

7 Literaturverzeichnis

1. Kaatsch P. Jahresbericht des Kinderkrebsregisters 2002, Mainz 2003.
2. Kinderkrebsstiftung. Pressemitteilung: 2004;
http://www.kinderkrebsstiftung.de/presse_art38.html.
3. Creuzig U, Henze G, Bielack S, et al. Krebserkrankungen bei Kindern. Dtsch Arztl 2003; 100:A 842-852.
4. Henze G. Leukämien. In Gutjahr, P.: Krebs bei Kindern und Jugendlichen, 4. Auflage Köln 1999, S. 241-242.
5. Virchow R. Weisses Blut. Froriep's Neue Notizen aus dem Gebiet der Natur- und Heilkunde, 180, 1845. Abgedruckt in: Gesammelte Abhandlungen zur Wissenschaftlichen Medicin von Rudolf Virchow, Frankfurt a. M. 1856.
6. Lafage-Pochitaloff M, Charrin C. [Cytogenetic abnormalities in acute lymphoblastic leukemia]. Pathol Biol (Paris) 2003; 51:329-36.
7. Borkhardt A. Akute lymphoblastische Leukämie (ALL) im Kindesalter. In: Ganten und Ruckpaul (Hrsg.): Molekularmedizinische Grundlagen von hämatologischen Neoplasien, Berlin und Heidelberg 2003, S. 356-362.
8. Lion T, Kovar H. Tumorgenetik. in P. Gutjahr: Krebs bei Kindern und Jugendlichen, 4. Auflage Köln 1999, S. 30-46.
9. Seeger K, Eckert C, Kirschner R, Henze G, Hernaiz-Driever P. Pädiatrische Onkologie. Molekulare Onkologie im Kindesalter. Monatsschr Kinderheilk 2002; 150:924-933.
10. Look AT. Oncogenic transcription factors in the human acute leukemias. Science 1997; 278:1059-64.
11. Borkhardt A. Hämatologische Neoplasien im Kindesalter. Sozialpädiatrie, Kinder- und Jugendheilkunde 2000; 22:6-10.
12. Hoelzer D, Gokbuget N, Ottmann O, et al. Acute lymphoblastic leukemia. Hematology (Am Soc Hematol Educ Program) 2002:162-92.
13. Digweed M, Sperling K. Chromosomeninstabilitätssyndrome. In: Ganten und Ruckpaul (Hrsg.): Molekularmedizinische Grundlagen von hämatologischen Neoplasien, Berlin und Heidelberg 2003, S. 3-20.
14. Hoeijmakers JH. Genome maintenance mechanisms for preventing cancer. Nature 2001; 411:366-74.

15. Grawunder U, Zimmer D, Kulesza P, Lieber MR. Requirement for an interaction of XRCC4 with DNA ligase IV for wild-type V(D)J recombination and DNA double-strand break repair in vivo. *J Biol Chem* 1998; 273:24708-14.
16. van Gent DC, Hoeijmakers JH, Kanaar R. Chromosomal stability and the DNA double-stranded break connection. *Nat Rev Genet* 2001; 2:196-206.
17. Lieber MR, Ma Y, Pannicke U, Schwarz K. Mechanism and regulation of human non-homologous DNA end-joining. *Nat Rev Mol Cell Biol* 2003; 4:712-20.
18. Khanna KK, Jackson SP. DNA double-strand breaks: signaling, repair and the cancer connection. *Nat Genet* 2001; 27:247-54.
19. Digweed M. aus: Kulozik, Hentze, Hagemeyer, Bartram: *Molekulare Medizin*, Berlin, New York 2000, S. 129.
20. Norbury CJ, Hickson ID. Cellular responses to DNA damage. *Annu Rev Pharmacol Toxicol* 2001; 41:367-401.
21. Kolodner RD. Mismatch repair: mechanisms and relationship to cancer susceptibility. *Trends Biochem Sci* 1995; 20:397-401.
22. Dasika GK, Lin SC, Zhao S, Sung P, Tomkinson A, Lee EY. DNA damage-induced cell cycle checkpoints and DNA strand break repair in development and tumorigenesis. *Oncogene* 1999; 18:7883-99.
23. Digweed M. Response to environmental carcinogens in DNA-repair-deficient disorders. *Toxicology* 2003; 193:111-24.
24. Varon R, Vissinga C, Platzer M, et al. Nibrin, a novel DNA double-strand break repair protein, is mutated in Nijmegen breakage syndrome. *Cell* 1998; 93:467-76.
25. Karran P. DNA double strand break repair in mammalian cells. *Curr Opin Genet Dev* 2000; 10:144-50.
26. Takata M, Sasaki MS, Sonoda E, et al. Homologous recombination and non-homologous end-joining pathways of DNA double-strand break repair have overlapping roles in the maintenance of chromosomal integrity in vertebrate cells. *Embo J* 1998; 17:5497-508.
27. Kulozik AE, Hentze MW, Hagemeyer C, Bartram CR. *Molekulare Medizin*, Berlin, New York 2000, S. 102-103.
28. Smith GC, Jackson SP. The DNA-dependent protein kinase. *Genes Dev* 1999; 13:916-34.

