

6. Literaturverzeichnis

1. World-Health-Organisation, *Definition, Diagnosis and Classification of Diabetes mellitus and its complications. pt1: Diagnosis and Classification of Diabetes mellitus*. World Health Organisation, 1999: p. 1-59.
2. *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)*. Jama, 2001. **285**(19): p. 2486-97.
3. Sacks, F.M., *Metabolic syndrome: epidemiology and consequences*. J Clin Psychiatry, 2004. **65 Suppl 18**: p. 3-12.
4. Ford, E.S. and W.H. Giles, *A comparison of the prevalence of the metabolic syndrome using two proposed definitions*. Diabetes Care, 2003. **26**(3): p. 575-81.
5. Hu, F.B., et al., *Diet, lifestyle, and the risk of type 2 diabetes mellitus in women*. N Engl J Med, 2001. **345**(11): p. 790-7.
6. Liese, A.D., et al., *Familial components of the multiple metabolic syndrome: the ARIC study*. Diabetologia, 1997. **40**(8): p. 963-70.
7. Edwards, K.L., et al., *Heritability of factors of the insulin resistance syndrome in women twins*. Genet Epidemiol, 1997. **14**(3): p. 241-53.
8. Isomaa, B., et al., *Cardiovascular morbidity and mortality associated with the metabolic syndrome*. Diabetes Care, 2001. **24**(4): p. 683-9.
9. Laaksonen, D.E., et al., *Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study*. Am J Epidemiol, 2002. **156**(11): p. 1070-7.
10. Sattar, N., et al., *Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study*. Circulation, 2003. **108**(4): p. 414-9.
11. Hill, J.O. and D. Bessesen, *What to do about the metabolic syndrome?* Arch Intern Med, 2003. **163**(4): p. 395-7.

12. Wilson, P.W. and S.M. Grundy, *The metabolic syndrome: a practical guide to origins and treatment: Part II.* Circulation, 2003. **108**(13): p. 1537-40.
13. Tuomilehto, J., et al., *Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance.* N Engl J Med, 2001. **344**(18): p. 1343-50.
14. Knowler, W.C., et al., *Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.* N Engl J Med, 2002. **346**(6): p. 393-403.
15. American Diabetes Association: *clinical practice recommendations 2002.* Diabetes Care, 2002. **25 Suppl 1:** p. S1-147.
16. Smith, S.C., Jr., et al., *AHA/ACC Guidelines for Preventing Heart Attack and Death in Patients With Atherosclerotic Cardiovascular Disease: 2001 update. A statement for healthcare professionals from the American Heart Association and the American College of Cardiology.* J Am Coll Cardiol, 2001. **38**(5): p. 1581-3.
17. National-Institutes-of-Health.National Heart, L., and Blood Institute., *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report.* National-Institutes-of-Health, 1998.
18. World-Health-Organisation, *Obesity - Preventing and managing the global epidemic.* WHO Consultation on Obesity, 1997: p. 1-276.
19. Kissebah, A.H. and G.R. Krakower, *Regional adiposity and morbidity.* Physiol Rev, 1994. **74**(4): p. 761-811.
20. Kuczmarski, R.J., et al., *Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 to 1991.* Jama, 1994. **272**(3): p. 205-11.
21. Flegal, K.M., et al., *Overweight and obesity in the United States: prevalence and trends, 1960-1994.* Int J Obes Relat Metab Disord, 1998. **22**(1): p. 39-47.
22. Seidell, J.C. and I. Deerenberg, *Obesity in Europe: prevalence and consequences for use of medical care.* Pharmacoconomics, 1994. **5**(Suppl 1): p. 38-44.
23. Thefeld, W., *Verbreitung der Herz-Kreislauf-Risikofaktoren Hypercholesterinämie, Übergewicht, Hypertonie und Rauchen in der*

