

7. Literaturverzeichnis

1. **Harris,N.L., Jaffe,E.S., Stein,H., Banks,P.M., Chan,J.K., Cleary,M.L., Delsol,G., Wolf-Peters,C., Falini,B., and Gatter,K.C.,** A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood* 1994. **84**: 1361-1392.
2. **World Health Organization,** Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. *IARC Press, Lyon* 2003.
3. **Hummel,M., Marafioti,T., Ziemann,K., and Stein,H.,** Ig rearrangements in isolated Reed-Sternberg cells: conclusions from four different studies. *Ann.Oncol.* 1996. **7 Suppl 4**: 31-33.
4. **Hodgkin,T.,** On some morbid appearances of the absorbent glands and spleen. *Med.Chir.Soc.Tr.* 1832. **17**: 68.
5. **Schwab,U., Stein,H., Gerdes,J., Lemke,H., Kirchner,H., Schaadt,M., and Diehl,V.,** Production of a monoclonal antibody specific for Hodgkin and Sternberg-Reed cells of Hodgkin's disease and a subset of normal lymphoid cells. *Nature* 1982. **299**: 65-67.
6. **Dallenbach,F.E. and Stein,H.,** Expression of T-cell-receptor beta chain in Reed-Sternberg cells. *Lancet* 1989. **2**: 828-830.
7. **Falini,B., Stein,H., Pileri,S., Canino,S., Farabbi,R., Martelli,M.F., Grignani,F., Fagioli,M., Minelli,O., Ciani,C., and .,** Expression of lymphoid-associated antigens on Hodgkin's and Reed- Sternberg cells of Hodgkin's disease. An immunocytochemical study on lymph node cytopins using monoclonal antibodies. *Histopathology* 1987. **11**: 1229-1242.
8. **Agnarsson,B.A. and Kadin,M.E.,** The immunophenotype of Reed-Sternberg cells. A study of 50 cases of Hodgkin's disease using fixed frozen tissues. *Cancer* 1989. **63**: 2083-2087.
9. **Schmid,C., Pan,L., Diss,T., and Isaacson,P.G.,** Expression of B-cell antigens by Hodgkin's and Reed-Sternberg cells. *Am.J.Pathol.* 1991. **139**: 701-707.
10. **Zukerberg,L.R., Collins,A.B., Ferry,J.A., and Harris,N.L.,** Coexpression of CD15 and CD20 by Reed-Sternberg cells in Hodgkin's disease. *Am.J.Pathol.* 1991. **139**: 475-483.
11. **Diehl,V., Kirchner,H.H., Burrichter,H., Stein,H., Fonatsch,C., Gerdes,J., Schaadt,M., Heit,W., Uchanska-Ziegler,B., Ziegler,A., Heintz,F., and Sueno,K.,** Characteristics of Hodgkin's disease-derived cell lines. *Cancer Treat.Rep.* 1982. **66**: 615-632.

12. **Diehl,V., Kirchner,H.H., Schaadt,M., Fonatsch,C., Stein,H., Gerdes,J., and Boie,C.,** Hodgkin's disease: establishment and characterization of four in vitro cell lines. *J.Cancer Res.Clin.Oncol.* 1981. **101**: 111-124.
13. **Yatabe,Y., Oka,K., Asai,J., and Mori,N.,** Poor correlation between clonal immunoglobulin gene rearrangement and immunoglobulin gene transcription in Hodgkin's disease. *Am.J.Pathol.* 1996. **149**: 1351-1361.
14. **Manzanal,A., Santon,A., Oliva,H., and Bellas,C.,** Evaluation of clonal immunoglobulin heavy chain rearrangements in Hodgkin's disease using the polymerase chain reaction (PCR). *Histopathology* 1995. **27**: 21-25.
15. **Orazi,A., Jiang,B., Lee,C.H., English,G.W., Cattoretti,G., John,K., and Neiman,R.S.,** Correlation between presence of clonal rearrangements of immunoglobulin heavy chain genes and B-cell antigen expression in Hodgkin's disease. *Am.J.Clin.Pathol.* 1995. **104**: 413-418.
16. **Al Saati,T., Galoin,S., Gravel,S., Lamant,L., Roda,D., Chittal,S.M., and Delsol,G.,** IgH and TcR-gamma gene rearrangements identified in Hodgkin's disease by PCR demonstrate lack of correlation between genotype, phenotype, and Epstein-Barr virus status. *J.Pathol.* 1997. **181**: 387-393.
17. **Tamaru,J., Hummel,M., Zemlin,M., Kalvelage,B., and Stein,H.,** Hodgkin's disease with a B-cell phenotype often shows a VDJ rearrangement and somatic mutations in the VH genes. *Blood* 1994. **84**: 708-715.
18. **Kueppers,R., Zhao,M., Hansmann,M.L., and Rajewsky,K.,** Tracing B cell development in human germinal centres by molecular analysis of single cells picked from histological sections. *EMBO J.* 1993. **12**: 4955-4967.
19. **Marafioti,T., Hummel,M., Foss,H.D., Laumen,H., Korbjuhn,P., Anagnostopoulos,I., Lammert,H., Demel,G., Theil,J., Wirth,T., and Stein,H.,** Hodgkin and reed-sternberg cells represent an expansion of a single clone originating from a germinal center B-cell with functional immunoglobulin gene rearrangements but defective immunoglobulin transcription. *Blood* 2000. **95**: 1443-1450.
20. **Kueppers,R., Sousa,A.B., Baur,A.S., Strickler,J.G., Rajewsky,K., and Hansmann,M.L.,** Common germinal-center B-cell origin of the malignant cells in two composite lymphomas, involving classical Hodgkin's disease and either follicular lymphoma or B-CLL. *Mol.Med.* 2001. **7**: 285-292.
21. **Kueppers,R., Rajewsky,K., Zhao,M., Simons,G., Laumann,R., Fischer,R., and Hansmann,M.L.,** Hodgkin disease: Hodgkin and Reed-Sternberg cells picked from histological sections show clonal immunoglobulin gene rearrangements and appear to be derived from B cells at various stages of development. *Proc.Natl.Acad.Sci.U.S.A* 1994. **91**: 10962-10966.
22. **Kanzler,H., Kueppers,R., Hansmann,M.L., and Rajewsky,K.,** Hodgkin and Reed-Sternberg cells in Hodgkin's disease represent the outgrowth of a dominant tumor clone derived from (crippled) germinal center B cells. *J.Exp.Med.* 1996. **184**: 1495-1505.

