

6. Literaturverzeichnis

1. Bertz J, Hentschel S, Hundsdörfer G, Kaatsch P, Katalinic A, Lehnert M Schön D, Stegmaier C, Ziegler H. Krebs in Deutschland. 4. überarbeitete, aktualisierte Ausgabe. Arbeitsgemeinschaft Bevölkerungsbezogener Krebsregister in Deutschland, Saarbrücken. 2004.
2. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-30.
3. The Research Group for Population-based Cancer Registration in Japan. Cancer incidence and incidence rates in Japan in 1997: estimates based on data from 12 population-based cancer registries. Jpn J Clin Oncol 2002;32:318–22.
4. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thurlimann B, Senn HJ. Meeting highlights: updated international expert consensus on the primary therapy of early breast cancer. J Clin Oncol 2003;21:3357–65.
5. Edmondson RJ, Monaghan JM. The epidemiology of ovarian cancer. Int J Gynecol Cancer 2001;11:423-29.
6. Cooperberg MR, Moul JW, Carroll PR. The changing face of prostate cancer. J Clin Oncol 2005;23:8146-51.
7. Chau I, Chan S, Cunningham D. Overview of preoperative and postoperative therapy for colorectal cancer: the European and United States perspectives. Clin Colorectal Cancer 2003;3:19-33.
8. Vanhoefer U. Molecular mechanisms and targeting of colorectal cancer. Semin Oncol 2005;32 Suppl 8:7-10.
9. Alberts SR, Cervantes A, van de Velde CJ. Gastric cancer: epidemiology, pathology and treatment. Ann Oncol. 2003;14 Suppl 2:ii31-6.

10. Haller DG: New perspectives in the management of pancreas cancer. *Semin Oncol* 2003;30:3-10.
11. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell* 2000;100:57-70.
12. Bell R, Verma S, Untch M, Cameron D, Smith I. Maximizing clinical benefit with trastuzumab. *Semin Oncol* 2004;31 Suppl 10:35-44.
13. Peggs K. Imatinib mesylate--gold standards and silver linings. *Clin Exp Med* 2004;4:1-9.
14. van der Zwan SM, DeMatteo RP. Gastrointestinal stromal tumor: 5 years later. *Cancer* 2005;104:1781-8.
15. Silvestri GA, Rivera MP. Targeted therapy for the treatment of advanced non-small cell lung cancer: a review of the epidermal growth factor receptor antagonists. *Chest*. 2005;128:3975-84.
16. Harari PM. Epidermal growth factor receptor inhibition strategies in oncology. *Endocr Relat Cancer* 2004;11:689-708.
17. Sunkel CE, Glover DM. Polo, a mitotic mutant of *Drosophila* displaying abnormal spindle poles. *J Cell Sci* 1988;89:25-38.
18. Llamazares S, Moreira A, Tavares A, Girdham C, Spruce BA, Gonzalez C, Karess RE, Glover DM, Sunkel CE. polo encodes a protein kinase homolog required for mitosis in *Drosophila*. *Genes Dev* 1991;5:2153-65.
19. Kitada K, Johnson AL, Johnston LH, Sugino A. A multicopy suppressor gene of the *Saccharomyces cerevisiae* G1 cell cycle mutant gene dbf4 encodes a protein kinase and is identified as CDC5. *Mol Cell Biol* 1993;13:4445-57.
20. Nigg EA. Polo-like kinases: positive regulators of cell division from start to finish. *Curr Opin Cell Biol* 1998;10:776-83.