- Bevölkerung.* Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 2000. **43**: p. 415-423.
24. Mokdad, A.H., et al., *The spread of the obesity epidemic in the United States, 1991-1998.* Jama, 1999. **282**(16): p. 1519-22.
25. Mokdad, A.H., et al., *The continuing epidemics of obesity and diabetes in the United States.* Jama, 2001. **286**(10): p. 1195-200.
26. Mokdad, A.H., et al., *Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001.* Jama, 2003. **289**(1): p. 76-9.
27. Must, A., et al., *The disease burden associated with overweight and obesity.* Jama, 1999. **282**(16): p. 1523-9.
28. Calle, E.E., et al., *Body-mass index and mortality in a prospective cohort of U.S. adults.* N Engl J Med, 1999. **341**(15): p. 1097-105.
29. Allison, D.B., et al., *Annual deaths attributable to obesity in the United States.* Jama, 1999. **282**(16): p. 1530-8.
30. Luyckx, F.H., P.J. Lefebvre, and A.J. Scheen, *Non-alcoholic steatohepatitis: association with obesity and insulin resistance, and influence of weight loss.* Diabetes Metab, 2000. **26**(2): p. 98-106.
31. Kortelainen, M.L., *Association between cardiac pathology and fat tissue distribution in an autopsy series of men without premortem evidence of cardiovascular disease.* Int J Obes Relat Metab Disord, 1996. **20**(3): p. 245-52.
32. Wirth, A., A.M. Sharma, and H. Schunkert, *[Cardiomyopathy in obesity--a disease entity?].* Dtsch Med Wochenschr, 2000. **125**(31-32): p. 944-9.
33. Jennette, J.C., L. Charles, and W. Grubb, *Glomerulomegaly and focal segmental glomerulosclerosis associated with obesity and sleep-apnea syndrome.* Am J Kidney Dis, 1987. **10**(6): p. 470-2.
34. Dwyer, T.M., et al., *The altered structure of renal papillary outflow tracts in obesity.* Ultrastruct Pathol, 2000. **24**(4): p. 251-7.
35. Reaven, G.M., *Banting lecture 1988. Role of insulin resistance in human disease.* Diabetes, 1988. **37**(12): p. 1595-607.
36. Kahn, B.B. and J.S. Flier, *Obesity and insulin resistance.* J Clin Invest, 2000. **106**(4): p. 473-81.
37. Ginsberg, H.N., *Insulin resistance and cardiovascular disease.* J Clin Invest, 2000. **106**(4): p. 453-8.

38. Haffner, S.M., *Epidemiology of insulin resistance and its relation to coronary artery disease*. Am J Cardiol, 1999. **84**(1A): p. 11J-14J.
39. DeFronzo, R.A., J.D. Tobin, and R. Andres, *Glucose clamp technique: a method for quantifying insulin secretion and resistance*. Am J Physiol, 1979. **237**(3): p. E214-23.
40. Bergman, R.N., et al., *Quantitative estimation of insulin sensitivity*. Am J Physiol, 1979. **236**(6): p. E667-77.
41. Matthews, D.R., et al., *Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man*. Diabetologia, 1985. **28**(7): p. 412-9.
42. Bonora, E., et al., *Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity*. Diabetes Care, 2000. **23**(1): p. 57-63.
43. Expert-Committee-on-the-Diagnosis-and- and Classification-of-Diabetes-Mellitus., *Report of Expert Committee on the Diagnosis and Classification of Diabetes Mellitus*. Diabetes Care, 1998. **21**(suppl 1):p.1-25.
44. International-Diabetes-Federation-Task-Force-on-Diabetes-Health-Economics, *Facts, Figures and Forecasts*. 1997.
45. King, H., R.E. Aubert, and W.H. Herman, *Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections*. Diabetes Care, 1998. **21**(9): p. 1414-31.
46. Thefeld, W., *Prävalenz des Diabetes mellitus in der erwachsenen Bevölkerung Deutschlands*. Gesundheitswesen, 2000. **61**(Sonderheft 2): p. 85-89.
47. Morgan, C.L., C.J. Currie, and J.R. Peters, *Relationship between diabetes and mortality: a population study using record linkage*. Diabetes Care, 2000. **23**(8): p. 1103-7.
48. Stamler, J., et al., *Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial*. Diabetes Care, 1993. **16**(2): p. 434-44.
49. Manson, J.E., et al., *A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women*. Arch Intern Med, 1991. **151**(6): p. 1141-7.

50. Skeggs, L.T., Jr., et al., *The amino acid sequence of hypertensin. II.* J Exp Med, 1956. **104**(2): p. 193-7.
51. Pals, D.T., et al., *A specific competitive antagonist of the vascular action of angiotensin. II.* Circ Res, 1971. **29**(6): p. 664-72.
52. Furakawa, Y., S. Kishimoto, and K. Nishikawa, *Hypotensive imidazole derivatives and hypotensive imidazole-5-acetic acid derivates.* US Patents, 1982: p. No. 4340598 and 4355040.
53. Timmermans, P.B., et al., *Angiotensin II receptors and angiotensin II receptor antagonists.* Pharmacol Rev, 1993. **45**(2): p. 205-51.
54. Buhlmayer, P., et al., *Valsartan, a potent, orally active angiotensin II antagonist developed from the structurally new amino acid series.* Bioorg Med Chem Lett, 1994. **4**: p. 29-34.
55. Bernhart, C.A., et al., *A new series of imidazolones: highly specific and potent nonpeptide AT1 angiotensin II receptor antagonists.* J Med Chem, 1993. **36**(22): p. 3371-80.
56. Noda, M., et al., *Inhibition of rabbit aortic angiotensin II (All) receptor by CV-11974, a new nonpeptide All antagonist.* Biochem Pharmacol, 1993. **46**(2): p. 311-8.
57. Wienen, W., et al., *Pharmacological characterization of the novel nonpeptide angiotensin II receptor antagonist, BIBR 277.* Br J Pharmacol, 1993. **110**(1): p. 245-52.
58. Koike, H., T. Sada, and M. Mizuno, *In vitro and in vivo pharmacology of olmesartan medoxomil, an angiotensin II type AT1 receptor antagonist.* J Hypertens Suppl, 2001. **19 Suppl 1**: p. S3-14.
59. Judd, D.B., et al., *Bromobenzofuran-based non-peptide antagonists of angiotensin II: GR138950, a potent antihypertensive agent with high oral bioavailability.* J Med Chem, 1994. **37**(19): p. 3108-20.
60. Weinstock, J., et al., *1-(carboxybenzyl)imidazole-5-acrylic acids: potent and selective angiotensin II receptor antagonists.* J Med Chem, 1991. **34**(4): p. 1514-7.
61. Unger, T., B. Schölkens, and (eds.), *Angiotensin. Handbook of Experimental Pharmacology*, 2004. **163/I**: p. 5-7.
62. Kaschina, E. and T. Unger, *Angiotensin AT1/AT2 receptors: regulation, signalling and function.* Blood Press, 2003. **12**(2): p. 70-88.