23. **Hummel,M., Ziemann,K., Lammert,H., Pileri,S., Sabbatini,E., and Stein,H.,** Hodgkin's disease with monoclonal and polyclonal populations of Reed- Sternberg cells. *N.Engl.J.Med.* 1995. **333**: 901-906.
24. **Hummel,M., Marafioti,T., and Stein,H.,** Immunoglobulin V genes in Reed- Sternberg cells-Reply to the letters to the Editor. *N.Engl.J.Med.* 1996. 334-405.
25. **Weiss,L.M., Strickler,J.G., Hu,E., Warnke,R.A., and Sklar,J.,** Immunoglobulin gene rearrangements in Hodgkin's disease. *Hum.Pathol.* 1986. **17**: 1009-1014.
26. **Herbst,H., Tippelmann,G., Anagnostopoulos,I., Gerdes,J., Schwarting,R., Boehm,T., Pileri,S., Jones,D.B., and Stein,H.,** Immunoglobulin and T-cell receptor gene rearrangements in Hodgkin's disease and Ki-1-positive anaplastic large cell lymphoma: dissociation between phenotype and genotype. *Leuk.Res.* 1989. **13**: 103-116.
27. **Ruprai,A.K., Pringle,J.H., Angel,C.A., Kind,C.N., and Lauder,I.,** Localization of immunoglobulin light chain mRNA expression in Hodgkin's disease by in situ hybridization. *J.Pathol.* 1991. **164**: 37-40.
28. **Rajewsky,K.,** Clonal selection and learning in the antibody system. *Nature* 1996. **381**: 751-758.
29. **Chilosi,M., Doglioni,C., Menestrina,F., Montagna,L., Rigo,A., Lestani,M., Barbareschi,M., Scarpa,A., Mariuzzi,G.M., and Pizzolo,G.,** Abnormal expression of the p53-binding protein MDM2 in Hodgkin's disease. *Blood* 1994. **84**: 4295-4300.
30. **Czader,M., Porwit,A., Ost,A., and Auer,G.,** DNA content and expression of PCNA and p53 in Hodgkin's disease and Hodgkin's-like B-cell lymphoma. *APMIS* 1994. **102**: 865-873.
31. **Doglioni,C., Pelosio,P., Mombello,A., Scarpa,A., and Chilosi,M.,** Immunohistochemical evidence of abnormal expression of the antioncogene- encoded p53 phosphoprotein in Hodgkin's disease and CD30+ anaplastic lymphomas. *Hematol.Pathol.* 1991. **5**: 67-73.
32. **Doussis,I.A., Pezzella,F., Lane,D.P., Gatter,K.C., and Mason,D.Y.,** An immunocytochemical study of p53 and bcl-2 protein expression in Hodgkin's disease. *Am.J.Clin.Pathol.* 1993. **99**: 663-667.
33. **Gupta,R.K., Norton,A.J., Lister,T.A., and Bodmer,J.G.,** p53 protein expression in Reed-Sternberg cells of Hodgkin's disease. *Leukemia* 1993. **7 Suppl 2**: S31-S33.
34. **Gupta,R.K., Norton,A.J., Thompson,I.W., Lister,T.A., and Bodmer,J.G.,** p53 expression in Reed-Sternberg cells of Hodgkin's disease. *Br.J.Cancer* 1992. **66**: 649-652.
35. **Niedobitek,G., Rowlands,D.C., Young,L.S., Herbst,H., Williams,A., Hall,P., Padfield,J., Rooney,N., and Jones,E.L.,** Overexpression of p53 in Hodgkin's disease: lack of correlation with Epstein-Barr virus infection. *J.Pathol.* 1993. **169**: 207-212.

36. **el Deiry,W.S.**, Regulation of p53 downstream genes. *Semin.Cancer Biol.* 1998. **8**: 345-357.
37. **Lohrum,M.A. and Vousden,K.H.**, Regulation and activation of p53 and its family members. *Cell Death.Differ.* 1999. **6**: 1162-1168.
38. **Levine,A.J., Momand,J., and Finlay,C.A.**, The p53 tumour suppressor gene. *Nature* 1991. **351**: 453-456.
39. **Wynford-Thomas,D.**, p53: guardian of cellular senescence. *J.Pathol.* 1996. **180**: 118-121.
40. **Hansen,R. and Oren,M.**, p53; from inductive signal to cellular effect. *Curr.Opin.Genet.Dev.* 1997. **7**: 46-51.
41. **Levine,A.J.**, p53, the cellular gatekeeper for growth and division. *Cell* 1997. **88**: 323-331.
42. **Vogelstein,B. and Kinzler,K.W.**, p53 function and dysfunction. *Cell* 1992. **70**: 523-526.
43. **Botuyan,M.V., Momand,J., and Chen,Y.**, Solution conformation of an essential region of the p53 transactivation domain. *Fold.Des* 1997. **2**: 331-342.
44. **Lee,H., Mok,K.H., Muhandiram,R., Park,K.H., Suk,J.E., Kim,D.H., Chang,J., Sung,Y.C., Choi,K.Y., and Han,K.H.**, Local structural elements in the mostly unstructured transcriptional activation domain of human p53. *J.Biol.Chem.* 2000. **275**: 29426-29432.
45. **Arrowsmith,C.H.**, Structure and function in the p53 family. *Cell Death.Differ.* 1999. **6**: 1169-1173.
46. **Arrowsmith,C.H. and Morin,P.**, New insights into p53 function from structural studies. *Oncogene* 1996. **12**: 1379-1385.
47. **Bargonetti,J., Manfredi,J.J., Chen,X., Marshak,D.R., and Prives,C.**, A proteolytic fragment from the central region of p53 has marked sequence-specific DNA-binding activity when generated from wild-type but not from oncogenic mutant p53 protein. *Genes Dev.* 1993. **7**: 2565-2574.
48. **Fields,S. and Jang,S.K.**, Presence of a potent transcription activating sequence in the p53 protein. *Science* 1990. **249**: 1046-1049.
49. **Jayaraman,L., Freulich,E., and Prives,C.**, Functional dissection of p53 tumor suppressor protein. *Methods Enzymol.* 1997. **283**: 245-256.
50. **Montano,X.**, Common amino acid sequence motifs in p53, 14-3-3 and Akt protein families. *FEBS Lett.* 2001. **507**: 237-240.
51. **Pavletich,N.P., Chambers,K.A., and Pabo,C.O.**, The DNA-binding domain of p53 contains the four conserved regions and the major mutation hot spots. *Genes Dev.* 1993. **7**: 2556-2564.