21. Hamanaka R, Maloid S, Smith MR, O'Connell CD, Longo DL, Ferris DK. Cloning and characterization of human and murine homologues of the *Drosophila* polo serine-threonine kinase. *Cell Growth Differ* 1994;5:249-57.
22. Simmons DL, Neel BG, Stevens R, Evett G, Erikson RL. Identification of an early-growth-response gene encoding a novel putative protein kinase. *Mol Cell Biol* 1992;12:4164-9.
23. Clay FJ, McEwen SJ, Bertoncello I, Wilks AF, Dunn AR. Identification and cloning of a protein kinase-encoding mouse gene, Plk, related to the polo gene of *Drosophila*. *Proc Natl Acad Sci USA* 1993;90:4882-6.
24. Lake RJ, Jelinek WR. Cell cycle- and terminal differentiation-associated regulation of the mouse mRNA encoding a conserved mitotic protein kinase. *Mol Cell Biol* 1993;13:7793-801.
25. Golsteyn RM, Schultz SJ, Bartek J, Ziemiczki A, Ried T, Nigg EA. Cell cycle analysis and chromosomal localization of human Plk1, a putative homologue of the mitotic kinases *Drosophila* polo and *Saccharomyces cerevisiae* Cdc5. *J Cell Sci* 1994;107:1509-17.
26. Holtrich U, Wolf G, Brauninger A, Karn T, Bohme B, Rubsam-Waigmann H, Strebhardt K. Induction and down-regulation of PLK, a human serine/threonine kinase expressed in proliferating cells and tumors. *Proc Natl Acad Sci USA* 1994;91:1736-40.
27. Holtrich U, Wolf G, Yuan J, Bereiter-Hahn J, Karn T, Weiler M, Kauselmann G, Rehli M, Andreesen R, Kaufmann M, Kuhl D, Strebhardt K. Adhesion induced expression of the serine/threonine kinase Fnk in human macrophages. *Oncogene* 2000;19:4832-9.
28. Li B, Ouyang B, Pan H, Reissmann PT, Slamon DJ, Arceci R, Lu L, Dai W. Prk, a cytokine-inducible human protein serine/threonine kinase whose expression appears to be down-regulated in lung carcinomas. *J Biol Chem* 1996;271:19402-8.
29. Lee KS, Grenfell TZ, Yarm FR, Erikson RL. Mutation of the polo-box disrupts localization and mitotic functions of the mammalian polo kinase Plk. *Proc Natl Acad Sci USA* 1998;95:9301-6.

30. Fode C, Motro B, Yousefi S, Heffernan M, Dennis JW. Sak, a murine protein-serine/threonine kinase that is related to the Drosophila polo kinase and involved in cell proliferation. *Proc Natl Acad Sci USA* 1994;91:6388-92.
31. Hudson JW, Chen L-Y, Fode C, Binkert C, Dennis J. Sak kinase gene structure and transcriptional regulation. *Gene* 2000;241:65–73.
32. Manning G, Whyte DB, Martinez R, Hunter T, Sudarsanam S. The protein kinase complement of the human genome. *Science* 2002;298:1912-34.
33. Barr FA, Sillje HH, Nigg EA. Polo-like kinases and the orchestration of cell division. *Nat Rev Mol Cell Biol* 2004;5:429-40.
34. van Vugt MA, Medema RH. Getting in and out of mitosis with Polo-like kinase-1. *Oncogene* 2005;24:2844-59.
35. Xie S, Xie B, Lee MY, Dai W. Regulation of cell cycle checkpoints by polo-like kinases. *Oncogene* 2005;24:277-86.
36. Abrieu A, Brassac T, Galas S, Fisher D, Labbe JC, Doree M. The Polo-like kinase Plx1 is a component of the MPF amplification loop at the G2/M-phase transition of the cell cycle in Xenopus eggs. *J Cell Sci* 1998;111:1751-7.
37. Qian YW, Erikson E, Li C, Maller JL. Activated polo-like kinase Plx1 is required at multiple points during mitosis in Xenopus laevis. *Mol Cell Biol* 1998;18:4262-71.
38. Roshak AK, Capper EA, Imburgia C, Fornwald J, Scott G, Marshall LA. The human polo-like kinase, PLK, regulates cdc2/cyclin B through phosphorylation and activation of the cdc25C phosphatase. *Cell Signal* 2000;12:405-11.
39. Toyoshima-Morimoto F, Taniguchi E, Nishida E. Plk1 promotes nuclear translocation of human Cdc25C during prophase. *EMBO Rep* 2002;3:341-48.