63. Unger, T., et al., *Angiotensin receptors*. J Hypertens Suppl, 1996. **14**(5): p. S95-103.
64. Blume, A., E. Kaschina, and T. Unger, *Angiotensin II type 2 receptors: signalling and pathophysiological role*. Curr Opin Nephrol Hypertens, 2001. **10**(2): p. 239-46.
65. Dzau, V. and E. Braunwald, *Resolved and unresolved issues in the prevention and treatment of coronary artery disease: a workshop consensus statement*. Am Heart J, 1991. **121**(4 Pt 1): p. 1244-63.
66. Unger, T., *The role of the renin-angiotensin system in the development of cardiovascular disease*. Am J Cardiol, 2002. **89**(2A): p. 3A-9A; discussion 10A.
67. Goldberg, M.R., et al., *Biochemical effects of losartan, a nonpeptide angiotensin II receptor antagonist, on the renin-angiotensin-aldosterone system in hypertensive patients*. Hypertension, 1995. **25**(1): p. 37-46.
68. Gradman, A.H., et al., *A randomized, placebo-controlled, double-blind, parallel study of various doses of losartan potassium compared with enalapril maleate in patients with essential hypertension*. Hypertension, 1995. **25**(6): p. 1345-50.
69. Larochelle, P., et al., *Effects and tolerability of irbesartan versus enalapril in patients with severe hypertension*. Irbesartan Multicenter Investigators. Am J Cardiol, 1997. **80**(12): p. 1613-5.
70. Himmelmann, A., et al., *The effect duration of candesartan cilexetil once daily, in comparison with enalapril once daily, in patients with mild to moderate hypertension*. Blood Press, 2001. **10**(1): p. 43-51.
71. Neutel, J.M., D.H. Smith, and P.A. Reilly, *The efficacy and safety of telmisartan compared to enalapril in patients with severe hypertension*. Int J Clin Pract, 1999. **53**(3): p. 175-8.
72. Zimmermann, M. and T. Unger, *Challenges in improving prognosis and therapy: the Ongoing Telmisartan Alone and in Combination with Ramipril Global End point Trial programme*. Expert Opin Pharmacother, 2004. **5**(5): p. 1201-8.
73. Dahlof, B., et al., *Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol*. Lancet, 2002. **359**(9311): p. 995-1003.

74. Pfeffer, M.A., et al., *Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme.* Lancet, 2003. **362**(9386): p. 759-66.
75. Julius, S., et al., *Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial.* Lancet, 2004. **363**(9426): p. 2022-31.
76. Henriksen, E.J., et al., *Selective angiotensin II receptor antagonism reduces insulin resistance in obese Zucker rats.* Hypertension, 2001. **38**(4): p. 884-90.
77. Shiuchi, T., et al., *Angiotensin II type-1 receptor blocker valsartan enhances insulin sensitivity in skeletal muscles of diabetic mice.* Hypertension, 2004. **43**(5): p. 1003-10.
78. Ran, J., T. Hirano, and M. Adachi, *Angiotensin II type 1 receptor blocker ameliorates overproduction and accumulation of Triglyceride in the liver of Zucker fatty rats.* Am J Physiol Endocrinol Metab, 2004. **287**(2): p. E227-32.
79. Bergman, R.N., *Lilly lecture 1989. Toward physiological understanding of glucose tolerance. Minimal-model approach.* Diabetes, 1989. **38**(12): p. 1512-27.
80. Yamauchi, T., et al., *The fat-derived hormone adiponectin reverses insulin resistance associated with both lipodystrophy and obesity.* Nat Med, 2001. **7**(8): p. 941-6.
81. Scherer, P.E., et al., *A novel serum protein similar to C1q, produced exclusively in adipocytes.* J Biol Chem, 1995. **270**(45): p. 26746-9.
82. Hu, E., P. Liang, and B.M. Spiegelman, *AdipoQ is a novel adipose-specific gene dysregulated in obesity.* J Biol Chem, 1996. **271**(18): p. 10697-703.
83. Maeda, K., et al., *cDNA cloning and expression of a novel adipose specific collagen-like factor, apM1 (AdiPose Most abundant Gene transcript 1).* Biochem Biophys Res Commun, 1996. **221**(2): p. 286-9.
84. Arita, Y., et al., *Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity.* Biochem Biophys Res Commun, 1999. **257**(1): p. 79-83.

