

6. Literaturverzeichnis

1. Bernard C. An Introduction to the Study of Experimental Medicine, 1865
2. Jelkmann W. Erythropoietin: Structure, control of production, and function. *Physiol. Rev.* 72: 449-489, 1992
3. Bonsdorf E, Jalavisto E. A humoral mechanism in hypoxic erythrocytosis. *Acta. Physiol. Scand.* 16: 150-170, 1948
4. Jacobson LO, Goldwasser E, Fried W, Plzak L. Role of the kidney in erythropiesis. *Nature.* 179: 633-634, 1957
5. Kuratowska Z, Lewartowski B, Michalak E. Studies on the production of erythropoietin by isolated perfused organs. *Blood.* 18: 527-534, 1961
6. Fisher JW, Birdwell BL. The production of an erythropoietic factor by the in situ perfused kidney. *Acta Haematol.* 26: 224-32, 1961
7. Erslev AJ. In vitro production of erythropoietin by kidneys perfused with a serum-free solution. *Blood.* 44 (1): 77-85, 1974
8. Beru N, McDonald J, Lacombe C, Goldwasser E. Expression of the erythropoietin gene. *Mol Cell Biol.* 6: 2571-2575, 1986
9. Bondurant MC, Koury MJ. Anemia induces accumulation of erythropoietin mRNA in the kidney and liver. *Mol Cell Biol.* 675-683, 1986
10. Schuster SJ, Wilson JH, Erslev AJ, Caro J. Physiologic regulation and tissue localization of renal erythropoietin messenger RNA. *Blood.* 70: 316-318, 1987
11. Lin FK, Suggs S, Lin CH et al. Cloning and Expression of the human erythropoietin gene. *Proc. Natl. Acad. Sci. U.S.A.* 82 (22): 7580-7584, 1985
12. Jacobs K, Shoemaker C, Rudersdorf R et al. Isolation and characterization of genomic and cDNA clones of human erythropoietin. *Nature.* 313 (6005): 860-810, 1985
13. Fisher JW. Erythropoietin: Physiology and pharmacology update. *Exp. Biol. Med.* 228 (1): 1-14, 2003
14. Jelkmann W, Hellwig-Burgel T. Biology of erythropoietin. *Adv. Exp. Med. Biol.* 502: 169-187, 2001
15. Fandrey J. Oxygen-dependent and tissue-specific regulation of erythropoietin gene expression. *Am J. Physiol. Regul. Integr. Comp. Physiol.* 286 (6): R977-988, 2004
16. Zanjani ED, Ascensao JL, McGlave PB, Banisadre M, Ash RC. Studies on the liver to kidney switch of erythropoietin production. *J. Clin. Invest.* 67: 1183-1188, 1981

17. Clemons GK, Fitzsimmons SL, Demanincor D. Immunoreactive erythropoietin concentrations in fetal and neonatal rats and the effects of hypoxia. *Blood*. 68: 892-899, 1986
18. Lacombe C, Da Silva JL, Bruneval P et al. Peritubular cells are the site of erythropoietin synthesis in the murine hypoxia kidney. *J. Clin. Invest.* 271: 69-74, 1988
19. Maxwell PH, Osmond MK, Pugh CW et al. Identification of the renal erythropoietin-producing cells using transgenic mice. *Kidney Int.* 44: 1149-1162, 1993
20. Bachmann S, Le Hir M, Eckardt KU. Colocalization of erythropoietin mRNA and ecto-5'-nucleotidase immunoreactivity in peritubulär cells of rat renal cortex indicates that fibroblasts produce erythropoietin. *The Journal of Histochemistry and Cytochemistry*. 41: 335-341, 1993
21. Maxwell PH, Ferguson DJ, Nicholls LG et al. Sites of erythropoietin production. *Kidney Int.* 51: 393-401, 1997
22. Pugh CW, Tan CC, Jones RW, Ratcliffe PJ. Functional analysis of an oxygen-regulated transcriptional enhancer lying 3' to the mouse erythropoietin gene. *Proc. Natl. Acad. Sci. U.S.A.* 88: 10553-10557, 1991
23. Semenza GL, Nejfelt MK, Chi SM, Antonarakis SE. Hypoxia-inducible nuclear factors bind to an enhancer element located 3' to the human erythropoietin gene. *Proc. Natl. Acad. Sci. U.S.A.* 88: 5680-5684, 1991
24. Beck I, Ramirez S, Weinmann R, Caro J. Enhancer element at the 3'-flanking region controls transcriptional response to hypoxia in the human erythropoietin gene. *J. Biol. Chem.* 266: 1230-1237, 1993
25. Wang GL, Semenza GL. Purification and characterization of Hypoxia-inducible Factor 1. *Biochem. Mol. Biol.* 270: 1230-1237, 1995
26. Semenza GL. Regulation of mammalian O₂-Homeostase by hypoxia-inducible factor 1. *Cell Dev Biol.* 15: 551-78, 1999
27. Wang GI, Jiang BH, Rue EA, Semenza GL. Hypoxia-inducible factor 1 is a basic helix-loop-helix-PAS heterodimer regulated by cellular O₂ tension. *Proc. Natl. Acad. Sci. USA*, 92: 5510-5514, 1995
28. Wang GL, Semenza GL. Purification and characterization of hypoxia-inducible factor 1. *J. Biol. Chem.* 270: 1230-1237, 1995