40. Yuan J, Eckerdt F, Bereiter-Hahn J, Kurunci-Csacsko E, Kaufmann M, Strebhardt K. Cooperative phosphorylation including the activity of polo-like kinase 1 regulates the subcellular localization of cyclin B1. *Oncogene* 2002;21:8282-92.
41. Lane HA, Nigg EA. Antibody microinjection reveals an essential role for human polo-like kinase 1 (Plk1) in the functional maturation of mitotic centrosomes. *J Cell Biol* 1996;135:1701-13.
42. de Carcer G, do Carmo Avides M, Lallena MJ, Glover DM, Gonzalez C. Requirement of Hsp90 for centrosomal function reflects its regulation of Polo kinase stability. *EMBO J* 2001;20:2878-84.
43. do Carmo Avides M, Tavares A, Glover DM. Polo kinase and Asp are needed to promote the mitotic organizing activity of centrosomes. *Nat Cell Biol* 2001;3:421-4.
44. Ohkura H, Hagan IM, Glover DM. The conserved *Schizosaccharomyces pombe* kinase plo1, required to form a bipolar spindle, the actin ring, and septum, can drive septum formation in G1 and G2 cells. *Genes Dev* 1995;9:1059-73.
45. Sumara I, Vorlaufer E, Stukenberg PT, Kelm O, Redemann N, Nigg EA, Peters JM. The dissociation of cohesin from chromosomes in prophase is regulated by Polo-like kinase. *Mol Cell* 2002;9:515-25.
46. Golan A, Yudkovsky Y, Hershko A. The cyclin-ubiquitin ligase activity of cyclosome/APC is jointly activated by protein kinases Cdk1-cyclin B and Plk. *J Biol Chem* 2002;277:15552-7.
47. Descombes P, Nigg EA. The polo-like kinase Plx1 is required for M phase exit and destruction of mitotic regulators in Xenopus egg extracts. *EMBO J* 1998;17:1328-35.
48. Zhou T, Aumais JP, Liu X, Yu-Lee LY, Erikson RL. A role for Plk1 phosphorylation of NudC in cytokinesis. *Dev Cell* 2003;5:127-38.
49. Carmena M, Riparbelli MG, Minestrini G, Tavares AM, Adams R, Callaini G, Glover DM. Drosophila polo kinase is required for cytokinesis. *J Cell Biol* 1998;143:659-71.

50. Mundt KE, Golsteyn RM, Lane HA, Nigg EA. On the regulation and function of human polo-like kinase 1 (PLK1): effects of overexpression on cell cycle progression. *Biochem Biophys Res Commun* 1997;239:377-85.
51. Smits VA, Klompmaker R, Arnaud L, Rijken G, Nigg EA, Medema RH. Polo-like kinase-1 is a target of the DNA damage checkpoint. *Nat Cell Biol* 2000;2:672-6.
52. Sanchez Y, Bachant J, Wang H, Hu F, Liu D, Tetzlaff M, Elledge SJ. Control of the DNA damage checkpoint by chk1 and rad53 protein kinases through distinct mechanisms. *Science* 1999;286:1166-71.
53. Ouyang B, Pan H, Lu L, Li J, Stambrook P, Li B, Dai W. Human Prk is a conserved protein serine/threonine kinase involved in regulating M phase functions. *J Biol Chem* 1997;272:28646-51.
54. Chase D, Feng Y, Hanshew B, Winkles JA, Longo DL, Ferris DK. Expression and phosphorylation of fibroblast-growth-factor-inducible kinase (Fnk) during cell-cycle progression. *Biochem J* 1998;333:655-60.
55. Bahassi el M, Conn CW, Myer DL, Hennigan RF, McGowan CH, Sanchez Y, Stambrook PJ. Mammalian Polo-like kinase 3 (Plk3) is a multifunctional protein involved in stress response pathways. *Oncogene* 2002;21:6633-40.
56. Glover DM, Hagan IM, Tavares AA. Polo-like kinases: a team that plays throughout mitosis. *Genes Dev* 1998;12:3777-87.
57. Dai W, Cogswell JP. Polo-like kinases and the microtubule organization center: targets for cancer therapies. *Prog Cell Cycle Res* 2003;5:327-34.
58. Wang Q, Xie S, Chen J, Fukasawa K, Naik U, Traganos F, Darzynkiewicz Z, Jhanwar-Uniyal M, Dai W. Cell cycle arrest and apoptosis induced by human Polo-like kinase 3 is mediated through perturbation of microtubule integrity. *Mol Cell Biol* 2002;22:3450-9.