52. **Soussi,T. and May,P.**, Structural aspects of the p53 protein in relation to gene evolution: a second look. *J.Mol.Biol.* 1996. **260**: 623-637.
53. **Wang,Y., Reed,M., Wang,P., Stenger,J.E., Mayr,G., Anderson,M.E., Schwedes,J.F., and Tegtmeier,P.**, p53 domains: identification and characterization of two autonomous DNA-binding regions. *Genes Dev.* 1993. **7**: 2575-2586.
54. **Yamane,K., Katayama,E., and Tsuruo,T.**, p53 contains a DNA break-binding motif similar to the functional part of BRCT-related region of Rb. *Oncogene* 2001. **20**: 2859-2867.
55. **Hollstein,M., Hergenhahn,M., Yang,Q., Bartsch,H., Wang,Z.Q., and Hainaut,P.**, New approaches to understanding p53 gene tumor mutation spectra. *Mutat.Res.* 1999. **431**: 199-209.
56. **Sigal,A. and Rotter,V.**, Oncogenic mutations of the p53 tumor suppressor: the demons of the guardian of the genome. *Cancer Res.* 2000. **60**: 6788-6793.
57. **Prives,C. and Hall,P.A.**, The p53 pathway. *J.Pathol.* 1999. **187**: 112-126.
58. **Hall,P.A., Meek,D., and Lane,D.P.**, p53--integrating the complexity. *J.Pathol.* 1996. **180**: 1-5.
59. **Ko,L.J. and Prives,C.**, p53: puzzle and paradigm. *Genes Dev.* 1996. **10**: 1054-1072.
60. **Agarwal,M.L., Taylor,W.R., Chernov,M.V., Chernova,O.B., and Stark,G.R.**, The p53 network. *J.Biol.Chem.* 1998. **273**: 1-4.
61. **Harris,C.C.**, p53 tumor suppressor gene: from the basic research laboratory to the clinic--an abridged historical perspective. *Carcinogenesis* 1996. **17**: 1187-1198.
62. **Dowell,S.P. and Hall,P.A.**, The p53 tumour suppressor gene and tumour prognosis: is there a relationship? *J.Pathol.* 1995. **177**: 221-224.
63. **el Deiry,W.S., Kern,S.E., Pietenpol,J.A., Kinzler,K.W., and Vogelstein,B.**, Definition of a consensus binding site for p53. *Nat.Genet.* 1992. **1**: 45-49.
64. **Yuan,Z.M., Huang,Y., Whang,Y., Sawyers,C., Weichselbaum,R., Kharbanda,S., and Kufe,D.**, Role for c-Abl tyrosine kinase in growth arrest response to DNA damage. *Nature* 1996. **382**: 272-274.
65. **Meek,D.W.**, Post-translational modification of p53. *Semin.Cancer Biol.* 1994. **5**: 203-210.
66. **Siliciano,J.D., Canman,C.E., Taya,Y., Sakaguchi,K., Appella,E., and Kastan,M.B.**, DNA damage induces phosphorylation of the amino terminus of p53. *Genes Dev.* 1997. **11**: 3471-3481.
67. **Sakaguchi,K., Herrera,J.E., Saito,S., Miki,T., Bustin,M., Vassilev,A., Anderson,C.W., and Appella,E.**, DNA damage activates p53 through a phosphorylation-acetylation cascade. *Genes Dev.* 1998. **12**: 2831-2841.

68. **Caspari,T.**, How to activate p53. *Curr.Biol.* 2000. **10**: R315-R317.
69. **Hickman,E.S., Moroni,M.C., and Helin,K.**, The role of p53 and pRB in apoptosis and cancer. *Curr.Opin.Genet.Dev.* 2002. **12**: 60-66.
70. **Maltzman,W. and Czyzyk,L.**, UV irradiation stimulates levels of p53 cellular tumor antigen in nontransformed mouse cells. *Mol.Cell Biol.* 1984. **4**: 1689-1694.
71. **Reich,N.C., Oren,M., and Levine,A.J.**, Two distinct mechanisms regulate the levels of a cellular tumor antigen, p53. *Mol.Cell Biol.* 1983. **3**: 2143-2150.
72. **Balint,E.E. and Vousden,K.H.**, Activation and activities of the p53 tumour suppressor protein. *Br.J.Cancer* 2001. **85**: 1813-1823.
73. **Jayaraman,L. and Prives,C.**, Covalent and noncovalent modifiers of the p53 protein. *Cell Mol.Life Sci.* 1999. **55**: 76-87.
74. **Oren,M.**, Regulation of the p53 tumor suppressor protein. *J.Biol.Chem.* 1999. **274**: 36031-36034.
75. **Somasundaram,K.**, Tumor suppressor p53: regulation and function. *Front Biosci.* 2000. **5**: D424-D437.
76. **Vousden,K.H.**, Activation of the p53 tumor suppressor protein. *Biochim.Biophys.Acta* 2002. **1602**: 47-59.
77. **Fang,S., Jensen,J.P., Ludwig,R.L., Vousden,K.H., and Weissman,A.M.**, Mdm2 is a RING finger-dependent ubiquitin protein ligase for itself and p53. *J.Biol.Chem.* 2000. **275**: 8945-8951.
78. **Honda,R. and Yasuda,H.**, Association of p19(ARF) with Mdm2 inhibits ubiquitin ligase activity of Mdm2 for tumor suppressor p53. *EMBO J.* 1999. **18**: 22-27.
79. **Kubbutat,M.H. and Vousden,K.H.**, Keeping an old friend under control: regulation of p53 stability. *Mol.Med.Today* 1998. **4**: 250-256.
80. **Piette,J., Neel,H., and Marechal,V.**, Mdm2: keeping p53 under control. *Oncogene* 1997. **15**: 1001-1010.
81. **Groll,M., Ditzel,L., Loewe,J., Stock,D., Bochtler,M., Bartunik,H.D., and Huber,R.**, Structure of 20S proteasome from yeast at 2.4 Å resolution. *Nature* 1997. **386**: 463-471.
82. **Weissman,A.M.**, Themes and variations on ubiquitylation. *Nat.Rev.Mol.Cell Biol.* 2001. **2**: 169-178.
83. **Jesenberger,V. and Jentsch,S.**, Deadly encounter: ubiquitin meets apoptosis. *Nat.Rev.Mol.Cell Biol.* 2002. **3**: 112-121.
84. **Bernier-Villamor,V., Sampson,D.A., Matunis,M.J., and Lima,C.D.**, Structural basis for E2-mediated SUMO conjugation revealed by a complex between ubiquitin-conjugating enzyme Ubc9 and RanGAP1. *Cell* 2002. **108**: 345-356.