29. Flamme I, Froelich T, von Reutern M, Koppel A, Damat A, Risau W. HRF, a putative basic helix-loop-helix-PAS-domain transkription factor is closely related to hypoxia-inducible factor-1 α and developmentally expressed in blood vessels. *Mech. Dev.*, 63: 51-60, 1997
30. Wiesener MS, Turley H, Allen WE et al. Induction of endothelial PAS domain protein-1 by hypoxia: characterization and comparison with hypoxia-inducible factor-1 α . *Blood* 92: 2260-2268, 1998
31. Jewell UR, Kvietikova I, Scheid A, Bauer C, Wenger RH, Gassmann M. Induction of HIF-1 α in response to hypoxia is instantaneous. *FASEB J.* 15 (7): 1312-1314, 2001
32. Ratcliffe, P.J. From erythropoietin to oxygen: hypoxia-inducible factor hydroxylases and the hypoxia signal pathway. *Blood* 20: 445-450, 2002
33. Salceda S, Caro J. Hypoxia-inducible factor 1 α protein is rapidly degraded by the ubiquitin-proteasome system under normoxic conditions its stabilization by hypoxia depends on redox-induced changes. *JBC*, 272: 22642-22647, 1997
34. Huang LE, Gu J, Schau M, Bunn HF. Regulation of hypoxia-inducible factor 1 α is mediated by an O₂ dependent degradation domain via the ubiquitin-proteasome pathway. *Proc. Natl. Acad. Sci. USA*, 95: 7987-7992, 1998
35. Masson N, Ratcliffe PJ. HIF prolyl and asparaginyl hydroxylases in the biological response to intracellular O₂ levels. *J. Cell. Sci.* 3041-3049, 2003
36. Kaelin Jr, WG. Proline hydroxylation and Gene Expression. *Annu. Rev. Biochem.* 2004
37. Lando D, Peet DJ, Whelan DA, Gorman JJ, Whitelaw ML. Asparagine hydroxylation of the HIF transactivation domain a hypoxic switch. *Science.* 295:858-851, 2002
38. Firth JD, Ebert BL, Pugh CW, Ratcliffe PJ. Oxygen-regulated control elements in the phosphoglycerate kinase 1 and lactat dehydrogenase A genes: similarities with the erythropoietin 3' enhancer. *Proc. Natl. Acad. Sci. USA.* 91: 6496-500, 1994
39. Forsythe JA, Jiang BH, Iyer NV et al. Activation of vascular endothelial growth factor gene transcription by hypoxia-inducible factor 1. *Moll. Cell. Biol.* 16: 4604-13, 1996
40. Semenza GL. Expression of Hypoxia-inducible factor 1: Mechanisms and Consequences. *Biochem. Pharma.* 59: 47-53, 2000
41. Warburg O. *The metabolism of tumors constable and co. Ltd., London, 1930*
42. Zhong H, De Marzo AM, Laughner E et al. Overexpression of Hypoxia-inducible Factor 1 α in Common Human Cancers and their metastases. *Cancer Res.* 59: 5830-5835, 1999