59. Bahassi el M, Hennigan RF, Myer DL, Stambrook PJ. Cdc25C phosphorylation on serine 191 by Plk3 promotes its nuclear translocation. *Oncogene* 2004;23:2658-63.
60. Ouyang B, Li W, Pan H, Meadows J, Hoffmann I, Dai W. The physical association and phosphorylation of Cdc25C protein phosphatase by Prk. *Oncogene* 1999;18:6029-36.
61. Takai N, Hamanaka R, Yoshimatsu J, Miyakawa I. Polo-like kinases (Plks) and cancer. *Oncogene* 2005;24:287-91.
62. Eckerdt F, Yuan J, Strebhardt K. Polo-like kinases and oncogenesis. *Oncogene* 2005;24:267-76.
63. Donaldson MM, Tavares AA, Ohkura H, Deak P, Glover DM. Metaphase arrest with centromere separation in polo mutants of *Drosophila*. *J Cell Biol* 2001;153:663-76.
64. Smith MR, Wilson ML, Hamanaka R, Chase D, Kung H, Longo DL, Ferris DK. Malignant transformation of mammalian cells initiated by constitutive expression of the polo-like kinase. *Biochem Biophys Res Commun* 1997;234:397-405.
65. van Vugt MA, van de Weerd BC, Vader G, Janssen H, Calafat J, Klompmaker R, Wolthuis RM, Medema RH. Polo-like kinase-1 is required for bipolar spindle formation but is dispensable for anaphase promoting complex/Cdc20 activation and initiation of cytokinesis. *J Biol Chem* 2004;279:36841-54.
66. Xie S, Wu H, Wang Q, Cogswell JP, Husain I, Conn C, Stambrook P, Jhanwar-Uniyal M, Dai W. Plk3 functionally links DNA damage to cell cycle arrest and apoptosis at least in part via the p53 pathway. *J Biol Chem* 2001;276:43305-12.
67. Ando K, Ozaki T, Yamamoto H, Furuya K, Hosoda M, Hayashi S, Fukuzawa M, Nakagawara A. Polo-like kinase 1 (Plk1) inhibits p53 function by physical interaction and phosphorylation. *J Biol Chem* 2004;279:25549-61.
68. Liu X, Erikson RL. Polo-like kinase (Plk)1 depletion induces apoptosis in cancer cells. *Proc Natl Acad Sci USA* 2003;100:5789-94.

69. Incassati A, Patel D, McCance DJ. Induction of tetraploidy through loss of p53 and upregulation of Plk1 by human papillomavirus type-16 E6. *Oncogene* 2005; [Epub ahead of print]
70. Patel D, Incassati A, Wang N, McCance DJ. Human papillomavirus type 16 E6 and E7 cause polyploidy in human keratinocytes and up-regulation of G2-M-phase proteins. *Cancer Res* 2004;64:1299-306.
71. Lin HR, Ting NS, Qin J, Lee WH. M phase-specific phosphorylation of BRCA2 by Polo-like kinase 1 correlates with the dissociation of the BRCA2-P/CAF complex. *J Biol Chem* 2003;278:35979-87.
72. Lee M, Daniels MJ, Venkitaraman AR. Phosphorylation of BRCA2 by the Polo-like kinase Plk1 is regulated by DNA damage and mitotic progression. *Oncogene* 2004;23:865-72.
73. Tsvetkov L, Xu X, Li J, Stern DF. Polo-like kinase 1 and Chk2 interact and co-localize to centrosomes and the midbody. *J Biol Chem* 2003;278:8468-75.
74. van Vugt MA, Smits VA, Klompmaker R, Medema RH. Inhibition of Polo-like kinase-1 by DNA damage occurs in an ATM- or ATR-dependent fashion. *J Biol Chem* 2001;276:41656-60.
75. Yuan JH, Feng Y, Fisher RH, Maloid S, Longo DL, Ferris DK. Polo-like kinase 1 inactivation following mitotic DNA damaging treatments is independent of ataxia telangiectasia mutated kinase. *Mol Cancer Res* 2004;2:417-26.
76. Gunawardena RW, Siddiqui H, Solomon DA, Mayhew CN, Held J, Angus SP, Knudsen ES. Hierarchical requirement of SWI/SNF in retinoblastoma tumor suppressor-mediated repression of Plk1. *J Biol Chem* 2004;279:29278-85.
77. Cogswell JP, Brown CE, Bisi JE, Neill SD. Dominant-negative polo-like kinase 1 induces mitotic catastrophe independent of cdc25C function. *Cell Growth Differ* 2000;11:615-23.

