl6, in obesity-induced insulin resistance. 2007.
158. Maxfield FR. Role of cholesterol and lipid organization in disease. 2005.
159. McCarthy MI, Abecasis GR, Cardon LR et al. Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nat Rev Genet* 2008;9:356-69.
160. McDonald GB, Saunders DR, Weidman M, Fisher L. Portal venous transport of long-chain fatty acids absorbed from rat intestine. *Am J Physiol* 1980;239:G141-G150.
161. Mensink M, Hesselink MK, Russell AP, Schaart G, Sels JP, Schrauwen P. Improved skeletal muscle oxidative enzyme activity and restoration of PGC-1 alpha and PPAR beta/delta gene expression upon rosiglitazone treatment in obese patients with type 2 diabetes mellitus. *Int J Obes (Lond)* 2007;31:1302-10.
162. Merrill AH, Jr., Wang E, Mullins RE. Kinetics of long-chain (sphingoid) base biosynthesis in intact LM cells: effects of varying the extracellular concentrations of serine and fatty acid precursors of this pathway. *Biochemistry* 1988;27:340-5.
163. Metges CC, Wolfram G. Medium- and long-chain triglycerides labeled with 13C: a comparison of oxidation after oral or parenteral administration in humans. *J Nutr* 1991;121:31-6.
164. Meyer C, Woerle HJ, Dostou JM, Welle SL, Gerich JE. Abnormal renal, hepatic, and muscle glucose metabolism following glucose ingestion in type 2 diabetes. *Am J Physiol Endocrinol Metab* 2004;287:E1049-E1056.
165. Minehira K, Young SG, Villanueva CJ et al. Blocking VLDL secretion causes hepatic steatosis but does not affect peripheral lipid stores or insulin sensitivity in mice. *J Lipid Res* 2008;49:2038-44.
166. Minnaard R, Drost MR, Wagenmakers AJ, van Kranenburg GP, Kuipers H, Hesselink MK. Skeletal Muscle wasting and contractile performance in septic rats. *Muscle Nerve* 2005;31:339-48.
167. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *JAMA* 2004;291:1238-45.

168. Moller L, Norrelund H, Jessen N et al. Impact of growth hormone receptor blockade on substrate metabolism during fasting in healthy subjects. *J Clin Endocrinol Metab* 2009;94:4524-32.
169. Montell E, Turini M, Marotta M et al. DAG accumulation from saturated fatty acids desensitizes insulin stimulation of glucose uptake in muscle cells. *Am J Physiol Endocrinol Metab* 2001;280:E229-E237.
170. Morioka T, Asilmaz E, Hu J et al. Disruption of leptin receptor expression in the pancreas directly affects beta cell growth and function in mice. *J Clin Invest* 2007;117:2860-8.
171. Morris MJ, Chen H, Watts R, Shulkes A, Cameron-Smith D. Brain neuropeptide Y and CCK and peripheral adipokine receptors: temporal response in obesity induced by palatable diet. *Int J Obes (Lond)* 2008;32:249-58.
172. Mostad IL, Bjerve KS, Bjorgaas MR, Lydersen S, Grill V. Effects of n-3 fatty acids in subjects with type 2 diabetes: reduction of insulin sensitivity and time-dependent alteration from carbohydrate to fat oxidation. *Am J Clin Nutr* 2006;84:540-50.
173. Muniyappa R, Iantorno M, Quon MJ. An integrated view of insulin resistance and endothelial dysfunction. *Endocrinol Metab Clin North Am* 2008;37:685-x.
174. Muoio DM, Newgard CB. Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. *Nat Rev Mol Cell Biol* 2008;9:193-205.
175. Nabben M, Hoeks J, Briede JJ et al. The effect of UCP3 overexpression on mitochondrial ROS production in skeletal muscle of young versus aged mice. *FEBS Lett* 2008;582:4147-52.
176. Nagle CA, Klett EL, Coleman RA. Hepatic triacylglycerol accumulation and insulin resistance. *J Lipid Res* 2009;50 Suppl:S74-S79.
177. Nascimento EB. Insulin-mediated phosphorylation of the proline-rich Akt substrate PRAS40 is impaired in insulin target tissues of high-fat diet-fed rats. 2006.
