

6. Literaturverzeichnis

1. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med.* 1999;341:709-17.
2. Borghi C, Boschi S, Ambrosioni E, Melandri G, Branzi A, Magnani B. Evidence of a partial escape of renin-angiotensin-aldosterone blockade in patients with acute myocardial infarction treated with ACE inhibitors. *J Clin Pharmacol.* 1993;33:40-5.
3. Swedberg K, Eneroth P, Kjekshus J, Wilhelmsen L. Hormones regulating cardiovascular function in patients with severe congestive heart failure and their relation to mortality. CONSENSUS Trial Study Group. *Circulation.* 1990;82:1730-6.
4. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators. *N Engl J Med.* 1991;325:293-302.
5. Klahr S, Morrissey J. Angiotensin II and gene expression in the kidney. *Am J Kidney Dis.* 1998;31:171-6.
6. Bader M, Peters J, Baltatu O, Muller DN, Luft FC, Ganter D. Tissue renin-angiotensin systems: new insights from experimental animal models in hypertension research. *J Mol Med.* 2001;79:76-102.
7. Dzau VJ, Re R. Tissue angiotensin system in cardiovascular medicine. A paradigm shift? *Circulation.* 1994;89:493-8.
8. Muller DN, Fischli W, Clozel JP, Hilgers KF, Bohlender J, Menard J, Busjahn A, Ganter D, Luft FC. Local angiotensin II generation in the rat heart: role of renin uptake. *Circ Res.* 1998;82:13-20.
9. Pitt B, Reichek N, Willenbrock R, Zannad F, Phillips RA, Roniker B, Kleiman J, Krause S, Burns D, Williams GH. Effects of Eplerenone, enalapril, and Eplerenone/enalapril in patients with essential hypertension and left ventricular hypertrophy: the 4E-left ventricular hypertrophy study. *Circulation.* 2003;108:1831-8.

10. Struthers AD, MacDonald TM. Review of aldosterone- and angiotensin II-induced target organ damage and prevention. *Cardiovasc Res*. 2004;61:663-70.
11. Funder JW, Feldman D, Edelman IS. Specific aldosterone binding in rat kidney and parotid. *J Steroid Biochem*. 1972;3:209-18.
12. Lakkis J, Lu WX, Weir MR. RAAS escape: a real clinical entity that may be important in the progression of cardiovascular and renal disease. *Curr Hypertens Rep*. 2003;5:408-17.
13. Geller DS, Farhi A, Pinkerton N, Fradley M, Moritz M, Spitzer A, Meinke G, Tsai FT, Sigler PB, Lifton RP. Activating mineralocorticoid receptor mutation in hypertension exacerbated by pregnancy. *Science*. 2000;289:119-23.
14. Berger S, Bleich M, Schmid W, Cole TJ, Peters J, Watanabe H, Kriz W, Warth R, Greger R, Schutz G. Mineralocorticoid receptor knockout mice: pathophysiology of Na⁺ metabolism. *Proc Natl Acad Sci U S A*. 1998;95:9424-9.
15. Pratt JH, Peacock M, Henry DP. Effect of recombinant human growth hormone on adreno-cortical function, and on sodium and potassium homeostasis. *Pharmacology*. 1993;47:36-42.
16. Sturtevant FM. Prevention by adrenal-regeneration hypertension by an aldosterone-blocker. *Endocrinology*. 1959;64:299-300.
17. Selye H. Protection by a steroid-spirolactone against certain types of cardiac necroses. *Proc Soc Exp Biol Med*. 1960;104:212-3.
18. de Gasparo M, Joss U, Ramjoue HP, Whitebread SE, Haenni H, Schenkel L, Krahenbuehl C, Biollaz M, Grob J, Schmidlin J, et al. Three new epoxy-spirolactone derivatives: characterization in vivo and in vitro. *J Pharmacol Exp Ther*. 1987;240:650-6.
19. Slight SH, Joseph J, Ganjam VK, Weber KT. Extra-adrenal mineralocorticoids and cardiovascular tissue. *J Mol Cell Cardiol*. 1999;31:1175-84.
20. Mizuno Y, Yasue H, Yoshimura M, Fujii H, Yamamoto N, Nakayama M, Harada E, Sakamoto T, Nakamura S, Ito T, Shimasaki Y, Ogawa H, Saito Y, Nakao K. Effects of perindopril on aldosterone production in the failing human heart. *Am J Cardiol*. 2002;89:1197-200.
21. Tsutamoto T, Wada A, Maeda K, Hayashi M, Tsutsui T, Ohnishi M, Fujii M, Matsumoto T, Yamamoto T, Takayama T, Ishii C. Transcardiac gradient of aldosterone before and after spironolactone in patients with congestive heart failure. *J Cardiovasc Pharmacol*. 2003;41 Suppl 1:S19-22.