29. Martensson S, Hammarsten O. DNA-dependent protein kinase catalytic subunit. Structural requirements for kinase activation by DNA ends. *J Biol Chem* 2002; 277:3020-9.
30. Bradbury JM, Jackson SP. The complex matter of DNA double-strand break detection. *Biochem Soc Trans* 2003; 31:40-4.
31. Christmann M, Tomicic MT, Roos WP, Kaina B. Mechanisms of human DNA repair: an update. *Toxicology* 2003; 193:3-34.
32. Bakkenist CJ, Kastan MB. DNA damage activates ATM through intermolecular autophosphorylation and dimer dissociation. *Nature* 2003; 421:499-506.
33. Banin S, Moyal L, Shieh S, et al. Enhanced phosphorylation of p53 by ATM in response to DNA damage. *Science* 1998; 281:1674-7.
34. Canman CE, Lim DS, Cimprich KA, et al. Activation of the ATM kinase by ionizing radiation and phosphorylation of p53. *Science* 1998; 281:1677-9.
35. Lim DS, Kim ST, Xu B, et al. ATM phosphorylates p95/nbs1 in an S-phase checkpoint pathway. *Nature* 2000; 404:613-7.
36. Wu X, Ranganathan V, Weisman DS, et al. ATM phosphorylation of Nijmegen breakage syndrome protein is required in a DNA damage response. *Nature* 2000; 405:477-82.
37. Zhao S, Weng YC, Yuan SS, et al. Functional link between ataxia-telangiectasia and Nijmegen breakage syndrome gene products. *Nature* 2000; 405:473-7.
38. Stewart ZA, Pietsenpol JA. p53 Signaling and cell cycle checkpoints. *Chem Res Toxicol* 2001; 14:243-63.
39. Helleday T. Pathways for mitotic homologous recombination in mammalian cells. *Mutat Res* 2003; 532:103-15.
40. New JH, Sugiyama T, Zaitseva E, Kowalczykowski SC. Rad52 protein stimulates DNA strand exchange by Rad51 and replication protein A. *Nature* 1998; 391:407-10.
41. van Dyck E, Stasiak AZ, Stasiak A, West SC. Binding of double-strand breaks in DNA by human Rad52 protein. *Nature* 1999; 398:728-31.
42. Kagawa W, Kurumizaka H, Ikawa S, Yokoyama S, Shibata T. Homologous pairing promoted by the human Rad52 protein. *J Biol Chem* 2001; 276:35201-8.
43. Benson FE, Baumann P, West SC. Synergistic actions of Rad51 and Rad52 in recombination and DNA repair. *Nature* 1998; 391:401-4.

44. Baumann P, West SC. Role of the human RAD51 protein in homologous recombination and double-stranded-break repair. *Trends Biochem Sci* 1998; 23:247-51.
45. Henning W, Sturzbecher HW. Homologous recombination and cell cycle checkpoints: Rad51 in tumour progression and therapy resistance. *Toxicology* 2003; 193:91-109.
46. Tan TL, Essers J, Citterio E, et al. Mouse Rad54 affects DNA conformation and DNA-damage-induced Rad51 foci formation. *Curr Biol* 1999; 9:325-8.
47. Yuan SS, Lee SY, Chen G, Song M, Tomlinson GE, Lee EY. BRCA2 is required for ionizing radiation-induced assembly of Rad51 complex in vivo. *Cancer Res* 1999; 59:3547-51.
48. Johnson RD, Jasin M. Sister chromatid gene conversion is a prominent double-strand break repair pathway in mammalian cells. *Embo J* 2000; 19:3398-407.
49. Pastink A, Eeken JC, Lohman PH. Genomic integrity and the repair of double-strand DNA breaks. *Mutat Res* 2001; 480-481:37-50.
50. Jeggo P, O'Neill P. The Greek Goddess, Artemis, reveals the secrets of her cleavage. *DNA Repair (Amst)* 2002; 1:771-7.
51. Wang J, Pluth J, Cooper P, Cowan M, Chen D, Yannone S. Artemis deficiency confers a DNA double-strand break repair defect and artemis phosphorylation status is altered by DNA damage and cell cycle progression. *DNA Repair (Amst)* 2005; 4:556-570.
52. Pastwa E, Blasiak J. Non-homologous DNA end joining. *Acta Biochim Pol* 2003; 50:891-908.
53. Nick McElhinny SA, Snowden CM, McCarville J, Ramsden DA. Ku recruits the XRCC4-ligase IV complex to DNA ends. *Mol Cell Biol* 2000; 20:2996-3003.
54. Mahajan KN, Nick McElhinny SA, Mitchell BS, Ramsden DA. Association of DNA polymerase mu (pol mu) with Ku and ligase IV: role for pol mu in end-joining double-strand break repair. *Mol Cell Biol* 2002; 22:5194-202.
55. Modesti M, Junop MS, Ghirlando R, et al. Tetramerization and DNA ligase IV interaction of the DNA double-strand break repair protein XRCC4 are mutually exclusive. *J Mol Biol* 2003; 334:215-28.
56. van Heemst D, Brugmans L, Verkaik NS, van Gent DC. End-joining of blunt DNA double-strand breaks in mammalian fibroblasts is precise and requires DNA-PK and XRCC4. *DNA Repair (Amst)* 2004; 3:43-50.