178. Nishimura S, Manabe I, Nagai R. Adipose tissue inflammation in obesity and metabolic syndrome. *Discov Med* 2009;8:55-60.

179. Nitsan Z, Nir I, Petahi I. The effect of meal-feeding and food restriction on body composition, food utilization and intestinal adaptation in light-breed chicks. *Br J Nutr* 1984;51:101-9.
180. Nkondjock A. Specific fatty acid intake and the risk of pancreatic cancer in Canada. 2005.
181. ntuna-Puente B, Feve B, Fellahi S, Bastard JP. Adipokines: the missing link between insulin resistance and obesity. *Diabetes Metab* 2008;34:2-11.
182. Oosterveer MH, van Dijk TH, Tietge UJ et al. High fat feeding induces hepatic fatty acid elongation in mice. *PLoS One* 2009;4:e6066.
183. Ooyama K, Kojima K, Aoyama T, Takeuchi H. Decrease of food intake in rats after ingestion of medium-chain triacylglycerol. *J Nutr Sci Vitaminol (Tokyo)* 2009;55:423-7.
184. Pai T. Stearic acid modifies very low density lipoprotein lipid composition and particle size differently from shorter-chain saturated fatty acids in cultured rat hepatocytes. 1997.
185. Pai T, Yeh YY. Stearic acid unlike shorter-chain saturated fatty acids is poorly utilized for triacylglycerol synthesis and beta-oxidation in cultured rat hepatocytes. *Lipids* 1996;31:159-64.
186. Paniagua JA, de la Sacristana AG, Sanchez E et al. A MUFA-rich diet improves postprandial glucose, lipid and GLP-1 responses in insulin-resistant subjects. *J Am Coll Nutr* 2007;26:434-44.
187. Paoletti R, Bolego C, Poli A, Cignarella A. Metabolic syndrome, inflammation and atherosclerosis. *Vasc Health Risk Manag* 2006;2:145-52.
188. Papamandjaris AA, MacDougall DE, Jones PJ. Medium chain fatty acid metabolism and energy expenditure: obesity treatment implications. *Life Sci* 1998;62:1203-15.
189. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med* 2003;163:427-36.
190. Peronnet F, Massicotte D. Table of nonprotein respiratory quotient: an update. *Can J Sport Sci* 1991;16:23-9.
191. Piers LS, Walker KZ, Stoney RM, Soares MJ, O'Dea K. The influence of the type of dietary fat on postprandial fat oxidation rates: monounsaturated

- (olive oil) vs saturated fat (cream). *Int J Obes Relat Metab Disord* 2002;26:814-21.
192. Piers LS, Walker KZ, Stoney RM, Soares MJ, O'Dea K. Substitution of saturated with monounsaturated fat in a 4-week diet affects body weight and composition of overweight and obese men. *Br J Nutr* 2003;90:717-27.
 193. Pischon T, Nothlings U, Boeing H. Obesity and cancer. *Proc Nutr Soc* 2008;67:128-45.
 194. Plasqui G, Joosen AM, Kester AD, Goris AH, Westerterp KR. Measuring free-living energy expenditure and physical activity with triaxial accelerometry. *Obes Res* 2005;13:1363-9.
 195. Prodi E, Obici S. Minireview: the brain as a molecular target for diabetic therapy. *Endocrinology* 2006;147:2664-9.
 196. Qi L, Kang K, Zhang C et al. Fat mass-and obesity-associated (FTO) gene variant is associated with obesity: longitudinal analyses in two cohort studies and functional test. *Diabetes* 2008;57:3145-51.
 197. Radonjic M, de H, Jr., van Erk MJ et al. Genome-wide mRNA expression analysis of hepatic adaptation to high-fat diets reveals switch from an inflammatory to steatotic transcriptional program. *PLoS One* 2009;4:e6646.
 198. Radonjic M, de H, Jr., van Erk MJ et al. Genome-wide mRNA expression analysis of hepatic adaptation to high-fat diets reveals switch from an inflammatory to steatotic transcriptional program. *PLoS One* 2009;4:e6646.