- 22.Yoshimura M, Nakamura S, Ito T, Nakayama M, Harada E, Mizuno Y, Sakamoto T, Yamamuro M, Saito Y, Nakao K, Yasue H, Ogawa H. Expression of aldosterone synthase gene in failing human heart: quantitative analysis using modified real-time polymerase chain reaction. *J Clin Endocrinol Metab.* 2002;87:3936-40.
- 23.Tsybouleva N, Zhang L, Chen S, Patel R, Lutucuta S, Nemoto S, DeFreitas G, Entman M, Carabello BA, Roberts R, Marian AJ. Aldosterone, through novel signaling proteins, is a fundamental molecular bridge between the genetic defect and the cardiac phenotype of hypertrophic cardiomyopathy. *Circulation.* 2004;109:1284-91.
- 24.Gomez-Sanchez EP, Ahmad N, Romero DG, Gomez-Sanchez CE. Origin of aldosterone in the rat heart. *Endocrinology.* 2004;145:4796-802.
- 25.Luft FC, Mervaala E, Muller DN, Gross V, Schmidt F, Park JK, Schmitz C, Lippoldt A, Breu V, Dechend R, Dragun D, Schneider W, Ganten D, Haller H. Hypertension-induced end-organ damage : A new transgenic approach to an old problem. *Hypertension.* 1999;33:212-8.
- 26.Mervaala E, Muller DN, Schmidt F, Park JK, Gross V, Bader M, Breu V, Ganten D, Haller H, Luft FC. Blood pressure-independent effects in rats with human renin and angiotensinogen genes. *Hypertension.* 2000;35:587-94.
- 27.Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet.* 1994;344:1383-9.
- 28.Davignon J, Laaksonen R. Low-density lipoprotein-independent effects of statins. *Curr Opin Lipidol.* 1999;10:543-59.
- 29.Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *N Engl J Med.* 2004;351:543-51.
- 30.Dechend R, Fiebeler A, Park JK, Muller DN, Theuer J, Mervaala E, Bieringer M, Gulba D, Dietz R, Luft FC, Haller H. Amelioration of angiotensin II-induced cardiac injury by a 3-hydroxy-3-methylglutaryl coenzyme a reductase inhibitor. *Circulation.* 2001;104:576-81.
- 31.Mervaala E, Muller DN, Park JK, Dechend R, Schmidt F, Fiebeler A, Bieringer M, Breu V, Ganten D, Haller H, Luft FC. Cyclosporin A protects against angiotensin

- II-induced end-organ damage in double transgenic rats harboring human renin and angiotensinogen genes. *Hypertension*. 2000;35:360-6.
32. Muller DN, Heissmeyer V, Dechend R, Hampich F, Park JK, Fiebeler A, Shagdarsuren E, Theuer J, Elger M, Pilz B, Breu V, Schroer K, Ganten D, Dietz R, Haller H, Scheidereit C, Luft FC. Aspirin inhibits NF-kappaB and protects from angiotensin II-induced organ damage. *Faseb J*. 2001;15:1822-4.
33. Muller DN, Mullally A, Dechend R, Park JK, Fiebeler A, Pilz B, Loffler BM, Blum-Kaelin D, Masur S, Dehmlow H, Aebi JD, Haller H, Luft FC. Endothelin-converting enzyme inhibition ameliorates angiotensin II-induced cardiac damage. *Hypertension*. 2002;40:840-6.
34. Theuer J, Shagdarsuren E, Muller DN, Kaergel E, Honeck H, Park JK, Fiebeler A, Dechend R, Haller H, Luft FC, Schunck WH. Inducible NOS inhibition, eicosapentaenoic acid supplementation, and angiotensin II-induced renal damage. *Kidney Int*. 2005;67:248-58.
35. Muller DN, Shagdarsuren E, Park JK, Dechend R, Mervaala E, Hampich F, Fiebeler A, Ju X, Finckenberg P, Theuer J, Viedt C, Kreuzer J, Heidecke H, Haller H, Zenke M, Luft FC. Immunosuppressive treatment protects against angiotensin II-induced renal damage. *Am J Pathol*. 2002;161:1679-93.
36. Anderson S, Rennke HG, Brenner BM. Therapeutic advantage of converting enzyme inhibitors in arresting progressive renal disease associated with systemic hypertension in the rat. *J Clin Invest*. 1986;77:1993-2000.
37. Su EJ, Lombardi DM, Siegal J, Schwartz SM. Angiotensin II induces vascular smooth muscle cell replication independent of blood pressure. *Hypertension*. 1998;31:1331-7.
38. Seshiah PN, Weber DS, Rocic P, Valppu L, Taniyama Y, Griendling KK. Angiotensin II stimulation of NAD(P)H oxidase activity: upstream mediators. *Circ Res*. 2002;91:406-13.
39. Wehling M, Kasmayr J, Theisen K. Rapid effects of mineralocorticoids on sodium-proton exchanger: genomic or nongenomic pathway? *Am J Physiol*. 1991;260:E719-26.
40. Liu SL, Schmuck S, Choraczewski JZ, Gros R, Feldman RD. Aldosterone regulates vascular reactivity: short-term effects mediated by phosphatidylinositol 3-kinase-dependent nitric oxide synthase activation. *Circulation*. 2003;108:2400-6.

