

Supplemental references:

1. Børresen AL, Hovig E, Smith-Sørensen B, et al (1991) Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations. *Proc Natl Acad Sci U S A* 88:8405–8409. <https://doi.org/10.1073/pnas.88.19.8405>
2. Coles C, Condie A, Chetty U, et al (1992) p53 mutations in breast cancer. *Cancer Res* 52:5291–5298
3. Sommer SS, Cunningham J, McGovern RM, et al (1992) Pattern of p53 gene mutations in breast cancers of women of the midwestern United States. *J Natl Cancer Inst* 84:246–252. <https://doi.org/10.1093/jnci/84.4.246>
4. Tsuda H, Iwaya K, Fukutomi T, Hirohashi S (1993) p53 mutations and c-erbB-2 amplification in intraductal and invasive breast carcinomas of high histologic grade. *Jpn J Cancer Res* 84:394–401. <https://doi.org/10.1111/j.1349-7006.1993.tb00149.x>
5. Andersen TI, Holm R, Nesland JM, et al (1993) Prognostic significance of TP53 alterations in breast carcinoma. *Br J Cancer* 68:540–548. <https://doi.org/10.1038/bjc.1993.383>
6. Thorlacius S, Børresen AL, Eyfjörd JE (1993) Somatic p53 mutations in human breast carcinomas in an Icelandic population: a prognostic factor. *Cancer Res* 53:1637–1641
7. Cornelis RS, van Vliet M, Vos CB, et al (1994) Evidence for a gene on 17p13.3, distal to TP53, as a target for allele loss in breast tumors without p53 mutations. *Cancer Res* 54:4200–4206
8. Blaszyk H, Vaughn CB, Hartmann A, et al (1994) Novel pattern of p53 gene mutations in an American black cohort with high mortality from breast cancer. *Lancet (London, England)* 343:1195–1197. [https://doi.org/10.1016/s0140-6736\(94\)92403-1](https://doi.org/10.1016/s0140-6736(94)92403-1)
9. Umekita Y, Kobayashi K, Saheki T, Yoshida H (1994) Nuclear accumulation of p53 protein correlates with mutations in the p53 gene on archival paraffin-embedded tissues of human breast cancer. *Jpn J Cancer Res* 85:825–830. <https://doi.org/10.1111/j.1349-7006.1994.tb02954.x>
10. Tsuda H, Hirohashi S (1994) Association among p53 gene mutation, nuclear accumulation of the p53 protein and aggressive phenotypes in breast cancer. *Int J Cancer* 57:498–503. <https://doi.org/10.1002/ijc.2910570410>
11. Saitoh S, Cunningham J, De Vries EM, et al (1994) p53 gene mutations in breast cancers in midwestern US women: null as well as missense-type mutations are associated with poor prognosis. *Oncogene* 9:2869–2875
12. Hartmann A, Rosanelli G, Blaszyk H, et al (1995) Novel pattern of P53 mutation in breast cancers from Austrian women. *J Clin Invest* 95:686–689. <https://doi.org/10.1172/JCI117714>
13. Shiao YH, Chen VW, Scheer WD, et al (1995) Racial disparity in the association of p53 gene alterations with breast cancer survival. *Cancer Res* 55:1485–1490
14. Hartmann A, Blaszyk H, McGovern RM, et al (1995) p53 gene mutations inside and outside of exons 5-8: the patterns differ in breast and other cancers. *Oncogene* 10:681–688
15. Karameris AM, Worthy E, Gorgoulis VG, et al (1995) p53 gene alterations in special types of breast carcinoma: a molecular and immunohistochemical study in archival material. *J Pathol*