 199. Ramirez I. High-fat diets stimulate transient hyperphagia whereas wet diets stimulate prolonged hyperphagia in Fischer rats. *Physiol Behav* 1991;49:1223-8.
 200. 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;1:785-9.
 201. Ravussin E, Bogardus C. A brief overview of human energy metabolism and its relationship to essential obesity. *Am J Clin Nutr* 1992;55:242S-245.
 202. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest* 1986;78:1568-78.

203. Ravussin E, Lillioja S, Knowler WC et al. Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Engl J Med* 1988;318:467-72.
204. Razzouk L, Muntner P. Ethnic, gender, and age-related differences in patients with the metabolic syndrome. *Curr Hypertens Rep* 2009;11:127-32.
205. Renfurm LN, Bandsma RH, Verkade HJ et al. Cholesterol synthesis and de novo lipogenesis in premature infants determined by mass isotopomer distribution analysis. *Pediatr Res* 2004;56:602-7.
206. Rivellese AA, Lilli S. Quality of dietary fatty acids, insulin sensitivity and type 2 diabetes. *Biomed Pharmacother* 2003;57:84-7.
207. Roberts DL, Dive C, Renahan AG. Biological Mechanisms Linking Obesity and Cancer Risk: New Perspectives. *Annu Rev Med* 2009.
208. Roberts SB. Use of the doubly labeled water method for measurement of energy expenditure, total body water, water intake, and metabolizable energy intake in humans and small animals. *Can J Physiol Pharmacol* 1989;67:1190-8.
209. Rolfe DF, Brown GC. Cellular energy utilization and molecular origin of standard metabolic rate in mammals. *Physiol Rev* 1997;77:731-58.
210. Rosenbaum M, Ravussin E, Matthews DE et al. A comparative study of different means of assessing long-term energy expenditure in humans. *Am J Physiol* 1996;270:R496-R504.
211. Rumawas ME, Meigs JB, Dwyer JT, McKeown NM, Jacques PF. Mediterranean-style dietary pattern, reduced risk of metabolic syndrome traits, and incidence in the Framingham Offspring Cohort. *Am J Clin Nutr* 2009.
212. Salgado-Delgado R, ngeles-Castellanos M, Saderi N, Buijs RM, Escobar C. Food intake during the normal activity phase prevents obesity and circadian desynchrony in a rat model of night work. *Endocrinology* 2010;151:1019-29.
213. Sampath H, Ntambi JM. The fate and intermediary metabolism of stearic acid. *Lipids* 2005;40:1187-91.
214. Savastano DM, Covasa M. Adaptation to a high-fat diet leads to hyperphagia and diminished sensitivity to cholecystokinin in rats. *J Nutr* 2005;135:1953-9.

215. Schaeffler A, Gross P, Buettner R et al. Fatty acid-induced induction of Toll-like receptor-4/nuclear factor-kappaB pathway in adipocytes links nutritional signalling with innate immunity. *Immunology* 2009;126:233-45.
216. Schrauwen P, Lichtenbelt WD, Saris WH, Westerterp KR. Fat balance in obese subjects: role of glycogen stores. *Am J Physiol* 1998;274:E1027-E1033.
217. Schutz Y, Flatt JP, Jequier E. Failure of dietary fat intake to promote fat oxidation: a factor favoring the development of obesity. *Am J Clin Nutr* 1989;50:307-14.
218. Segal KR, Presta E, Gutin B. Thermic effect of food during graded exercise in normal weight and obese men. *Am J Clin Nutr* 1984;40:995-1000.
219. Sell H, Eckel J. Chemotactic cytokines, obesity and type 2 diabetes: in vivo and in vitro evidence for a possible causal correlation? *Proc Nutr Soc* 2009;68:378-84.
220. Shi H. TLR4 links innate immunity and fatty acid-induced insulin resistance. 2006.
221. Singh M, Kesterson RA, Jacobs MM, Joers JM, Gore JC, Emeson RB. Hyperphagia-mediated obesity in transgenic mice misexpressing the RNA-editing enzyme ADAR2. *J Biol Chem* 2007;282:22448-59.