85. **Kahyo,T., Nishida,T., and Yasuda,H.,** Involvement of PIAS1 in the sumoylation of tumor suppressor p53. *Mol.Cell* 2001. **8**: 713-718.
86. **Mueller,S., Berger,M., Lehenbre,F., Seeler,J.S., Haupt,Y., and Dejean,A.,** c-Jun and p53 activity is modulated by SUMO-1 modification. *J.Biol.Chem.* 2000. **275**: 13321-13329.
87. **Buschmann,T., Fuchs,S.Y., Lee,C.G., Pan,Z.Q., and Ronai,Z.,** SUMO-1 modification of Mdm2 prevents its self-ubiquitination and increases Mdm2 ability to ubiquitinate p53. *Cell* 2000. **101**: 753-762.
88. **Steegenga,W.T., van der Eb,A.J., and Jochemsen,A.G.,** How phosphorylation regulates the activity of p53. *J.Mol.Biol.* 1996. **263**: 103-113.
89. **Khanna,K.K.,** Cancer risk and the ATM gene: a continuing debate. *J.Natl.Cancer Inst.* 2000. **92**: 795-802.
90. **Banin,S., Moyal,L., Shieh,S., Taya,Y., Anderson,C.W., Chessa,L., Smorodinsky,N.I., Prives,C., Reiss,Y., Shiloh,Y., and Ziv,Y.,** Enhanced phosphorylation of p53 by ATM in response to DNA damage. *Science* 1998. **281**: 1674-1677.
91. **Canman,C.E., Lim,D.S., Cimprich,K.A., Taya,Y., Tamai,K., Sakaguchi,K., Appella,E., Kastan,M.B., and Siliciano,J.D.,** Activation of the ATM kinase by ionizing radiation and phosphorylation of p53. *Science* 1998. **281**: 1677-1679.
92. **Khosravi,R., Maya,R., Gottlieb,T., Oren,M., Shiloh,Y., and Shkedy,D.,** Rapid ATM-dependent phosphorylation of MDM2 precedes p53 accumulation in response to DNA damage. *Proc.Natl.Acad.Sci.U.S.A* 1999. **96**: 14973-14977.
93. **Grossman,S.R.,** p300/CBP/p53 interaction and regulation of the p53 response. *Eur.J.Biochem.* 2001. **268**: 2773-2778.
94. **Gu,W. and Roeder,R.G.,** Activation of p53 sequence-specific DNA binding by acetylation of the p53 C-terminal domain. *Cell* 1997. **90**: 595-606.
95. **Gu,W., Shi,X.L., and Roeder,R.G.,** Synergistic activation of transcription by CBP and p53. *Nature* 1997. **387**: 819-823.
96. **Vaziri,H., Dessain,S.K., Ng,E.E., Imai,S.I., Frye,R.A., Pandita,T.K., Guarente,L., and Weinberg,R.A.,** hSIR2(SIRT1) functions as an NAD-dependent p53 deacetylase. *Cell* 2001. **107**: 149-159.
97. **Barlev,N.A., Liu,L., Chehab,N.H., Mansfield,K., Harris,K.G., Halazonetis,T.D., and Berger,S.L.,** Acetylation of p53 activates transcription through recruitment of coactivators/histone acetyltransferases. *Mol.Cell* 2001. **8**: 1243-1254.
98. **Liang,S.H. and Clarke,M.F.,** Regulation of p53 localization. *Eur.J.Biochem.* 2001. **268**: 2779-2783.

99. **Roth,J., Dobbelstein,M., Freedman,D.A., Shenk,T., and Levine,A.J.,** Nucleocytoplasmic shuttling of the hdm2 oncoprotein regulates the levels of the p53 protein via a pathway used by the human immunodeficiency virus rev protein. *EMBO J.* 1998. **17:** 554-564.
100. **Stommel,J.M., Marchenko,N.D., Jimenez,G.S., Moll,U.M., Hope,T.J., and Wahl,G.M.,** A leucine-rich nuclear export signal in the p53 tetramerization domain: regulation of subcellular localization and p53 activity by NES masking. *EMBO J.* 1999. **18:** 1660-1672.
101. **Zhang,Y. and Xiong,Y.,** Control of p53 ubiquitination and nuclear export by MDM2 and ARF. *Cell Growth Differ.* 2001. **12:** 175-186.
102. **Cahilly-Snyder,L., Yang-Feng,T., Francke,U., and George,D.L.,** Molecular analysis and chromosomal mapping of amplified genes isolated from a transformed mouse 3T3 cell line. *Somat. Cell Mol. Genet.* 1987. **13:** 235-244.
103. **Fakharzadeh,S.S., Trusko,S.P., and George,D.L.,** Tumorigenic potential associated with enhanced expression of a gene that is amplified in a mouse tumor cell line. *EMBO J.* 1991. **10:** 1565-1569.
104. **Momand,J., Zambetti,G.P., Olson,D.C., George,D., and Levine,A.J.,** The mdm-2 oncogene product forms a complex with the p53 protein and inhibits p53-mediated transactivation. *Cell* 1992. **69:** 1237-1245.
105. **Haupt,Y., Maya,R., Kazaz,A., and Oren,M.,** Mdm2 promotes the rapid degradation of p53. *Nature* 1997. **387:** 296-299.
106. **Momand,J. and Zambetti,G.P.,** Analysis of the proportion of p53 bound to mdm-2 in cells with defined growth characteristics. *Oncogene* 1996. **12:** 2279-2289.
107. **Haines,D.S., Landers,J.E., Engle,L.J., and George,D.L.,** Physical and functional interaction between wild-type p53 and mdm2 proteins. *Mol. Cell Biol.* 1994. **14:** 1171-1178.
108. **Sigalas,I., Calvert,A.H., Anderson,J.J., Neal,D.E., and Lunec,J.,** Alternatively spliced mdm2 transcripts with loss of p53 binding domain sequences: transforming ability and frequent detection in human cancer. *Nat. Med.* 1996. **2:** 912-917.
109. **Juven-Gershon,T. and Oren,M.,** Mdm2: the ups and downs. *Mol. Med.* 1999. **5:** 71-83.
110. **Freedman,D.A. and Levine,A.J.,** Regulation of the p53 protein by the MDM2 oncoprotein--thirty-eighth G.H.A. Clowes Memorial Award Lecture. *Cancer Res.* 1999. **59:** 1-7.
111. **Freedman,D.A., Wu,L., and Levine,A.J.,** Functions of the MDM2 oncoprotein. *Cell Mol. Life Sci.* 1999. **55:** 96-107.
112. **Momand,J., Wu,H.H., and Dasgupta,G.,** MDM2--master regulator of the p53 tumor suppressor protein. *Gene* 2000. **242:** 15-29.