57. Wang H, Perrault AR, Takeda Y, Qin W, Iliakis G. Biochemical evidence for Ku-independent backup pathways of NHEJ. *Nucleic Acids Res* 2003; 31:5377-88.
58. Taylor AM, Metcalfe JA, Thick J, Mak YF. Leukemia and lymphoma in ataxia telangiectasia. *Blood* 1996; 87:423-38.
59. Boultonwood J. Ataxia telangiectasia gene mutations in leukaemia and lymphoma. *J Clin Pathol* 2001; 54:512-6.
60. Stewart GS, Maser RS, Stankovic T, et al. The DNA double-strand break repair gene hMRE11 is mutated in individuals with an ataxia-telangiectasia-like disorder. *Cell* 1999; 99:577-87.
61. Digweed M, Reis A, Sperling K. Nijmegen breakage syndrome: consequences of defective DNA double strand break repair. *Bioessays* 1999; 21:649-56.
62. Plowman PN, Bridges BA, Arlett CF, Hinney A, Kingston JE. An instance of clinical radiation morbidity and cellular radiosensitivity, not associated with ataxia-telangiectasia. *Br J Radiol* 1990; 63:624-8.
63. Riballo E, Critchlow SE, Teo SH, et al. Identification of a defect in DNA ligase IV in a radiosensitive leukaemia patient. *Curr Biol* 1999; 9:699-702.
64. Riballo E, Doherty AJ, Dai Y, et al. Cellular and biochemical impact of a mutation in DNA ligase IV conferring clinical radiosensitivity. *J Biol Chem* 2001; 276:31124-32.
65. Human protein: Q8IY66 - Lig4 protein. EMBL Bioinformatic Harvester; <http://harvester.embl.de/harvester/Q8IY/Q8IY66.htm>.
66. Grawunder U, Zimmer D, Lieber MR. DNA ligase IV binds to XRCC4 via a motif located between rather than within its BRCT domains. *Curr Biol* 1998; 8:873-6.
67. O'Driscoll M, Cerosaletti KM, Girard PM, et al. DNA ligase IV mutations identified in patients exhibiting developmental delay and immunodeficiency. *Mol Cell* 2001; 8:1175-85.
68. Timson DJ, Singleton MR, Wigley DB. DNA ligases in the repair and replication of DNA. *Mutat Res* 2000; 460:301-18.
69. Martin IV, MacNeill SA. ATP-dependent DNA ligases. *Genome Biol* 2002; 3:REVIEWS3005.
70. Sanger. Protein families database of alignments and HMM; <http://www.sanger.ac.uk/cgi-bin/Pfam/swisspfamget.pl?name=P49917>.