85. Nakano, Y., et al., *Isolation and characterization of GBP28, a novel gelatin-binding protein purified from human plasma.* J Biochem (Tokyo), 1996. **120**(4): p. 803-12.
86. Kishore, U. and K.B. Reid, *C1q: structure, function, and receptors.* Immunopharmacology, 2000. **49**(1-2): p. 159-70.
87. Shapiro, L. and P.E. Scherer, *The crystal structure of a complement-1q family protein suggests an evolutionary link to tumor necrosis factor.* Curr Biol, 1998. **8**(6): p. 335-8.
88. Berg, A.H., T.P. Combs, and P.E. Scherer, *ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism.* Trends Endocrinol Metab, 2002. **13**(2): p. 84-9.
89. Yamauchi, T., et al., *Cloning of adiponectin receptors that mediate antidiabetic metabolic effects.* Nature, 2003. **423**(6941): p. 762-9.
90. Fasshauer, M., et al., *Growth hormone is a positive regulator of adiponectin receptor 2 in 3T3-L1 adipocytes.* FEBS Lett, 2004. **558**(1-3): p. 27-32.
91. Hotta, K., 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**(5): p. 1126-33.
92. Hotta, K., et al., *Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients.* Arterioscler Thromb Vasc Biol, 2000. **20**(6): p. 1595-9.
93. Yang, W.S., et al., *Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin.* J Clin Endocrinol Metab, 2001. **86**(8): p. 3815-9.
94. Weyer, C., et al., *Hypo adiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia.* J Clin Endocrinol Metab, 2001. **86**(5): p. 1930-5.
95. Berg, A.H., et al., *The adipocyte-secreted protein Acrp30 enhances hepatic insulin action.* Nat Med, 2001. **7**(8): p. 947-53.
96. Maeda, N., et al., *PPARgamma ligands increase expression and plasma concentrations of adiponectin, an adipose-derived protein.* Diabetes, 2001. **50**(9): p. 2094-9.

97. Yu, J.G., et al., *The effect of thiazolidinediones on plasma adiponectin levels in normal, obese, and type 2 diabetic subjects*. Diabetes, 2002. **51**(10): p. 2968-74.
98. Combatsiaris, T., M. Tanen, and J. Berger, *Induction of Acrp30 levels by PPARgamma agonists: a potential mechanism of insulin sensitization*. Diabetes, 2001. **50**(suppl 2): p. 1118-P.
99. Fruebis, J., et al., *Proteolytic cleavage product of 30-kDa adipocyte complement-related protein increases fatty acid oxidation in muscle and causes weight loss in mice*. Proc Natl Acad Sci U S A, 2001. **98**(4): p. 2005-10.
100. Kappes, A. and G. Loffler, *Influences of ionomycin, dibutyryl-cycloAMP and tumour necrosis factor-alpha on intracellular amount and secretion of apM1 in differentiating primary human preadipocytes*. Horm Metab Res, 2000. **32**(11-12): p. 548-54.
101. Moitra, J., et al., *Life without white fat: a transgenic mouse*. Genes Dev, 1998. **12**(20): p. 3168-81.
102. Shimomura, I., et al., *Leptin reverses insulin resistance and diabetes mellitus in mice with congenital lipodystrophy*. Nature, 1999. **401**(6748): p. 73-6.
103. Yamauchi, T., et al., *Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase*. Nat Med, 2002. **8**(11): p. 1288-95.
104. Wu, X., et al., *Involvement of AMP-activated protein kinase in glucose uptake stimulated by the globular domain of adiponectin in primary rat adipocytes*. Diabetes, 2003. **52**(6): p. 1355-63.
105. Maeda, N., et al., *Diet-induced insulin resistance in mice lacking adiponectin/ACRP30*. Nat Med, 2002. **8**(7): p. 731-7.
106. Fasshauer, M., R. Paschke, and M. Stumvoll, *Adiponectin, obesity, and cardiovascular disease*. Biochimie, 2004. **86**(11): p. 779-84.
107. Tomas, E., et al., *Enhanced muscle fat oxidation and glucose transport by ACRP30 globular domain: acetyl-CoA carboxylase inhibition and AMP-activated protein kinase activation*. Proc Natl Acad Sci U S A, 2002. **99**(25): p. 16309-13.