113. **Lohrum,M.A. and Vousden,K.H.**, Regulation and function of the p53-related proteins: same family, different rules. *Trends Cell Biol.* 2000. **10**: 197-202.
114. **Barak,Y., Juven,T., Haffner,R., and Oren,M.**, mdm2 expression is induced by wild type p53 activity. *EMBO J.* 1993. **12**: 461-468.
115. **Wu,X., Bayle,J.H., Olson,D., and Levine,A.J.**, The p53-mdm-2 autoregulatory feedback loop. *Genes Dev.* 1993. **7**: 1126-1132.
116. **Bottger,A., Bottger,V., Sparks,A., Liu,W.L., Howard,S.F., and Lane,D.P.**, Design of a synthetic Mdm2-binding mini protein that activates the p53 response in vivo. *Curr.Biol.* 1997. **7**: 860-869.
117. **Jones,S.N., Roe,A.E., Donehower,L.A., and Bradley,A.**, Rescue of embryonic lethality in Mdm2-deficient mice by absence of p53. *Nature* 1995. **378**: 206-208.
118. **Montes de Oca,L.R., Wagner,D.S., and Lozano,G.**, Rescue of early embryonic lethality in mdm2-deficient mice by deletion of p53. *Nature* 1995. **378**: 203-206.
119. **Oliner,J.D., Kinzler,K.W., Meltzer,P.S., George,D.L., and Vogelstein,B.**, Amplification of a gene encoding a p53-associated protein in human sarcomas. *Nature* 1992. **358**: 80-83.
120. **Hall,A.R. and Milner,J.**, Specific p53-DNA complexes contain an mdm2-related protein. *Oncogene* 1997. **14**: 1371-1376.
121. **Leng,P., Brown,D.R., Shivakumar,C.V., Deb,S., and Deb,S.P.**, N-terminal 130 amino acids of MDM2 are sufficient to inhibit p53-mediated transcriptional activation. *Oncogene* 1995. **10**: 1275-1282.
122. **Oliner,J.D., Pietenpol,J.A., Thiagalingam,S., Gyuris,J., Kinzler,K.W., and Vogelstein,B.**, Oncoprotein MDM2 conceals the activation domain of tumour suppressor p53. *Nature* 1993. **362**: 857-860.
123. **Vousden,K.H. and Woude,G.F.**, The ins and outs of p53. *Nat.Cell Biol.* 2000. **2**: E178-E180.
124. **Ashcroft,M. and Vousden,K.H.**, Regulation of p53 stability. *Oncogene* 1999. **18**: 7637-7643.
125. **Haupt,Y., Maya,R., Kazaz,A., and Oren,M.**, Mdm2 promotes the rapid degradation of p53. *Nature* 1997. **387**: 296-299.
126. **Kubbutat,M.H., Jones,S.N., and Vousden,K.H.**, Regulation of p53 stability by Mdm2. *Nature* 1997. **387**: 299-303.
127. **Lane,D.P. and Hall,P.A.**, MDM2--arbiter of p53's destruction. *Trends Biochem.Sci.* 1997. **22**: 372-374.
128. **Juven,T., Barak,Y., Zauberman,A., George,D.L., and Oren,M.**, Wild type p53 can mediate sequence-specific transactivation of an internal promoter within the mdm2 gene. *Oncogene* 1993. **8**: 3411-3416.