43. Talks KL, Turley H, Gatter KC et al. The expression and distribution of the hypoxia-inducible factors HIF-1 α and HIF-2 α in normal human tissues, cancers, and tumor-associated macrophages. *Am. J. Pathol.* 157: 411-421, 2000
44. Maxwell PH, Dachs GU, Gleadle JM et al. Hypoxia-inducible factor-1 modulates gene expression in solid tumors and influences both angiogenesis and tumor growth. *Proc. Natl. Acad. Sci. U.S.A.* 94: 8104-8109, 1997
45. Ryan HE, Lo J, Johnson RS. HIF-1 α is required for solid tumor formation and embryonic vascularization. *EMBO J.* 17 (11): 3005-3015, 1998
46. Ryan HE, Poloni M, McNulty W et al. Hypoxia-inducible factor-1 α is a positive factor in solid tumor growth. *Cancer res.* 60: 4010-4015, 2000
47. Carmeliet P, Dor Y, Herbert JM et al. Role of HIF-1 α in hypoxia-mediated apoptosis, cell proliferation, and tumor angiogenesis. *Nature.* 394: 435-439, 1998
48. Blouw B, Song H, Tihan T et al. The hypoxic response of tumors is dependent on their microenvironment. *Cancer Cell.* 4 (2): 133-146, 2003
49. Mandriota SJ, Turner KJ, Davies DR et al. HIF activation identifies early lesions in VHL kidneys: evidence for site specific tumor suppressor function in the nephron. *Cancer Cell*; 1: 459-468, 2002
50. Kondo K, Klcó J, Nakamura E, Lechpammer M, Kaelin WGJr. Inhibition of HIF is necessary for tumor suppression by the von Hippel-Lindau protein. *Cancer Cell*; 1: 237-246, 2002
51. Maranchie JK, Vasselli JR, Riss J, Bonifacino JS, Lineham WM, Klausner RD. The contribution of VHL substrate binding and HIF-1 α to the phenotype of VHL loss in renal cell carcinoma. *Cancer Cell*; 1: 247-255, 2002
52. Seizinger BR, Rouleau GA, Ozelius LJ et al. Von Hippel-Lindau disease maps to the region of chromosome 3 associated with renal cell carcinoma. *Nature.* 332 (6161): 268-9, 1988
53. Latif F, Tory K, Gnarrá J et al. Identification of the von Hippel-Lindau disease tumor suppressor gene. *Science.* 260: 1317-1320, 1993
54. Mircea I, William G, Kaelin JR. The von Hippel-Lindau tumor suppressor protein. *Genet.* 11: 27-34, 2001
55. William G, Kaelin JR. Cancer: Many vessels, faulty gene. *Nature.* 399: 203-204, 1999
56. Kaelin WG, Maher ER. The VHL tumor-suppressor gene paradigm. *Trends Genet.* 14: 423-426, 1998

57. Gnarr JR, Tory K, Weng Y et al. Mutations of the VHL tumor suppressor gene in renal carcinoma. *Nat. Genet.* 7: 85-90, 1994
58. Herman JG, Latif F, Weng Y et al. Silencing of the VHL tumor-suppressor gene by DNA methylation in renal carcinoma. *Proc. Natl. Acad. Sci. U.S.A.* 91: 9700-9704, 1994
59. Maxwell PH, Wiesener MS, Chang GW et al. The tumor suppressor protein VHL targets hypoxia-inducible factors for oxygen-dependent proteolysis. *Nature.* 399: 271-275, 1999
60. Wiesener MS, Munchenhagen PM, Berger I et al.. Constitutive activation of hypoxia-inducible genes related to overexpression of HIF-1 alpha in clear cell renal carcinomas. *Cancer Res.* 61: 5215-5222, 2001
61. Turner KJ, Moore JW, Jones A et al. Expression of hypoxia-inducible factors in human renal cancer: relationship to angiogenesis and to the von Hippel-Lindau gene mutation. *Cancer Res.* 62: 2957-2961, 2002
62. Kosary CL, Mc Laughlin JK. Kidney and renal pelvis. National Cancer Institute. 93-2789, 1993
63. Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. *N Engl J Med.* 335: 865-873, 1996
64. Vogelzang NJ, Stadler WM. Kidney cancer. *Lancet.* 352: 1691-1696, 1998
65. Mc Credie M, Pommer W, Mc Laughlin JK et al. International renal-cell cancer study.II. Analgesics. *Int J Cancer.* 60: 345-9, 1995
66. Wolk A, Gridley G, Niwa S et al. International renal-cell cancer study.VII. Role of diet. *Int J Cancer.* 65: 67-73, 1996
67. Yu MC, Mack TM, Hanisch R, Cicioni C, Henderson BE. Cigarette smoking, obesity, diuretic use, and coffee consumption as risk factors for renal cell carcinoma. *J Natl Cancer inst.* 77: 351-6, 1986
68. Kovacs G, Akhtar M, Beckwith BJ et al. The Heidelberg Classification of renal cell tumours. *J of Pathol.* 183: 131-133. 1997
69. van den Berg E, van der Hout AH, Oosterhuis JW et al. Cytogenetic analysis of epithelial renal-cell tumors: relationship with a new histopathological classification. *Int J Cancer.* 55: 223-7, 1993
70. Bander NH, Finstad CL, Cordon-Cardo C et al. Analysis of a mouse monoclonal antibody that reacts with a specific region of the human proximal tubule and subsets of renal cell carcinomas. *Cancer Res.* 49: 6774-80, 1989