222. Sirtori CR, Galli C. N-3 fatty acids and diabetes. *Biomed Pharmacother* 2002;56:397-406.
223. Smilde AK, Jansen JJ, Hoefsloot HC, Lamers RJ, van der GJ, Timmerman ME. ANOVA-simultaneous component analysis (ASCA): a new tool for analyzing designed metabolomics data. *Bioinformatics* 2005;21:3043-8.
224. Song SH, Hardisty CA. Early-onset Type 2 diabetes mellitus: an increasing phenomenon of elevated cardiovascular risk. *Expert Rev Cardiovasc Ther* 2008;6:315-22.
225. St-Onge MP, Ross R, Parsons WD, Jones PJ. Medium-chain triglycerides increase energy expenditure and decrease adiposity in overweight men. *Obes Res* 2003;11:395-402.
226. Storlien LH, Jenkins AB, Chisholm DJ, Pascoe WS, Khouri S, Kraegen EW. Influence of dietary fat composition on development of insulin resistance in rats. Relationship to muscle triglyceride and omega-3 fatty acids in muscle phospholipid. *Diabetes* 1991;40:280-9.

227. Stubbs RJ. Nutrition Society Medal Lecture. Appetite, feeding behaviour and energy balance in human subjects. *Proc Nutr Soc* 1998;57:341-56.
228. Stubbs RJ, Whybrow S. Energy density, diet composition and palatability: influences on overall food energy intake in humans. *Physiol Behav* 2004;81:755-64.
229. Stucki JW. The optimal efficiency and the economic degrees of coupling of oxidative phosphorylation. *Eur J Biochem* 1980;109:269-83.
230. Summermatter S, Mainieri D, Russell AP et al. Thrifty metabolism that favors fat storage after caloric restriction: a role for skeletal muscle phosphatidylinositol-3-kinase activity and AMP-activated protein kinase. *FASEB J* 2008;22:774-85.
231. Summers SA. Ceramides in insulin resistance and lipotoxicity. *Prog Lipid Res* 2006;45:42-72.
232. Swinburn B, Sacks G, Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. *Am J Clin Nutr* 2009.
233. Szendroedi J, Roden M. Ectopic lipids and organ function. *Curr Opin Lipidol* 2009;20:50-6.
234. Tagami S, Inokuchi JJ, Kabayama K et al. Ganglioside GM3 participates in the pathological conditions of insulin resistance. *J Biol Chem* 2002;277:3085-92.
235. Tao YX. Molecular mechanisms of the neural melanocortin receptor dysfunction in severe early onset obesity. *Mol Cell Endocrinol* 2005;239:1-14.
236. Tataranni PA, Harper IT, Snitker S et al. Body weight gain in free-living Pima Indians: effect of energy intake vs expenditure. *Int J Obes Relat Metab Disord* 2003;27:1578-83.
237. Taylor PD, Khan IY, Lakasing L et al. Uterine artery function in pregnant rats fed a diet supplemented with animal lard. *Exp Physiol* 2003;88:389-98.
238. Temme EH, Mensink RP, Hornstra G. Comparison of the effects of diets enriched in lauric, palmitic, or oleic acids on serum lipids and lipoproteins in healthy women and men. *Am J Clin Nutr* 1996;63:897-903.

239. Teusink B, Voshol PJ, Dahlmans VE et al. Contribution of fatty acids released from lipolysis of plasma triglycerides to total plasma fatty acid flux and tissue-specific fatty acid uptake. *Diabetes* 2003;52:614-20.
240. Thissen U, Wopereis S, van den Berg SA et al. Improving the analysis of designed studies by combining statistical modelling with study design information. *BMC Bioinformatics* 2009;10:52.
241. Thorleifsson G, Walters GB, Gudbjartsson DF et al. Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity. *Nat Genet* 2009;41:18-24.
242. Timmers S, Schrauwen P, de Vogel J. Muscular diacylglycerol metabolism and insulin resistance. *Physiology & Behavior* 2008;94:242-51.
243. Trayhurn P, Fuller L. The development of obesity in genetically diabetic-obese (db/db) mice pair-fed with lean siblings. The importance of thermoregulatory thermogenesis. *Diabetologia* 1980;19:148-53.
244. Tserng KY, Griffin RL. Ceramide metabolite, not intact ceramide molecule, may be responsible for cellular toxicity. *Biochem J* 2004;380:715-22.