129. **Picksley,S.M. and Lane,D.P.**, The p53-mdm2 autoregulatory feedback loop: a paradigm for the regulation of growth control by p53? *Bioessays* 1993. **15**: 689-690.
130. **Lev Bar-Or,R., Maya,R., Segel,L.A., Alon,U., Levine,A.J., and Oren,M.**, Generation of oscillations by the p53-Mdm2 feedback loop: a theoretical and experimental study. *Proc.Natl.Acad.Sci.U.S.A* 2000. **97**: 11250-11255.
131. **Shieh,S.Y., Ikeda,M., Taya,Y., and Prives,C.**, DNA damage-induced phosphorylation of p53 alleviates inhibition by MDM2. *Cell* 1997. **91**: 325-334.
132. **Unger,T., Juven-Gershon,T., Moallem,E., Berger,M., Vogt,S.R., Lozano,G., Oren,M., and Haupt,Y.**, Critical role for Ser20 of human p53 in the negative regulation of p53 by Mdm2. *EMBO J.* 1999. **18**: 1805-1814.
133. **Bean,L.J. and Stark,G.R.**, Regulation of the accumulation and function of p53 by phosphorylation of two residues within the domain that binds to Mdm2. *J.Biol.Chem.* 2002. **277**: 1864-1871.
134. **Lai,Z., Auger,K.R., Manubay,C.M., and Copeland,R.A.**, Thermodynamics of p53 binding to hdm2(1-126): effects of phosphorylation and p53 peptide length. *Arch.Biochem.Biophys.* 2000. **381**: 278-284.
135. **Sakaguchi,K., Saito,S., Higashimoto,Y., Roy,S., Anderson,C.W., and Appella,E.**, Damage-mediated phosphorylation of human p53 threonine 18 through a cascade mediated by a casein 1-like kinase. Effect on Mdm2 binding. *J.Biol.Chem.* 2000. **275**: 9278-9283.
136. **Sherr,C.J. and Weber,J.D.**, The ARF/p53 pathway. *Curr.Opin.Genet.Dev.* 2000. **10**: 94-99.
137. **Asker,C., Wiman,K.G., and Selivanova,G.**, p53-induced apoptosis as a safeguard against cancer. *Biochem.Biophys.Res.Comm.* 1999. **265**: 1-6.
138. **Serrano,M., Lee,H., Chin,L., Cordon-Cardo,C., Beach,D., and DePinho,R.A.**, Role of the INK4a locus in tumor suppression and cell mortality. *Cell* 1996. **85**: 27-37.
139. **Sherr,C.J.**, Tumor surveillance via the ARF-p53 pathway. *Genes Dev.* 1998. **12**: 2984-2991.
140. **DiGiammarino,E.L., Filippov,I., Weber,J.D., Bothner,B., and Kriwacki,R.W.**, Solution structure of the p53 regulatory domain of the p19Arf tumor suppressor protein. *Biochemistry* 2001. **40**: 2379-2386.
141. **Pomerantz,J., Schreiber-Agus,N., Liegeois,N.J., Silverman,A., Alland,L., Chin,L., Potes,J., Chen,K., Orlow,I., Lee,H.W., Cordon-Cardo,C., and DePinho,R.A.**, The Ink4a tumor suppressor gene product, p19Arf, interacts with MDM2 and neutralizes MDM2's inhibition of p53. *Cell* 1998. **92**: 713-723.
142. **Tao,W. and Levine,A.J.**, P19(ARF) stabilizes p53 by blocking nucleo-cytoplasmic shuttling of Mdm2. *Proc.Natl.Acad.Sci.U.S.A* 1999. **96**: 6937-6941.

143. **Weber,J.D., Taylor,L.J., Roussel,M.F., Sherr,C.J., and Bar-Sagi,D.,** Nucleolar Arf sequesters Mdm2 and activates p53. *Nat. Cell Biol.* 1999. **1**: 20-26.
144. **Xirodimas,D., Saville,M.K., Edling,C., Lane,D.P., and Lain,S.,** Different effects of p14ARF on the levels of ubiquitinated p53 and Mdm2 in vivo. *Oncogene* 2001. **20**: 4972-4983.
145. **Stott,F.J., Bates,S., James,M.C., McConnell,B.B., Starborg,M., Brookes,S., Palmero,I., Ryan,K., Hara,E., Vousden,K.H., and Peters,G.,** The alternative product from the human CDKN2A locus, p14(ARF), participates in a regulatory feedback loop with p53 and MDM2. *EMBO J.* 1998. **17**: 5001-5014.
146. **Hsieh,J.K., Chan,F.S., O'Connor,D.J., Mitnacht,S., Zhong,S., and Lu,X.,** RB regulates the stability and the apoptotic function of p53 via MDM2. *Mol. Cell* 1999. **3**: 181-193.
147. **Halevy,O., Hall,A., and Oren,M.,** Stabilization of the p53 transformation-related protein in mouse fibrosarcoma cell lines: effects of protein sequence and intracellular environment. *Mol. Cell Biol.* 1989. **9**: 3385-3392.
148. **Hollstein,M., Sidransky,D., Vogelstein,B., and Harris,C.C.,** p53 mutations in human cancers. *Science* 1991. **253**: 49-53.
149. **Hainaut,P., Soussi,T., Shomer,B., Hollstein,M., Greenblatt,M., Hovig,E., Harris,C.C., and Montesano,R.,** Database of p53 gene somatic mutations in human tumors and cell lines: updated compilation and future prospects. *Nucleic Acids Res.* 1997. **25**: 151-157.
150. **Blagosklonny,M.V.,** Loss of function and p53 protein stabilization. *Oncogene* 1997. **15**: 1889-1893.
151. **Zhang,Y., Xiong,Y., and Yarbrough,W.G.,** ARF promotes MDM2 degradation and stabilizes p53: ARF-INK4a locus deletion impairs both the Rb and p53 tumor suppression pathways. *Cell* 1998. **92**: 725-734.
152. **Keleti,J., Quezado,M.M., Abaza,M.M., Raffeld,M., and Tsokos,M.,** The MDM2 oncoprotein is overexpressed in rhabdomyosarcoma cell lines and stabilizes wild-type p53 protein. *Am.J.Pathol.* 1996. **149**: 143-151.
153. **Maestro,R., Gloghini,A., Doglioni,C., Gasparotto,D., Vukosavljevic,T., De,R., V, Laurino,L., Carbone,A., and Boiocchi,M.,** MDM2 overexpression does not account for stabilization of wild-type p53 protein in non-Hodgkin's lymphomas. *Blood* 1995. **85**: 3239-3246.
154. **Finnegan,M.C., Goepel,J.R., Royds,J., Hancock,B.W., and Goyns,M.H.,** Elevated levels of MDM-2 and p53 expression are associated with high grade non-Hodgkin's lymphomas. *Cancer Lett.* 1994. **86**: 215-221.
155. **Piris,M.A., Villuendas,R., Martinez,J.C., Sanchez-Beato,M., Orradre,J.L., Mateo,M.S., and Martinez,P.,** p53 expression in non-Hodgkin's lymphomas: a marker of p53 inactivation? *Leuk.Lymphoma* 1995. **17**: 35-42.