71. Prchal JT. Pathogenetic mechanisms of polycythemia vera and congenital polycythemic disorders. *Semin. Hematol.* 38: 10-20, 2001
72. Ang SO, Chen H, Hirota K et al. Disruption of oxygen homeostasis underlies congenital Chuvash polycythemia. *Nat. Genet.* 32: 614-621, 2002
73. Pastore YD, Jelinek J, Ang S et al. Mutations in the VHL Gene in Sporadic Apparently Congenital Polycythemia. *Blood.* 101: 1591-1595, 2003
74. Noguchi Y, Goto T, Yufu Y et al. Gene expression of erythropoietin in renal cell carcinoma. *Intern. Med.* 38: 991-994, 1999
75. Katsuoka Y, McGonigle R, Rege AB, Beckam B, Fisher JW. Erythropoietin production in human renal carcinoma cells passaged in nude mice and in tissue culture. *Gann.* 74: 534-41, 1983
76. Okabe T, Urabe A, Kato T, Chiba S, Takaku F. Production of erythropoietin-like activity by human renal and hepatic carcinomas in cell culture. *Cancer.* 55: 1918-23, 1985
77. Shouval D, Anton M, Galun E, Sherwood JB. Erythropoietin-induced polycythemia in athymic mice following transplantation of a human renal carcinoma cell line. *Cancer Res.* 48: 3430-4, 1988
78. Thoenes W, Störkel S, Rumpelt HJ. Histopathology and classification of renal cell tumors (adenomas, oncocytomas and carcinomas). *Pathol. Res. Pract.* 181: 125-143, 1986
79. Sobin LH, Fleming ID. TMN Classification of Malignant Tumors, fifth edition (1997). Union Internationale Contre le Cancer and the American Joint Committee on Cancer. *Cancer.* 80: 1803-1804, 1997
80. Janout V, Janoutova G. Epidemiology and risk factors of kidney cancer. *Biomed. Pap. Med. Fac.* 148: 95-1001, 2004
81. Wykoff CC, Beasley NJ, Watson PH et al. Hypoxia-inducible expression of tumor-associated carbonic anhydrases. *Cancer Res.* 60: 7075-83, 2000
82. Da Silva JL, Lacombe C, Bruneval P et al. Tumor cells are the site of erythropoietin synthesis in human renal cancers associated with polycythemia. *Blood.* 75: 577-82, 1990
83. Wiesener MS, Seyfarth M, Warnecke C et al. Paraneoplastic erythrocytosis with an inactivating point mutation of the von Hippel-Lindau gene in a renal cell carcinoma. *Blood.* 99: 35-62-5, 2002
84. Kaelin WJ. The von Hippel-Lindau tumor suppressor gene and kidney cancer. *Clin. Cancer Res.* 10: 6290S-5S, 2004