245. Turinsky J, O'Sullivan DM, Bayly BP. 1,2-Diacylglycerol and ceramide levels in insulin-resistant tissues of the rat *in vivo*. *Journal of Biological Chemistry* 1990;265:16880-5.
246. Turner N, Hariharan K, TidAng J et al. Enhancement of muscle mitochondrial oxidative capacity and alterations in insulin action are lipid species dependent: potent tissue-specific effects of medium-chain fatty acids. *Diabetes* 2009;58:2547-54.
247. Turner SM, Linfoot PA, Neese RA, Hellerstein MK. Sources of plasma glucose and liver glycogen in fasted ob/ob mice. *Acta Diabetol* 2005;42:187-93.
248. van Dale D, Saris WH, ten Hoor F. Weight maintenance and resting metabolic rate 18-40 months after a diet/exercise treatment. *Int J Obes* 1990;14:347-59.
249. van den Berg RA, Hoefsloot HC, Westerhuis JA, Smilde AK, van der Werf MJ. Centering, scaling, and transformations: improving the biological information content of metabolomics data. *BMC Genomics* 2006;7:142.
250. van den Berg SA, Guigas B, Bijland S et al. High levels of dietary stearate promote adiposity and deteriorate hepatic insulin sensitivity. *Nutr Metab (Lond)* 2010;7:24.

251. van den Hoek AM, Heijboer AC, Voshol PJ et al. Chronic PYY3-36 treatment promotes fat oxidation and ameliorates insulin resistance in C57BL6 mice. *Am J Physiol Endocrinol Metab* 2007;292:E238-E245.
252. van den Hoek AM, Teusink B, Voshol PJ, Havekes LM, Romijn JA, Pijl H. Leptin deficiency per se dictates body composition and insulin action in ob/ob mice. *J Neuroendocrinol* 2008;20:120-7.
253. van Eijk M, Aten J, Bijl N et al. Reducing glycosphingolipid content in adipose tissue of obese mice restores insulin sensitivity, adipogenesis and reduces inflammation. *PLoS One* 2009;4:e4723.
254. van Herpen NA, Schrauwen-Hinderling VB. Lipid accumulation in non-adipose tissue and lipotoxicity. *Physiol Behav* 2008;94:231-41.
255. van Wymelbeke V, Himaya A, Louis-Sylvestre J, Fantino M. Influence of medium-chain and long-chain triacylglycerols on the control of food intake in men. *Am J Clin Nutr* 1998;68:226-34.
256. Vernoched C, Peres SB, Farmer SR. Mechanisms of obesity and related pathologies: transcriptional control of adipose tissue development. *FEBS J* 2009;276:5729-37.
257. Vis DJ, Westerhuis JA, Smilde AK, van der GJ. Statistical validation of megavariate effects in ASCA. *BMC Bioinformatics* 2007;8:322.
258. Voshol PJ. In muscle-specific lipoprotein lipase-overexpressing mice, muscle triglyceride content is increased without inhibition of insulin-stimulated whole-body and muscle-specific glucose uptake. 2001.
259. Vrang N, Madsen AN, Tang-Christensen M, Hansen G, Larsen PJ. PYY(3-36) reduces food intake and body weight and improves insulin sensitivity in rodent models of diet-induced obesity. *Am J Physiol Regul Integr Comp Physiol* 2006;291:R367-R375.
260. Wadden TA, Vogt RA, Andersen RE et al. Exercise in the treatment of obesity: effects of four interventions on body composition, resting energy expenditure, appetite, and mood. *J Consult Clin Psychol* 1997;65:269-77.
261. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocr Rev* 2000;21:697-738.
262. Wang Z, Heshka S, Wang J et al. Metabolically active portion of fat-free mass: a cellular body composition level modeling analysis. *Am J Physiol Endocrinol Metab* 2007;292:E49-E53.

263. Wein S, Wolffram S, Schrezenmeir J, Gasperikova D, Klimes I, Sebokova E. Medium-chain fatty acids ameliorate insulin resistance caused by high-fat diets in rats. *Diabetes Metab Res Rev* 2009;25:185-94.