156. **Chen,W.G., Chen,Y.Y., Kamel,O.W., Koo,C.H., and Weiss,L.M.**, p53 mutations in Hodgkin's disease. *Lab Invest* 1996. **75**: 519-527.
157. **Elenitoba-Johnson,K.S., Medeiros,L.J., Khorsand,J., and King,T.C.**, P53 expression in Reed-Sternberg cells does not correlate with gene mutations in Hodgkin's disease. *Am.J.Clin.Pathol.* 1996. **106**: 728-738.
158. **Kuepper,M., Joos,S., von Bonin,F., Daus,H., Pfreundschuh,M., Lichter,P., and Trumper,L.**, MDM2 gene amplification and lack of p53 point mutations in Hodgkin and Reed-Sternberg cells: results from single-cell polymerase chain reaction and molecular cytogenetic studies. *Br.J.Haematol.* 2001. **112**: 768-775.
159. **Lorenzen,J., Thiele,J., and Fischer,R.**, The mummified Hodgkin cell: cell death in Hodgkin's disease. *J.Pathol.* 1997. **182**: 288-298.
160. **Montesinos-Rongen,M., Roers,A., Kueppers,R., Rajewsky,K., and Hansmann,M.L.**, Mutation of the p53 gene is not a typical feature of Hodgkin and Reed-Sternberg cells in Hodgkin's disease. *Blood* 1999. **94**: 1755-1760.
161. **Kawamata,N., Miller,C., Levy,V., Shintaku,I.P., Koeffler,H.P., and Said,J.W.**, mdm-2 oncogene expression in non-Hodgkin's lymphomas. *Diagn.Mol.Pathol.* 1996. **5**: 33-38.
162. **Watanabe,T., Ichikawa,A., Saito,H., and Hotta,T.**, Overexpression of the MDM2 oncogene in leukemia and lymphoma. *Leuk.Lymphoma* 1996. **21**: 391-7, color.
163. **Watanabe,T., Hotta,T., Ichikawa,A., Kinoshita,T., Nagai,H., Uchida,T., Murate,T., and Saito,H.**, The MDM2 oncogene overexpression in chronic lymphocytic leukemia and low-grade lymphoma of B-cell origin. *Blood* 1994. **84**: 3158-3165.
164. **Sanger,F., Nicklen,S., and Coulson,A.R.**, DNA sequencing with chain-terminating inhibitors. 1977. *Biotechnology* 1992. **24**: 104-108.
165. **Burnette,W.N.**, "Western blotting": electrophoretic transfer of proteins from sodium dodecyl sulfate--polyacrylamide gels to unmodified nitrocellulose and radiographic detection with antibody and radioiodinated protein A. *Anal.Biochem.* 1981. **112**: 195-203.
166. **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**: 248-254.
167. **Whang-Peng,J., Lee,E.C., Kao-Shan,C.S., Seibert,K., and Lippman,M.**, Cytogenetic studies of human breast cancer lines: MCF-7 and derived variant sublines. *J.Natl.Cancer Inst.* 1983. **71**: 687-695.
168. **Wolf,J., Kapp,U., Bohlen,H., Kornacker,M., Schoch,C., Stahl,B., Mucke,S., von Kalle,C., Fonatsch,C., Schaefer,H.E., Hansmann,M.L., and Diehl,V.**, Peripheral blood mononuclear cells of a patient with advanced Hodgkin's lymphoma give rise to permanently growing Hodgkin-Reed Sternberg cells. *Blood* 1996. **87**: 3418-3428.

169. **Staratschek-Jox,A., Thomas,R.K., Zander,T., Massoudi,N., Kornacker,M., Bullerdiek,J., Fonatsch,C., Diehl,V., and Wolf,J.,** Loss of heterozygosity in the Hodgkin-Reed Sternberg cell line L1236. *Br.J.Cancer* 2001. **84**: 381-387.
170. **Duthu,A., Debuire,B., Romano,J., Ehrhart,J.C., Fiscella,M., May,E., Appella,E., and May,P.,** p53 mutations in Raji cells: characterization and localization relative to other Burkitt's lymphomas. *Oncogene* 1992. **7**: 2161-2167.
171. **Garcia,J.F., Villuendas,R., Sanchez-Beato,M., Sanchez-Aguilera,A., Sanchez,L., Prieto,I., and Piris,M.A.,** Nucleolar p14(ARF) overexpression in Reed-Sternberg cells in Hodgkin's lymphoma: absence of p14(ARF)/Hdm2 complexes is associated with expression of alternatively spliced Hdm2 transcripts. *Am.J.Pathol.* 2002. **160**: 569-578.
172. **Leach,F.S., Tokino,T., Meltzer,P., Burrell,M., Oliner,J.D., Smith,S., Hill,D.E., Sidransky,D., Kinzler,K.W., and Vogelstein,B.,** p53 Mutation and MDM2 amplification in human soft tissue sarcomas. *Cancer Res.* 1993. **53**: 2231-2234.
173. **Reifenberger,G., Liu,L., Ichimura,K., Schmidt,E.E., and Collins,V.P.,** Amplification and overexpression of the MDM2 gene in a subset of human malignant gliomas without p53 mutations. *Cancer Res.* 1993. **53**: 2736-2739.
174. **Taylor,A.M., Metcalfe,J.A., Thick,J., and Mak,Y.F.,** Leukemia and lymphoma in ataxia telangiectasia. *Blood* 1996. **87**: 423-438.
175. **Starczynski,J., Simmons,W., Flavell,J.R., Byrd,P.J., Stewart,G.S., Kullar,H.S., Groom,A., Crocker,J., Moss,P.A., Reynolds,G.M., Glavina-Durdov,M., Taylor,A.M., Fegan,C., Stankovic,T., and Murray,P.G.,** Variations in ATM protein expression during normal lymphoid differentiation and among B-cell-derived neoplasias. *Am.J.Pathol.* 2003. **163**: 423-432.
176. **Ohshima,K., Haraoka,S., Fujiki,T., Yoshioka,S., Suzumiya,J., Kanda,M., and Kikuchi,M.,** Expressions of cyclin E, A, and B1 in Hodgkin and Reed-Sternberg cells: not suppressed by cyclin-dependent kinase inhibitor p21 expression. *Pathol.Int.* 1999. **49**: 506-512.
177. **Sanchez-Beato,M., Piris,M.A., Martinez-Montero,J.C., Garcia,J.F., Villuendas,R., Garcia,F.J., Orradre,J.L., and Martinez,P.,** MDM2 and p21WAF1/CIP1, wild-type p53-induced proteins, are regularly expressed by Sternberg-Reed cells in Hodgkin's disease. *J.Pathol.* 1996. **180**: 58-64.
178. **Tzankov,A., Zimpfer,A., Lugli,A., Krugmann,J., Went,P., Schraml,P., Maurer,R., Ascani,S., Pileri,S., Geley,S., and Dirnhofner,S.,** High-throughput tissue microarray analysis of G1-cyclin alterations in classical Hodgkin's lymphoma indicates overexpression of cyclin E1. *J.Pathol.* 2003. **199**: 201-207.
179. **Garcia,J.F., Camacho,F.I., Morente,M., Fraga,M., Montalban,C., Alvaro,T., Bellas,C., Castano,A., Diez,A., Flores,T., Martin,C., Martinez,M.A., Mazorra,F., Menarguez,J., Mestre,M.J., Mollejo,M., Saez,A.I., Sanchez,L., and Piris,M.A.,** Hodgkin and Reed-Sternberg cells harbor alterations in the major tumor suppressor pathways and cell-cycle checkpoints: analyses using tissue microarrays. *Blood* 2003. **101**: 681-689.