78. Elez R, Piiper A, Kronenberger B, Kock M, Brendel M, Hermann E, Pliquett U, Neumann E, Zeuzem S. Tumor regression by combination antisense therapy against Plk1 and Bcl-2. *Oncogene* 2003;22:69-80.
79. Spankuch-Schmitt B, Bereiter-Hahn J, Kaufmann M, Strebhardt K. Effect of RNA silencing of polo-like kinase-1 (PLK1) on apoptosis and spindle formation in human cancer cells. *J Natl Cancer Inst* 2002;94:1863-77.
80. Guan R, Tapang P, Leverson JD, Albert D, Giranda VL, Luo Y. Small interfering RNA-mediated Polo-like kinase 1 depletion preferentially reduces the survival of p53-defective, oncogenic transformed cells and inhibits tumor growth in animals. *Cancer Res* 2005;65:2698-704.
81. Nogawa M, Yuasa T, Kimura S, Tanaka M, Kuroda J, Sato K, Yokota A, Segawa H, Toda Y, Kageyama S, Yoshiki T, Okada Y, Maekawa T. Intravesical administration of small interfering RNA targeting PLK-1 successfully prevents the growth of bladder cancer. *J Clin Invest* 2005;115:978-85.
82. Gumireddy K, Reddy MV, Cosenza SC, Boominathan R, Baker SJ, Papathi N, Jiang J, Holland J, Reddy EP. ON01910, a non-ATP-competitive small molecule inhibitor of Plk1, is a potent anticancer agent. *Cancer Cell* 2005;7:275-86.
83. Knosel T, Schluns K, Stein U, Schwabe H, Schlag PM, Dietel M, Petersen I. Chromosomal alterations during lymphatic and liver metastasis formation of colorectal cancer. *Neoplasia* 2004;6:23-8.
84. Wolf G, Elez R, Doermer A, Holtrich U, Ackermann H, Stutte HJ, Altmannsberger HM, Rubsamen-Waigmann H, Strebhardt K. Prognostic significance of polo-like kinase (PLK) expression in non-small cell lung cancer. *Oncogene* 1997;14:543-9.
85. Knecht R, Oberhauser C, Strebhardt K. PLK (polo-like kinase), a new prognostic marker for oropharyngeal carcinomas. *Int J Cancer* 2000;89:535-6.
86. Seeburg DP, Pak D, Sheng M. Polo-like kinases in the nervous system. *Oncogene* 2005;24:292-8.