108. Tan, K.C., et al., *Hypo adiponectinemia is associated with impaired endothelium-dependent vasodilation*. J Clin Endocrinol Metab, 2004. **89**(2): p. 765-9.
109. Chen, H., et al., *Adiponectin stimulates production of nitric oxide in vascular endothelial cells*. J Biol Chem, 2003. **278**(45): p. 45021-6.
110. Ouchi, N., et al., *Adiponectin stimulates angiogenesis by promoting cross-talk between AMP-activated protein kinase and Akt signaling in endothelial cells*. J Biol Chem, 2004. **279**(2): p. 1304-9.
111. Arita, Y., et al., *Adipocyte-derived plasma protein adiponectin acts as a platelet-derived growth factor-BB-binding protein and regulates growth factor-induced common postreceptor signal in vascular smooth muscle cell*. Circulation, 2002. **105**(24): p. 2893-8.
112. Matsuda, M., et al., *Role of adiponectin in preventing vascular stenosis. The missing link of adipo-vascular axis*. J Biol Chem, 2002. **277**(40): p. 37487-91.
113. Ouchi, N., et al., *Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages*. Circulation, 2001. **103**(8): p. 1057-63.
114. Furukawa, K., et al., *Adiponectin down-regulates acyl-coenzyme A:cholesterol acyltransferase-1 in cultured human monocyte-derived macrophages*. Biochem Biophys Res Commun, 2004. **317**(3): p. 831-6.
115. Kubota, N., et al., *Disruption of adiponectin causes insulin resistance and neointimal formation*. J Biol Chem, 2002. **277**(29): p. 25863-6.
116. Motoshima, H., et al., *Adiponectin suppresses proliferation and superoxide generation and enhances eNOS activity in endothelial cells treated with oxidized LDL*. Biochem Biophys Res Commun, 2004. **315**(2): p. 264-71.
117. Ouchi, N., et al., *Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway*. Circulation, 2000. **102**(11): p. 1296-301.
118. Campbell, D.J. and J.F. Habener, *Cellular localization of angiotensinogen gene expression in brown adipose tissue and mesentery: quantification of messenger ribonucleic acid abundance using hybridization in situ*. Endocrinology, 1987. **121**(5): p. 1616-26.

119. Engeli, S., R. Negrel, and A.M. Sharma, *Physiology and pathophysiology of the adipose tissue renin-angiotensin system*. Hypertension, 2000. **35**(6): p. 1270-7.
120. Crandall, D.L., et al., *Identification and characterization of angiotensin II receptors in rat epididymal adipocyte membranes*. Metabolism, 1993. **42**(4): p. 511-5.
121. Crandall, D.L., et al., *Distribution of angiotensin II receptors in rat and human adipocytes*. J Lipid Res, 1994. **35**(8): p. 1378-85.
122. Darimont, C., et al., *Differentiation of preadipose cells: paracrine role of prostacyclin upon stimulation of adipose cells by angiotensin-II*. Endocrinology, 1994. **135**(5): p. 2030-6.
123. Jones, B.H., M.K. Standridge, and N. Moustaid, *Angiotensin II increases lipogenesis in 3T3-L1 and human adipose cells*. Endocrinology, 1997. **138**(4): p. 1512-9.
124. Sambrook, J., E.F. Fritsch, and T. Maniatis, *Molecular Cloning*. Cold Spring Harbor Lab Press, 1989.
125. Tamori, Y., et al., *Role of peroxisome proliferator-activated receptor-gamma in maintenance of the characteristics of mature 3T3-L1 adipocytes*. Diabetes, 2002. **51**(7): p. 2045-55.
126. Lindl, T. and J. Bauer, *Zell- und Gewebekultur*. Gustav Fischer Verlag, Stuttgart, 1987. **2. Aufl.**
127. Frost, S.C. and M.D. Lane, *Evidence for the involvement of vicinal sulphydryl groups in insulin-activated hexose transport by 3T3-L1 adipocytes*. J Biol Chem, 1985. **260**(5): p. 2646-52.
128. Chomczynski, P. and N. Sacchi, *Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction*. Anal Biochem, 1987. **162**(1): p. 156-9.
129. Chirgwin, J.M., et al., *Isolation of biologically active ribonucleic acid from sources enriched in ribonuclease*. Biochemistry, 1979. **18**(24): p. 5294-9.
130. Bradford, M.M., *A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding*. Anal Biochem, 1976. **72**: p. 248-54.
131. Laemmli, U.K., *Cleavage of structural proteins during the assembly of the head of bacteriophage T4*. Nature, 1970. **227**(5259): p. 680-5.