180. **Gerdes,J., Van Baarlen,J., Pileri,S., Schwarting,R., Van Unnik,J.A., and Stein,H.,** Tumor cell growth fraction in Hodgkin's disease. *Am.J.Pathol.* 1987. **128**: 390-393.
181. **Spruck,C.H., Won,K.A., and Reed,S.I.,** Deregulated cyclin E induces chromosome instability. *Nature* 1999. **401**: 297-300.
182. **Sanchez-Aguilera,A., Sanchez-Beato,M., Garcia,J.F., Prieto,I., Pollan,M., and Piris,M.A.,** p14(ARF) nuclear overexpression in aggressive B-cell lymphomas is a sensor of malfunction of the common tumor suppressor pathways. *Blood* 2002. **99**: 1411-1418.
183. **Barkett,M. and Gilmore,T.D.,** Control of apoptosis by Rel/NF-kappaB transcription factors. *Oncogene* 1999. **18**: 6910-6924.
184. **Giri,D.K. and Aggarwal,B.B.,** Constitutive activation of NF-kappaB causes resistance to apoptosis in human cutaneous T cell lymphoma HuT-78 cells. Autocrine role of tumor necrosis factor and reactive oxygen intermediates. *J.Biol.Chem.* 1998. **273**: 14008-14014.
185. **Nakshatri,H., Bhat-Nakshatri,P., Martin,D.A., Goulet,R.J., Jr., and Sledge,G.W., Jr.,** Constitutive activation of NF-kappaB during progression of breast cancer to hormone-independent growth. *Mol.Cell Biol.* 1997. **17**: 3629-3639.
186. **Chen,F.E. and Ghosh,G.,** Regulation of DNA binding by Rel/NF-kappaB transcription factors: structural views. *Oncogene* 1999. **18**: 6845-6852.
187. **Inoue,J., Kerr,L.D., Ransone,L.J., Bengal,E., Hunter,T., and Verma,I.M.,** c-rel activates but v-rel suppresses transcription from kappa B sites. *Proc.Natl.Acad.Sci.U.S.A* 1991. **88**: 3715-3719.
188. **Henkel,T., Machleidt,T., Alkalay,I., Kronke,M., Ben Neriah,Y., and Baeuerle,P.A.,** Rapid proteolysis of I kappa B-alpha is necessary for activation of transcription factor NF-kappa B. *Nature* 1993. **365**: 182-185.
189. **Miyamoto,S., Maki,M., Schmitt,M.J., Hatanaka,M., and Verma,I.M.,** Tumor necrosis factor alpha-induced phosphorylation of I kappa B alpha is a signal for its degradation but not dissociation from NF-kappa B. *Proc.Natl.Acad.Sci.U.S.A* 1994. **91**: 12740-12744.
190. **Naumann,M. and Scheidereit,C.,** Activation of NF-kappa B in vivo is regulated by multiple phosphorylations. *EMBO J.* 1994. **13**: 4597-4607.
191. **Mellits,K.H., Hay,R.T., and Goodbourn,S.,** Proteolytic degradation of MAD3 (I kappa B alpha) and enhanced processing of the NF-kappa B precursor p105 are obligatory steps in the activation of NF-kappa B. *Nucleic Acids Res.* 1993. **21**: 5059-5066.
192. **Gilmore,T.D.,** The Rel/NF-kappaB signal transduction pathway: introduction. *Oncogene* 1999. **18**: 6842-6844.

193. **Bargou,R.C., Leng,C., Krappmann,D., Emmerich,F., Mapara,M.Y., Bommert,K., Royer,H.D., Scheidereit,C., and Doerken,B.,** High-level nuclear NF-kappa B and Oct-2 is a common feature of cultured Hodgkin/Reed-Sternberg cells. *Blood* 1996. **87**: 4340-4347.
194. **Bargou,R.C., Emmerich,F., Krappmann,D., Bommert,K., Mapara,M.Y., Arnold,W., Royer,H.D., Grinstein,E., Greiner,A., Scheidereit,C., and Doerken,B.,** Constitutive nuclear factor-kappaB-RelA activation is required for proliferation and survival of Hodgkin's disease tumor cells. *J.Clin.Invest* 1997. **100**: 2961-2969.
195. **Krappmann,D., Emmerich,F., Kordes,U., Scharschmidt,E., Doerken,B., and Scheidereit,C.,** Molecular mechanisms of constitutive NF-kappaB/Rel activation in Hodgkin/Reed-Sternberg cells. *Oncogene* 1999. **18**: 943-953.
196. **Emmerich,F., Meiser,M., Hummel,M., Demel,G., Foss,H.D., Jundt,F., Mathas,S., Krappmann,D., Scheidereit,C., Stein,H., and Doerken,B.,** Overexpression of I kappa B alpha without inhibition of NF-kappaB activity and mutations in the I kappa B alpha gene in Reed-Sternberg cells. *Blood* 1999. **94**: 3129-3134.
197. **Emmerich,F., Theurich,S., Hummel,M., Haeffker,A., Vry,M.S., Dohner,K., Bommert,K., Stein,H., and Doerken,B.,** Inactivating I kappa B epsilon mutations in Hodgkin/Reed-Sternberg cells. *J.Pathol.* 2003. **201**: 413-420.
198. **Hinz,M., Loser,P., Mathas,S., Krappmann,D., Doerken,B., and Scheidereit,C.,** Constitutive NF-kappaB maintains high expression of a characteristic gene network, including CD40, CD86, and a set of antiapoptotic genes in Hodgkin/Reed-Sternberg cells. *Blood* 2001. **97**: 2798-2807.