- 41.Braun S, Losel R, Wehling M, Boldyreff B. Aldosterone rapidly activates Src kinase in M-1 cells involving the mineralocorticoid receptor and HSP84. *FEBS Lett.* 2004;570:69-72.
- 42.Simoncini T, Hafezi-Moghadam A, Brazil DP, Ley K, Chin WW, Liao JK. Interaction of oestrogen receptor with the regulatory subunit of phosphatidylinositol-3-OH kinase. *Nature*. 2000;407:538-41.
- 43.Xiao F, Puddefoot JR, Barker S, Vinson GP. Mechanism for aldosterone potentiation of angiotensin II-stimulated rat arterial smooth muscle cell proliferation. *Hypertension*. 2004;44:340-5.
- 44.Schiffrin EL, Gutkowska J, Genest J. Effect of angiotensin II and deoxycorticosterone infusion on vascular angiotensin II receptors in rats. *Am J Physiol*. 1984;246:H608-14.
- 45.Callera GE, Tostes R, Paulo S, Schiffrin EL, Touyz RM. Aldosterone increases activation of vascular p38MAP Kinase and NADPH Oxidase via c-src-dependent processes: Role of ETA receptors. *Council for High Blood Pressure Research*. 2004;Abstract.
- 46.Schmidt BM, Oehmer S, Delles C, Bratke R, Schneider MP, Klingbeil A, Fleischmann EH, Schmieder RE. Rapid nongenomic effects of aldosterone on human forearm vasculature. *Hypertension*. 2003;42:156-60.
- 47.Farquharson CA, Struthers AD. Spironolactone increases nitric oxide bioactivity, improves endothelial vasodilator dysfunction, and suppresses vascular angiotensin I/angiotensin II conversion in patients with chronic heart failure. *Circulation*. 2000;101:594-7.
- 48.Li L, Chu Y, Fink GD, Engelhardt JF, Heistad DD, Chen AF. Endothelin-1 stimulates arterial VCAM-1 expression via NADPH oxidase-derived superoxide in mineralocorticoid hypertension. *Hypertension*. 2003;42:997-1003.
- 49.Stockand JD, Spier BJ, Worrell RT, Yue G, Al-Baldawi N, Eaton DC. Regulation of Na(+) reabsorption by the aldosterone-induced small G protein K-Ras2A. *J Biol Chem*. 1999;274:35449-54.
- 50.Staruschenko A, Patel P, Tong Q, Medina JL, Stockand JD. Ras activates the epithelial Na(+) channel through phosphoinositide 3-OH kinase signaling. *J Biol Chem*. 2004;279:37771-8.