132. Nishina, T., et al., *Initial effects of the left ventricular repair by plication may not last long in a rat ischemic cardiomyopathy model.* Circulation, 2001. **104**(12 Suppl 1): p. I241-5.
133. Zimmer, H.G., et al., *Right heart catheterization in rats with pulmonary hypertension and right ventricular hypertrophy.* Basic Res Cardiol, 1988. **83**(1): p. 48-57.
134. Hsu, S.M., L. Raine, and H. Fanger, *The use of antiavidin antibody and avidin-biotin-peroxidase complex in immunoperoxidase technics.* Am J Clin Pathol, 1981. **75**(6): p. 816-21.
135. Hsu, S.M. and L. Raine, *Protein A, avidin, and biotin in immunohistochemistry.* J Histochem Cytochem, 1981. **29**(11): p. 1349-53.
136. Ntambi, J.M. and K. Young-Cheul, *Adipocyte differentiation and gene expression.* J Nutr, 2000. **130**(12): p. 3122S-3126S.
137. Green, H. and O. Kehinde, *An established preadipose cell line and its differentiation in culture. II. Factors affecting the adipose conversion.* Cell, 1975. **5**(1): p. 19-27.
138. Green, H. and M. Meuth, *An established pre-adipose cell line and its differentiation in culture.* Cell, 1974. **3**(2): p. 127-33.
139. Novikoff, A.B., et al., *Organelle relationships in cultured 3T3-L1 preadipocytes.* J Cell Biol, 1980. **87**(1): p. 180-96.
140. Clasen, R., et al., *The angiotensin type 1 receptor blocker Irbesartan induces Adiponectin expression via PPARgamma activation.* Circulation, 2004. **110**(Suppl. No.17): p. III-835.
141. Combs, T.P., et al., *Induction of adipocyte complement-related protein of 30 kilodaltons by PPARgamma agonists: a potential mechanism of insulin sensitization.* Endocrinology, 2002. **143**(3): p. 998-1007.
142. Lee, D.H. and A.L. Goldberg, *Proteasome inhibitors: valuable new tools for cell biologists.* Trends Cell Biol, 1998. **8**(10): p. 397-403.
143. Rock, K.L., et al., *Inhibitors of the proteasome block the degradation of most cell proteins and the generation of peptides presented on MHC class I molecules.* Cell, 1994. **78**(5): p. 761-71.
144. Dick, L.R., et al., *Mechanistic studies on the inactivation of the proteasome by lactacystin: a central role for clasto-lactacystin beta-lactone.* J Biol Chem, 1996. **271**(13): p. 7273-6.

145. Lowe, J., et al., *Crystal structure of the 20S proteasome from the archaeon T. acidophilum at 3.4 Å resolution*. Science, 1995. **268**(5210): p. 533-9.
146. Omura, S., et al., *Structure of lactacystin, a new microbial metabolite which induces differentiation of neuroblastoma cells*. J Antibiot (Tokyo), 1991. **44**(1): p. 117-8.
147. Fenteany, G., et al., *Inhibition of proteasome activities and subunit-specific amino-terminal threonine modification by lactacystin*. Science, 1995. **268**(5211): p. 726-31.
148. Pickart, C.M. and R.E. Cohen, *Proteasomes and their kin: proteases in the machine age*. Nat Rev Mol Cell Biol, 2004. **5**(3): p. 177-87.
149. Zucker, L.M., *Heredity obesity in the rat associated with hyperlipemia*. Ann N Y Acad Sci, 1965. **131**(1): p. 447-58.
150. Phillips, M.S., et al., *Leptin receptor missense mutation in the fatty Zucker rat*. Nat Genet, 1996. **13**(1): p. 18-9.
151. Ogawa, Y., et al., *Molecular cloning of rat obese cDNA and augmented gene expression in genetically obese Zucker fatty (fa/fa) rats*. J Clin Invest, 1995. **96**(3): p. 1647-52.
152. Takaya, K., et al., *Molecular cloning of rat leptin receptor isoform complementary DNAs--identification of a missense mutation in Zucker fatty (fa/fa) rats*. Biochem Biophys Res Commun, 1996. **225**(1): p. 75-83.
153. Karasik, A. and H. Masakazu, *Use of animal models in the study of diabetes*. Joslinss Diabetes, 1985(Joslin EP et al): p. 317-350.
154. Bjorntop, P., "Portal adipose tissue as a generator of risk factors for cardiovascular disease and diabetes". Arteriosclerosis, 1990. **10**: p. 493-496.
155. Gabriely, I., et al., *Removal of visceral fat prevents insulin resistance and glucose intolerance of aging: an adipokine-mediated process?* Diabetes, 2002. **51**(10): p. 2951-8.
156. Carey, D.G., et al., *Abdominal fat and insulin resistance in normal and overweight women: Direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM*. Diabetes, 1996. **45**(5): p. 633-8.
157. Saye, J.A., et al., *Angiotensinogen gene expression in 3T3-L1 cells*. Am J Physiol, 1989. **256**(2 Pt 1): p. C448-51.