71. Wei YF, Robins P, Carter K, et al. Molecular cloning and expression of human cDNAs encoding a novel DNA ligase IV and DNA ligase III, an enzyme active in DNA repair and recombination. *Mol Cell Biol* 1995; 15:3206-16.
72. Roddam PL, Rollinson S, O'Driscoll M, Jeggo PA, Jack A, Morgan GJ. Genetic variants of NHEJ DNA ligase IV can affect the risk of developing multiple myeloma, a tumour characterised by aberrant class switch recombination. *J Med Genet* 2002; 39:900-5.
73. Girard PM, Kysela B, Harer CJ, Doherty AJ, Jeggo PA. Analysis of DNA ligase IV mutations found in LIG4 syndrome patients: the impact of two linked polymorphisms. *Hum Mol Genet* 2004; 13:2369-76.
74. Kuklin A, Munson K, Gjerde D, Haefele R, Taylor P. Detection of single-nucleotide polymorphisms with the WAVE DNA fragment analysis system. *Genet Test* 1997; 1:201-6.
75. Inc. T. Preinstallation Guide for WAVE (TM) DNA Fragment Analysis System. 1998.
76. Xiao W, Oefner PJ. Denaturing high-performance liquid chromatography: A review. *Hum Mutat* 2001; 17:439-74.
77. O'Donovan MC, Oefner PJ, Roberts SC, et al. Blind analysis of denaturing high-performance liquid chromatography as a tool for mutation detection. *Genomics* 1998; 52:44-9.
78. Liu W, Smith DI, Rechtzigel KJ, Thibodeau SN, James CD. Denaturing high performance liquid chromatography (DHPLC) used in the detection of germline and somatic mutations. *Nucleic Acids Res* 1998; 26:1396-400.
79. Gross E, Arnold N, Goette J, Schwarz-Boeger U, Kiechle M. A comparison of BRCA1 mutation analysis by direct sequencing, SSCP and DHPLC. *Hum Genet* 1999; 105:72-8.
80. Roberts PS, Jozwiak S, Kwiatkowski DJ, Dabora SL. Denaturing high-performance liquid chromatography (DHPLC) is a highly sensitive, semi-automated method for identifying mutations in the TSC1 gene. *J Biochem Biophys Methods* 2001; 47:33-7.
81. Boutin P, Vasseur F, Samson C, Wahl C, Froguel P. Routine mutation screening of HNF-1alpha and GCK genes in MODY diagnosis: how effective are the techniques of DHPLC and direct sequencing used in combination? *Diabetologia* 2001; 44:775-8.

82. Oldenburg J, Ivaskevicius V, Rost S, et al. Evaluation of DHPLC in the analysis of hemophilia A. *J Biochem Biophys Methods* 2001; 47:39-51.
83. Wolford JK, Blunt D, Ballecer C, Prochazka M. High-throughput SNP detection by using DNA pooling and denaturing high performance liquid chromatography (DHPLC). *Hum Genet* 2000; 107:483-7.
84. Jones AC, Sampson JR, Cheadle JP. Low level mosaicism detectable by DHPLC but not by direct sequencing. *Hum Mutat* 2001; 17:233-4.
85. Hayashi K, Yandell DW. How sensitive is PCR-SSCP? *Hum Mutat* 1993; 2:338-46.
86. Goode EL, Dunning AM, Kuschel B, et al. Effect of germ-line genetic variation on breast cancer survival in a population-based study. *Cancer Res* 2002; 62:3052-7.
87. Han J, Hankinson SE, Ranu H, De Vivo I, Hunter DJ. Polymorphisms in DNA double-strand break repair genes and breast cancer risk in the Nurses' Health Study. *Carcinogenesis* 2004; 25:189-95.
88. Han J, Colditz GA, Samson LD, Hunter DJ. Polymorphisms in DNA double-strand break repair genes and skin cancer risk. *Cancer Res* 2004; 64:3009-13.
89. Heidenreich E, Novotny R, Kneidinger B, Holzmann V, Wintersberger U. Non-homologous end joining as an important mutagenic process in cell cycle-arrested cells. *Embo J* 2003; 22:2274-83.
90. Rothkamm K, Kuhne M, Jeggo PA, Lobrich M. Radiation-induced genomic rearrangements formed by nonhomologous end-joining of DNA double-strand breaks. *Cancer Res* 2001; 61:3886-93.
91. Iliakis G, Wang H, Perrault AR, et al. Mechanisms of DNA double strand break repair and chromosome aberration formation. *Cytogenet Genome Res* 2004; 104:14-20.
92. Smith J, Riballo E, Kysela B, et al. Impact of DNA ligase IV on the fidelity of end joining in human cells. *Nucleic Acids Res* 2003; 31:2157-67.
93. Kuhne M, Rothkamm K, Lobrich M. No dose-dependence of DNA double-strand break misrejoining following alpha-particle irradiation. *Int J Radiat Biol* 2000; 76:891-900.
94. Kuhne M, Rothkamm K, Lobrich M. Physical and biological parameters affecting DNA double strand break misrejoining in mammalian cells. *Radiat Prot Dosimetry* 2002; 99:129-32.