51. Ahokas RA, Sun Y, Bhattacharya SK, Gerling IC, Weber KT. Aldosteronism and a proinflammatory vascular phenotype: role of Mg²⁺, Ca²⁺, and H₂O₂ in peripheral blood mononuclear cells. *Circulation*. 2005;111:51-7.
52. O'Bryan JP, Frye RA, Cogswell PC, Neubauer A, Kitch B, Prokop C, Espinosa R, 3rd, Le Beau MM, Earp HS, Liu ET. Axl, a transforming gene isolated from primary human myeloid leukemia cells, encodes a novel receptor tyrosine kinase. *Mol Cell Biol*. 1991;11:5016-31.
53. Yanagita M, Arai H, Ishii K, Nakano T, Ohashi K, Mizuno K, Varnum B, Fukatsu A, Doi T, Kita T. Gas6 regulates mesangial cell proliferation through Axl in experimental glomerulonephritis. *Am J Pathol*. 2001;158:1423-32.
54. Yanagita M, Ishimoto Y, Arai H, Nagai K, Ito T, Nakano T, Salant DJ, Fukatsu A, Doi T, Kita T. Essential role of Gas6 for glomerular injury in nephrotoxic nephritis. *J Clin Invest*. 2002;110:239-46.
55. Melaragno MG, Wuthrich DA, Poppa V, Gill D, Lindner V, Berk BC, Corson MA. Increased expression of Axl tyrosine kinase after vascular injury and regulation by G protein-coupled receptor agonists in rats. *Circ Res*. 1998;83:697-704.
56. Fiebeler A, Park JK, Muller DN, Lindschau C, Mengel M, Merkel S, Banas B, Luft FC, Haller H. Growth arrest specific protein 6/Axl signaling in human inflammatory renal diseases. *Am J Kidney Dis*. 2004;43:286-95.
57. Fitzgibbon WR, Greene EL, Grewal JS, Hutchison FN, Self SE, Latten SY, Ullian ME. Resistance to remnant nephropathy in the Wistar-Furth rat. *J Am Soc Nephrol*. 1999;10:814-21.
58. Rocha R, Stier CT, Jr., Kifor I, Ochoa-Maya MR, Rennke HG, Williams GH, Adler GK. Aldosterone: a mediator of myocardial necrosis and renal arteriopathy. *Endocrinology*. 2000;141:3871-8.
59. de Paula RB, da Silva AA, Hall JE. Aldosterone antagonism attenuates obesity-induced hypertension and glomerular hyperfiltration. *Hypertension*. 2004;43:41-7.
60. Chander PN, Rocha R, Ranaudo J, Singh G, Zuckerman A, Stier CT, Jr. Aldosterone plays a pivotal role in the pathogenesis of thrombotic microangiopathy in SHRSP. *J Am Soc Nephrol*. 2003;14:1990-7.
61. Qin W, Rudolph AE, Bond BR, Rocha R, Blomme EA, Goellner JJ, Funder JW, McMahon EG. Transgenic model of aldosterone-driven cardiac hypertrophy and heart failure. *Circ Res*. 2003;93:69-76.

- 62.Hayashi M, Tsutamoto T, Wada A, Tsutsui T, Ishii C, Ohno K, Fujii M, Taniguchi A, Hamatani T, Nozato Y, Kataoka K, Morigami N, Ohnishi M, Kinoshita M, Horie M. Immediate administration of mineralocorticoid receptor antagonist spironolactone prevents post-infarct left ventricular remodeling associated with suppression of a marker of myocardial collagen synthesis in patients with first anterior acute myocardial infarction. *Circulation*. 2003;107:2559-65.
- 63.Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, Bittman R, Hurley S, Kleiman J, Gatlin M. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med*. 2003;348:1309-21.
- 64.Bendtzen K, Hansen PR, Rieneck K. Spironolactone inhibits production of proinflammatory cytokines, including tumour necrosis factor-alpha and interferon-gamma, and has potential in the treatment of arthritis. *Clin Exp Immunol*. 2003;134:151-8.
- 65.Sato A, Hayashi K, Naruse M, Saruta T. Effectiveness of aldosterone blockade in patients with diabetic nephropathy. *Hypertension*. 2003;41:64-8.
- 66.Naruse M, Tanabe A, Sato A, Takagi S, Tsuchiya K, Imaki T, Takano K. Aldosterone breakthrough during angiotensin II receptor antagonist therapy in stroke-prone spontaneously hypertensive rats. *Hypertension*. 2002;40:28-33.
- 67.Funder JW. Mineralocorticoid Receptors and Cardiovascular Disease. *Council for High Blood Pressure Research*. 2004;Abstract.
- 68.Michel F, Ambroisine ML, Duriez M, Delcayre C, Levy BI, Silvestre JS. Aldosterone enhances ischemia-induced neovascularization through angiotensin II-dependent pathway. *Circulation*. 2004;109:1933-7.
- 69.Beggah AT, Escoubet B, Puttini S, Cailmail S, Delage V, Ouvrard-Pascaud A, Bocchi B, Peuchmaur M, Delcayre C, Farman N, Jaisser F. Reversible cardiac fibrosis and heart failure induced by conditional expression of an antisense mRNA of the mineralocorticoid receptor in cardiomyocytes. *Proc Natl Acad Sci U S A*. 2002;99:7160-5.
- 70.Rubera I, Loffing J, Palmer LG, Frindt G, Fowler-Jaeger N, Sauter D, Carroll T, McMahon A, Hummler E, Rossier BC. Collecting duct-specific gene inactivation of alphaENaC in the mouse kidney does not impair sodium and potassium balance. *J Clin Invest*. 2003;112:554-65.

71. Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso L, Gomez-Sanchez CE, Veglio F, Young WF, Jr. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. *J Clin Endocrinol Metab*. 2004;89:1045-50.
72. Vasan RS, Evans JC, Larson MG, Wilson PW, Meigs JB, Rifai N, Benjamin EJ, Levy D. Serum aldosterone and the incidence of hypertension in nonhypertensive persons. *N Engl J Med*. 2004;351:33-41.