158. Mallow, H. and G. Löffler, *Methylisobutylxanthin increases the angiotensin II production in 3T3-L1 preadipocytes*. International Journal of Obesity, 1997. **21**(Supplement 1): p. S92.
159. Mallow, H., A. Trindl, and G. Loffler, *Production of angiotensin II receptors type one (AT1) and type two (AT2) during the differentiation of 3T3-L1 preadipocytes*. Horm Metab Res, 2000. **32**(11-12): p. 500-3.
160. Student, A.K., R.Y. Hsu, and M.D. Lane, *Induction of fatty acid synthetase synthesis in differentiating 3T3-L1 preadipocytes*. J Biol Chem, 1980. **255**(10): p. 4745-50.
161. Reinecke, K., et al., *Angiotensin II accelerates functional recovery in the rat sciatic nerve in vivo: role of the AT2 receptor and the transcription factor NF-kappaB*. Faseb J, 2003. **17**(14): p. 2094-6.
162. Fasshauer, M., et al., *Hormonal regulation of adiponectin gene expression in 3T3-L1 adipocytes*. Biochem Biophys Res Commun, 2002. **290**(3): p. 1084-9.
163. Schling, P., et al., *Evidence for a local renin angiotensin system in primary cultured human preadipocytes*. Int J Obes Relat Metab Disord, 1999. **23**(4): p. 336-41.
164. Karlsson, C., et al., *Human adipose tissue expresses angiotensinogen and enzymes required for its conversion to angiotensin II*. J Clin Endocrinol Metab, 1998. **83**(11): p. 3925-9.
165. Gohlke, P., C. Pees, and T. Unger, *AT2 receptor stimulation increases aortic cyclic GMP in SHRSP by a kinin-dependent mechanism*. Hypertension, 1998. **31**(1 Pt 2): p. 349-55.
166. van Kats, J.P., et al., *Angiotensin-converting enzyme inhibition and angiotensin II type 1 receptor blockade prevent cardiac remodeling in pigs after myocardial infarction: role of tissue angiotensin II*. Circulation, 2000. **102**(13): p. 1556-63.
167. Varagic, J., D. Susic, and E.D. Frohlich, *Coronary hemodynamic and ventricular responses to angiotensin type 1 receptor inhibition in SHR: interaction with angiotensin type 2 receptors*. Hypertension, 2001. **37**(6): p. 1399-403.
168. Folli, F., et al., *Angiotensin II inhibits insulin signaling in aortic smooth muscle cells at multiple levels. A potential role for serine phosphorylation in insulin/angiotensin II crosstalk*. J Clin Invest, 1997. **100**(9): p. 2158-69.

169. Coimbra, C.C., et al., *Gluconeogenesis activation after intravenous angiotensin II in freely moving rats*. Peptides, 1999. **20**(7): p. 823-7.
170. Whitton, P.D., L.M. Rodrigues, and D.A. Hems, *Stimulation by vasopressin, angiotensin and oxytocin of gluconeogenesis in hepatocyte suspensions*. Biochem J, 1978. **176**(3): p. 893-8.
171. DeWitt, L.M. and J.W. Putney, Jr., *Stimulation of glycogenolysis in hepatocytes by angiotensin II may involve both calcium release and calcium influx*. FEBS Lett, 1983. **160**(1-2): p. 259-63.
172. Hems, D.A., L.M. Rodrigues, and P.D. Whitton, *Glycogen phosphorylase, glucose output and vasoconstriction in the perfused rat liver. Concentration-dependence of actions of adrenaline, vasopressin and angiotensin II*. Biochem J, 1976. **160**(2): p. 367-74.
173. Benson, S.C., et al., *Identification of telmisartan as a unique angiotensin II receptor antagonist with selective PPARgamma-modulating activity*. Hypertension, 2004. **43**(5): p. 993-1002.
174. Yang, W.S., et al., *Synthetic peroxisome proliferator-activated receptor-gamma agonist, rosiglitazone, increases plasma levels of adiponectin in type 2 diabetic patients*. Diabetes Care, 2002. **25**(2): p. 376-80.
175. Desvergne, B. and W. Wahli, *Peroxisome proliferator-activated receptors: nuclear control of metabolism*. Endocr Rev, 1999. **20**(5): p. 649-88.
176. Iwaki, M., et al., *Induction of adiponectin, a fat-derived antidiabetic and antiatherogenic factor, by nuclear receptors*. Diabetes, 2003. **52**(7): p. 1655-63.
177. Das, K., et al., *Chromosomal localization, expression pattern, and promoter analysis of the mouse gene encoding adipocyte-specific secretory protein Acrp30*. Biochem Biophys Res Commun, 2001. **280**(4): p. 1120-9.
178. Schaffler, A., et al., *The human apM-1, an adipocyte-specific gene linked to the family of TNF's and to genes expressed in activated T cells, is mapped to chromosome 1q21.3-q23, a susceptibility locus identified for familial combined hyperlipidaemia (FCH)*. Biochem Biophys Res Commun, 1999. **260**(2): p. 416-25.
179. Glaumann, H., F.J. Ballard, and (eds.), *Lysosomes: Their Role in Protein Breakdown*. Academic Press Invest., 1987. **100**: p. 197203.