95. Ford AM, Ridge SA, Cabrera ME, et al. In utero rearrangements in the trithorax-related oncogene in infant leukaemias. *Nature* 1993; 363:358-60.
96. Strick R, Strissel PL, Borgers S, Smith SL, Rowley JD. Dietary bioflavonoids induce cleavage in the MLL gene and may contribute to infant leukemia. *Proc Natl Acad Sci U S A* 2000; 97:4790-5.
97. Betti CJ, Villalobos MJ, Diaz MO, Vaughan AT. Apoptotic triggers initiate translocations within the MLL gene involving the nonhomologous end joining repair system. *Cancer Res* 2001; 61:4550-5.
98. Yoshida H, Naoe T, Fukutani H, Kiyoi H, Kubo K, Ohno R. Analysis of the joining sequences of the t(15;17) translocation in human acute promyelocytic leukemia: sequence non-specific recombination between the PML and RARA genes within identical short stretches. *Genes Chromosomes Cancer* 1995; 12:37-44.
99. Wiemels JL, Alexander FE, Cazzaniga G, Biondi A, Mayer SP, Greaves M. Microclustering of TEL-AML1 translocation breakpoints in childhood acute lymphoblastic leukemia. *Genes Chromosomes Cancer* 2000; 29:219-28.
100. Rassool FV. DNA double strand breaks (DSB) and non-homologous end joining (NHEJ) pathways in human leukemia. *Cancer Lett* 2003; 193:1-9.
101. Gaymes TJ, Mufti GJ, Rassool FV. Myeloid leukemias have increased activity of the nonhomologous end-joining pathway and concomitant DNA misrepair that is dependent on the Ku70/86 heterodimer. *Cancer Res* 2002; 62:2791-7.
102. Brady N, Gaymes TJ, Cheung M, Mufti GJ, Rassool FV. Increased error-prone NHEJ activity in myeloid leukemias is associated with DNA damage at sites that recruit key nonhomologous end-joining proteins. *Cancer Res* 2003; 63:1798-805.
103. Smogorzewska A, Karlseder J, Holtgreve-Grez H, Jauch A, de Lange T. DNA Ligase IV-Dependent NHEJ of Deprotected Mammalian Telomeres in G1 and G2. *Current Biology* 2002; 12:1635-1644.
104. Bertuch AA. Telomeres: The Molecular Events Driving End-To-End Fusions. *Current Biology* 2002; 12:R738-R740.
105. Pardo B, Marcand S. Rap1 prevents telomere fusions by nonhomologous end joining. *EMBO J* 2005; 24:3117-3127.
106. Gao Y, Chaudhuri J, Zhu C, Davidson L, Weaver DT, Alt FW. A targeted DNA-PKcs-null mutation reveals DNA-PK-independent functions for KU in V(D)J recombination. *Immunity* 1998; 9:367-76.

107. Gao Y, Sun Y, Frank KM, et al. A critical role for DNA end-joining proteins in both lymphogenesis and neurogenesis. *Cell* 1998; 95:891-902.
108. Frank KM, Sekiguchi JM, Seidl KJ, et al. Late embryonic lethality and impaired V(D)J recombination in mice lacking DNA ligase IV. *Nature* 1998; 396:173-7.
109. Kurimasa A, Ouyang H, Dong LJ, et al. Catalytic subunit of DNA-dependent protein kinase: impact on lymphocyte development and tumorigenesis. *Proc Natl Acad Sci U S A* 1999; 96:1403-8.
110. Lim DS, Vogel H, Willerford DM, Sands AT, Platt KA, Hasty P. Analysis of ku80-mutant mice and cells with deficient levels of p53. *Mol Cell Biol* 2000; 20:3772-80.
111. Adachi N, Ishino T, Ishii Y, Takeda S, Koyama H. DNA ligase IV-deficient cells are more resistant to ionizing radiation in the absence of Ku70: Implications for DNA double-strand break repair. *Proc Natl Acad Sci U S A* 2001; 98:12109-13.
112. Barnes DE, Stamp G, Rosewell I, Denzel A, Lindahl T. Targeted disruption of the gene encoding DNA ligase IV leads to lethality in embryonic mice. *Curr Biol* 1998; 8:1395-8.
113. Frank KM, Sharpless NE, Gao Y, et al. DNA ligase IV deficiency in mice leads to defective neurogenesis and embryonic lethality via the p53 pathway. *Mol Cell* 2000; 5:993-1002.
114. Lee Y, McKinnon PJ. DNA ligase IV suppresses medulloblastoma formation. *Cancer Res* 2002; 62:6395-9.
115. Sharpless NE, Ferguson DO, O'Hagan RC, et al. Impaired nonhomologous end-joining provokes soft tissue sarcomas harboring chromosomal translocations, amplifications, and deletions. *Mol Cell* 2001; 8:1187-96.