87. Knecht R, Elez R, Oehler M, Solbach C, von Ilberg C, Strebhardt K. Prognostic significance of polo-like kinase (PLK) expression in squamous cell carcinomas of the head and neck. *Cancer Res* 1999;59:2794-7.
88. Tokumitsu Y, Mori M, Tanaka S, Akazawa K, Nakano S, Niho Y. Prognostic significance of polo-like kinase expression in esophageal carcinoma. *Int J Oncol* 1999;15:687-92.
89. Macmillan JC, Hudson JW, Bull S, Dennis JW, Swallow CJ. Comparative Expression of the Mitotic Regulators SAK and PLK in Colorectal Cancer. *Ann Surg Oncol* 2001;8:729-40.
90. Yamada S, Ohira M, Horie H, Ando K, Takayasu H, Suzuki Y, Sugano S, Hirata T, Goto T, Matsunaga T, Hiyama E, Hayashi Y, Ando H, Suita S, Kaneko M, Sasaki F, Hashizume K, Ohnuma N, Nakagawara A. Expression profiling and differential screening between hepatoblastomas and the corresponding normal livers: identification of high expression of the PLK1 oncogene as a poor-prognostic indicator of hepatoblastomas. *Oncogene* 2004;23:5901-11.
91. Kneisel L, Strebhardt K, Bernd A, Wolter M, Binder A, Kaufmann R. Expression of polo-like kinase (PLK1) in thin melanomas: a novel marker of metastatic disease. *J Cutan Pathol* 2002;29:354-8.
92. Strebhardt K, Kneisel L, Linhart C, Bernd A, Kaufmann R. Prognostic value of pololike kinase expression in melanomas. *JAMA* 2000;283:479-80.
93. Wolf G, Hildenbrand R, Schwar C, Grobholz R, Kaufmann M, Stutte HJ, Strebhardt K, Bleyl U. Polo-like kinase: a novel marker of proliferation: correlation with estrogen-receptor expression in human breast cancer. *Pathol Res Pract* 2000;196:753-9.
94. Takai N, Miyazaki T, Fujisawa K, Nasu K, Hamanaka R, Miyakawa I. Expression of polo-like kinase in ovarian cancer is associated with histological grade and clinical stage. *Cancer Lett* 2001;164:41-9.
95. Takai N, Miyazaki T, Fujisawa K, Nasu K, Hamanaka R, Miyakawa I. Polo-like kinase (PLK) expression in endometrial carcinoma. *Cancer Lett* 2001;169:41-9.

96. Takahashi T, Sano B, Nagata T, Kato H, Sugiyama Y, Kunieda K, Kimura M, Okano Y, Saji S. Polo-like kinase 1 (PLK1) is overexpressed in primary colorectal cancers. *Cancer Sci* 2003;94:148-52.
97. Dietzmann K, Kirches E, von Bossanyi, Jachau K, Mawrin C. Increased human polo-like kinase-1 expression in gliomas. *J Neurooncol* 2001;53:1-11.
98. Ito Y, Miyoshi E, Sasaki N, Kakudo K, Yoshida H, Tomoda C, Uruno T, Takamura Y, Miya A, Kobayashi K, Matsuzuka F, Matsuura N, Kuma K, Miyauchi A. Polo-like kinase 1 overexpression is an early event in the progression of papillary carcinoma. *Br J Cancer* 2004;90:414-8.
99. Ito Y, Nakamura Y, Yoshida H, Tomoda C, Uruno T, Takamura Y, Miya A, Kobayashi K, Matsuzuka F, Kuma K, Kakudo K, Miyauchi A. Polo-like kinase 1 expression in medullary carcinoma of the thyroid: its relationship with clinicopathological features. *Pathobiology* 2005;72:186-90.
100. Dai W, Li Y, Ouyang B, Pan H, Reissmann P, Li J, Wiest J, Stambrook P, Gluckman JL, Noffsinger A, Bejarano P. PRK, a cell cycle gene localized to 8p21, is downregulated in head and neck cancer. *Genes Chromosomes Cancer* 2000;27:332-6.
101. McLeod HL, Murray GI. Tumour markers of prognosis in colorectal cancer. *Br J Cancer* 1999;79:191-203.
102. Tirkkonen M, Tanner M, Karhu R, Kallioniemi A, Isola J, Kallioniemi OP. Molecular cytogenetics of primary breast cancer by CGH. *Genes Chromosomes Cancer* 1998;21:177-84.
103. Tay ST, Leong SH, Yu K, Aggarwal A, Tan SY, Lee CH, Wong K, Visvanathan J, Lim D, Wong WK, Soo KC, Kon OL, Tan P. A combined comparative genomic hybridization and expression microarray analysis of gastric cancer reveals novel molecular subtypes. *Cancer Res*. 2003;63:3309-16.