180. Goldberg, A.L., *Functions of the proteasome: the lysis at the end of the tunnel*. Science, 1995. **268**(5210): p. 522-3.
181. Ciechanover, A., *The ubiquitin-proteasome proteolytic pathway*. Cell, 1994. **79**(1): p. 13-21.
182. Coux, O., K. Tanaka, and A.L. Goldberg, *Structure and functions of the 20S and 26S proteasomes*. Annu Rev Biochem, 1996. **65**: p. 801-47.
183. Lee, D.H. and A.L. Goldberg, *Selective inhibitors of the proteasome-dependent and vacuolar pathways of protein degradation in Saccharomyces cerevisiae*. J Biol Chem, 1996. **271**(44): p. 27280-4.
184. Myung, J., K.B. Kim, and C.M. Crews, *The ubiquitin-proteasome pathway and proteasome inhibitors*. Med Res Rev, 2001. **21**(4): p. 245-73.
185. Motomura, W., et al., *Growth arrest by troglitazone is mediated by p27kip1 accumulation, which results from dual inhibition of proteasome activity and Skp2 expression in human hepatocellular carcinoma cells*. Int J Cancer, 2004. **108**(1): p. 41-6.
186. Bokkala, S. and S.K. Joseph, *Angiotensin II-induced down-regulation of inositol trisphosphate receptors in WB rat liver epithelial cells. Evidence for involvement of the proteasome pathway*. J Biol Chem, 1997. **272**(19): p. 12454-61.
187. Kenyon, C.J., *Mineralocorticoid-induced hypertension in obese Zucker rats*. J Hypertens, 2002. **20**(11): p. 2151-2.
188. Uphues, I., et al., *Failure of insulin-regulated recruitment of the glucose transporter GLUT4 in cardiac muscle of obese Zucker rats is associated with alterations of small-molecular-mass GTP-binding proteins*. Biochem J, 1995. **311** (Pt 1): p. 161-6.
189. Altomonte, J., et al., *Fat depot-specific expression of adiponectin is impaired in Zucker fatty rats*. Metabolism, 2003. **52**(8): p. 958-63.
190. Weber, M.A., et al., *Blood pressure dependent and independent effects of antihypertensive treatment on clinical events in the VALUE Trial*. Lancet, 2004. **363**(9426): p. 2049-51.
191. Furuhashi, M., et al., *Blockade of the renin-angiotensin system increases adiponectin concentrations in patients with essential hypertension*. Hypertension, 2003. **42**(1): p. 76-81.

192. Motley, E.D., et al., *Insulin-induced Akt activation is inhibited by angiotensin II in the vasculature through protein kinase C-alpha*. Hypertension, 2003. **41**(3 Pt 2): p. 775-80.
193. Krotkiewski, M., et al., *Impact of obesity on metabolism in men and women. Importance of regional adipose tissue distribution*. J Clin Invest, 1983. **72**(3): p. 1150-62.
194. Kisseebah, A.H., et al., *Relation of body fat distribution to metabolic complications of obesity*. J Clin Endocrinol Metab, 1982. **54**(2): p. 254-60.
195. Gillum, R.F., *The association of body fat distribution with hypertension, hypertensive heart disease, coronary heart disease, diabetes and cardiovascular risk factors in men and women aged 18-79 years*. J Chronic Dis, 1987. **40**(5): p. 421-8.
196. Kannel, W.B., et al., *Regional obesity and risk of cardiovascular disease; the Framingham Study*. J Clin Epidemiol, 1991. **44**(2): p. 183-90.
197. Lohn, M., et al., *Periadventitial fat releases a vascular relaxing factor*. Faseb J, 2002. **16**(9): p. 1057-63.
198. Fried, S.K., D.A. Bunkin, and A.S. Greenberg, *Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid*. J Clin Endocrinol Metab, 1998. **83**(3): p. 847-50.
199. Bruun, J.M., et al., *Higher production of IL-8 in visceral vs. subcutaneous adipose tissue. Implication of nonadipose cells in adipose tissue*. Am J Physiol Endocrinol Metab, 2004. **286**(1): p. E8-13.
200. Eriksson, P., et al., *Regional variation in plasminogen activator inhibitor-1 expression in adipose tissue from obese individuals*. Thromb Haemost, 2000. **83**(4): p. 545-8.
201. Yang, W.S., et al., *Adiponectin mRNA levels in the abdominal adipose depots of nondiabetic women*. Int J Obes Relat Metab Disord, 2003. **27**(8): p. 896-900.
202. Fisher, F.M., et al., *Differences in adiponectin protein expression: effect of fat depots and type 2 diabetic status*. Horm Metab Res, 2002. **34**(11-12): p. 650-4.
203. Zhou, Y.T., et al., *Lipotoxic heart disease in obese rats: implications for human obesity*. Proc Natl Acad Sci U S A, 2000. **97**(4): p. 1784-9.

204. Shibata, R., et al., *Adiponectin-mediated modulation of hypertrophic signals in the heart*. Nat Med, 2004. **10**(12): p. 1384-9.