264. Weinsier RL, Hunter GR, Zuckerman PA, Darnell BE. Low resting and sleeping energy expenditure and fat use do not contribute to obesity in women. *Obes Res* 2003;11:937-44.
265. Weinsier RL, Nelson KM, Hensrud DD, Darnell BE, Hunter GR, Schutz Y. Metabolic predictors of obesity. Contribution of resting energy expenditure, thermic effect of food, and fuel utilization to four-year weight gain of post-obese and never-obese women. *J Clin Invest* 1995;95:980-5.
266. Weinstein AR, Sesso HD, Lee IM et al. The joint effects of physical activity and body mass index on coronary heart disease risk in women. *Arch Intern Med* 2008;168:884-90.
267. Westerterp KR. Dietary fat oxidation as a function of body fat. *Curr Opin Lipidol* 2009;20:45-9.
268. Westerterp KR, Schols AMWJ. Basics in clinical nutrition: Energy metabolism. e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 2008;3:e281-e284.
269. Westerterp-Plantenga MS, Lejeune MP, Smeets AJ, Luscombe-Marsh ND. Sex differences in energy homeostasis following a diet relatively high in protein exchanged with carbohydrate, assessed in a respiration chamber in humans. *Physiol Behav* 2009;97:414-9.
270. White MD, Papamandjaris AA, Jones PJ. Enhanced postprandial energy expenditure with medium-chain fatty acid feeding is attenuated after 14 d in premenopausal women. *Am J Clin Nutr* 1999;69:883-9.
271. Wilkes JJ, Bonen A, Bell RC. A modified high-fat diet induces insulin resistance in rat skeletal muscle but not adipocytes. *Am J Physiol* 1998;275:E679-E686.
272. Willer CJ, Speliotes EK, Loos RJ et al. Six new loci associated with body mass index highlight a neuronal influence on body weight regulation. *Nat Genet* 2009;41:25-34.
273. Wittamer V, Franssen JD, Vulcano M et al. Specific recruitment of antigen-presenting cells by chemerin, a novel processed ligand from human inflammatory fluids. *J Exp Med* 2003;198:977-85.

274. Xiao GG, Garg M, Lim S, Wong D, Go VL, Lee WNP. Determination of protein synthesis in vivo using labeling from deuterated water and analysis of MALDI-TOF spectrum. *J Appl Physiol* 2008;104:828-36.
275. Xu H, Barnes GT, Yang Q et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. *J Clin Invest* 2003;112:1821-30.
276. Yang LY, Kuksis A, Myher JJ, Steiner G. Contribution of de novo fatty acid synthesis to very low density lipoprotein triacylglycerols: evidence from mass isotopomer distribution analysis of fatty acids synthesized from [2H6]ethanol. *J Lipid Res* 1996;37:262-74.
277. Yang N, Wang C, Xu M, Mao L, Liu L, Sun X. Interaction of dietary composition and PYY gene expression in diet-induced obesity in rats. *J Huazhong Univ Sci Technolog Med Sci* 2005;25:243-6.
278. Yuan R, Tsaih SW, Petkova SB et al. Aging in inbred strains of mice: study design and interim report on median lifespans and circulating IGF1 levels. *Aging Cell* 2009;8:277-87.
279. Yusuf S, Hawken S, Ounpuu S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937-52.
280. Zadelaar S, Kleemann R, Verschuren L et al. Mouse models for atherosclerosis and pharmaceutical modifiers. *Arterioscler Thromb Vasc Biol* 2007;27:1706-21.
281. Zhao H, Przybylska M, Wu IH et al. Inhibiting glycosphingolipid synthesis improves glycemic control and insulin sensitivity in animal models of type 2 diabetes. *Diabetes* 2007;56:1210-8.
282. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001;414:782-7.
283. Ziotopoulou M, Mantzoros CS, Hileman SM, Flier JS. Differential expression of hypothalamic neuropeptides in the early phase of diet-induced obesity in mice. *Am J Physiol Endocrinol Metab* 2000;279:E838-E845.
284. Zurlo F, Larson K, Bogardus C, Ravussin E. Skeletal muscle metabolism is a major determinant of resting energy expenditure. *J Clin Invest* 1990;86:1423-7.