85. Randi ML, Murgia A, Putti MC et al. Low frequency of VHL gene mutations in young individuals with polycythemia and high serum erythropoietin. *Haematologica*. 90: 689-91, 2005
86. Cario H, Goerttler PS, Steimle C, Levine RL, Pahl HL. The JAK2V617F mutation is acquired secondary to the predisposing alteration in familial polycythaemia vera. *Br. J. Haematol*. 130: 800-1, 2005
87. Stebbins CE, Kaelin WJ, Pavletich NP. Structure of the VHL-ElonginC-ElonginB complex: implications for VHL tumor suppressor function. *Science*. 284: 455-61, 1999
88. Sekido Y, Bader S, Latif F et al. Molecular analysis of the von Hippel-Lindau disease tumor suppressor gene in human lung cancer cell lines. *Oncogene*. 9:1599-604, 1994
89. Kuwai T, Kitadai Y, Tanaka S, Hiyama T, Tanimoto K, Chayama K. Mutation of the von Hippel-Lindau (VHL) gene in human colorectal carcinoma: association with cytoplasmic accumulation of hypoxia-inducible factor (HIF)-1 alpha). *Cancer Sci*. 95: 149-53, 2004
90. Cheng TI, Tsou MH, Yang PS, Sung SM, Chuang VP, Sung JL. Dermatomyositis and erythrocytosis associated with hepatocellular carcinoma. *J. Gastroenterol. Hepatol*. 17: 1239-1240, 2002
91. Wang LY, Shih LY, Chen SH, Liu HC, Chai IJ, Liang DC. Neuroblastoma with expression of erythropoietin resulting in erythrocytosis. *J. Pediatr. Hematol. Oncol*. 25: 649-650, 2003
92. Matsuo M, Koga S, Kanetake H et al. EPO-producing gastric carcinoma in a hemodialysis patient. *Am J. Kidney Dis*. 42: E3-4, 2003
93. Kaito K, Otsubo H, Usui N, Kobayashi M. Secondary polythemia as a paraneoplastic syndrome of testicular seminoma. *Ann. Hematol*. 83: 55-57, 2004
94. Dagnon K, Pacary E, Commo F, Antoine M, Bernaudin JF, Callard P. Expression of erythropoietin and erythropoietin receptor in non-small cell lung carcinomas. *Clin. Cancer Res*. 11: 993-9, 2005
95. Vogel TW, Brouwers FM, Lubensky IA et al. Differential expression of erythropoietin and its receptor in von hippel-lindau-associated and multiple endocrine neoplasia type 2-associated pheochromocytomas. *J. Clin. Endocrinol. Metab*. 90: 3747-51, 2005
96. Westenfelder C, Baranowski RL. Erythropoietin stimulates proliferation of human renal carcinoma cells. *Kidney Int*. 58: 647-57, 2000

97. Rosenberger C, Mandriota S, Juergensen JS et al. Expression of hypoxia-inducible factor-1alpha and -2alpha in hypoxic and ischemic rat kidneys. *J. Am. Soc. Nephrol.* 13: 1721-1732, 2002
98. Warnecke C, Zaborowska Z, Kurreck J, Erdmann VA, Frei U, Wiesener MS, Eckardt KU. Differentiating the functional role of hypoxia-inducible factor (HIF)-1alpha and -2alpha (EPAS-1) by the use of RNA interference: erythropoietin is a HIF-2alpha target gene in Hep3B and Kelly cells. *Faseb J.* 18: 1462-1464, 2004
99. Scortegagna M, Ding K, Zhang Q et al. HIF-2alpha regulates murine hematopoietic development in an erythropoietin-dependent manner. *Blood.* 105: 313-3140, 2005
100. Maynard MA, Ohh M. Von Hippel-Lindau tumor suppressor protein and hypoxia-inducible factor in kidney cancer. *Am J. Nephrol.* 24:1-13, 2004
101. Hagiwara M, Chen IL, McGonigle R, Beckmann B, Kasten FH, Fisher JW. Erythropoietin producing in a primary culture of human renal cell carcinoma maintained in nude mice. *Blood.* 63: 828-35, 1984
102. Toyama K, Fujiyama N, Suzuki H, Chen TP, Tamaoki N, Ueyama Y. Erythropoietin levels in course of a patient with erythropoietin-producing renal cell carcinoma and transplantation of this tumor in nude mice. *Blood.* 54: 245-53, 1979
103. Means RTJr, Krantz SB. Progress in understanding the pathogenesis of the anemia of chronic disease. *Blood.* 80: 1639-47, 1992;
104. Faquin WC, Schneider TJ, Goldberg MA. Effect of inflammatory cytokines on hypoxia-induced erythropoietin production. *Blood.* 79: 1987-94, 1992;
105. Sadoff L. Erythropoietin and cancer. *JAMA.* 293: 1858-9, 2005