176:361–372. <https://doi.org/10.1002/path.1711760407>

16. Sato T, Okazaki A, Okazaki M, et al (1995) Detection of p53 gene mutations in aspiration biopsy specimens from suspected breast cancers by polymerase chain reaction-single strand conformation polymorphism analysis. *Jpn J Cancer Res* 86:140–145.
<https://doi.org/10.1111/j.1349-7006.1995.tb03031.x>
17. Thorlaci S, Thorgilsson B, Björnsson J, et al (1995) TP53 mutations and abnormal p53 protein staining in breast carcinomas related to prognosis. *Eur J Cancer* 31A:1856–1861.
[https://doi.org/10.1016/0959-8049\(95\)00399-4](https://doi.org/10.1016/0959-8049(95)00399-4)
18. Blaszyk H, Hartmann A, Tamura Y, et al (1996) Molecular epidemiology of breast cancers in northern and southern Japan: the frequency, clustering, and patterns of p53 gene mutations differ among these two low-risk populations. *Oncogene* 13:2159–2166
19. Aas T, Børresen AL, Geisler S, et al (1996) Specific P53 mutations are associated with de novo resistance to doxorubicin in breast cancer patients. *Nat Med* 2:811–814.
<https://doi.org/10.1038/nm0796-811>
20. Gretarsdottir S, Tryggvadottir L, Jonasson JG, et al (1996) TP53 mutation analyses on breast carcinomas: a study of paraffin-embedded archival material. *Br J Cancer* 74:555–561.
<https://doi.org/10.1038/bjc.1996.400>
21. Hartmann A, Blaszyk H, Saitoh S, et al (1996) High frequency of p53 gene mutations in primary breast cancers in Japanese women, a low-incidence population. *Br J Cancer* 73:896–901.
<https://doi.org/10.1038/bjc.1996.179>
22. Kovach JS, Hartmann A, Blaszyk H, et al (1996) Mutation detection by highly sensitive methods indicates that p53 gene mutations in breast cancer can have important prognostic value. *Proc Natl Acad Sci U S A* 93:1093–1096. <https://doi.org/10.1073/pnas.93.3.1093>
23. Chakravarty G, Redkar A, Mittra I (1996) A comparative study of detection of p53 mutations in human breast cancer by flow cytometry, single-strand conformation polymorphism and genomic sequencing. *Br J Cancer* 74:1181–1187. <https://doi.org/10.1038/bjc.1996.514>
24. Lou MA, Tseng SL, Chang SF, et al (1997) Novel patterns of p53 abnormality in breast cancer from Taiwan: experience from a low-incidence area. *Br J Cancer* 75:746–751.
<https://doi.org/10.1038/bjc.1997.132>
25. Valgardsdottir R, Tryggvadottir L, Steinarsdottir M, et al (1997) Genomic instability and poor prognosis associated with abnormal TP53 in breast carcinomas. Molecular and immunohistochemical analysis. *APMIS* 105:121–130. <https://doi.org/10.1111/j.1699-0463.1997.tb00550.x>
26. Zelada-Hedman M, Børresen-Dale AL, Claro A, et al (1997) Screening for TP53 mutations in patients and tumours from 109 Swedish breast cancer families. *Br J Cancer* 75:1201–1204.
<https://doi.org/10.1038/bjc.1997.205>
27. Günther T, Schneider-Stock R, Rys J, et al (1997) p53 gene mutations and expression of p53 and mdm2 proteins in invasive breast carcinoma. A comparative analysis with clinico-pathological factors. *J Cancer Res Clin Oncol* 123:388–394. <https://doi.org/10.1007/BF01240122>
28. Berns EM, van Staveren IL, Look MP, et al (1998) Mutations in residues of TP53 that directly

- contact DNA predict poor outcome in human primary breast cancer. *Br J Cancer* 77:1130–1136. <https://doi.org/10.1038/bjc.1998.187>
- 29. Lavarino C, Corletto V, Mezzelani A, et al (1998) Detection of TP53 mutation, loss of heterozygosity and DNA content in fine-needle aspirates of breast carcinoma. *Br J Cancer* 77:125–130. <https://doi.org/10.1038/bjc.1998.20>
 - 30. Williams C, Norberg T, Ahmadian A, et al (1998) Assessment of sequence-based p53 gene analysis in human breast cancer: messenger RNA in comparison with genomic DNA targets. *Clin Chem* 44:455–462
 - 31. Wernert N, Hügel A, Löcherbach C (1998) [Genetic alterations in the fibroblastic stroma of invasive colon and breast carcinomas]. *Verh Dtsch Ges Pathol* 82:317–321
 - 32. Kucera E, Speiser P, Gnant M, et al (1999) Prognostic significance of mutations in the p53 gene, particularly in the zinc-binding domains, in lymph node- and steroid receptor positive breast cancer patients. Austrian Breast Cancer Study Group. *Eur J Cancer* 35:398–405. [https://doi.org/10.1016/s0959-8049\(98\)00400-6](https://doi.org/10.1016/s0959-8049(98)00400-6)
 - 33. Gentile M, Bergman Jungeström M, Olsen KE, et al (1999) p53 and survival in early onset breast cancer: analysis of gene mutations, loss of heterozygosity and protein accumulation. *Eur J Cancer* 35:1202–1207. [https://doi.org/10.1016/s0959-8049\(99\)00121-5](https://doi.org/10.1016/s0959-8049(99)00121-5)
 - 34. Tanyi J, Tory K, Bánkfalvi A, et al (1999) Analysis of p53 mutation and cyclin D1 expression in breast tumors. *Pathol Oncol Res* 5:90–94. <https://doi.org/10.1053/poor.1999.0201>
 - 35. Tomita S, Muto Y, Kusano T, Toda T (1999) [Genetic alterations in human malignant tumor]. *Rinsho Byori* 47:20–26
 - 36. Patrinos GP, Garinis G, Kounelis S, et al (1999) A novel 23-bp deletion in exon 5 of the p53 tumor suppressor gene. *J Mol Med (Berl)* 77:686–689. <https://doi.org/10.1007/s001099900043>
 - 37. Maitra A, Tavassoli FA, Albores-Saavedra J, et al (1999) Molecular abnormalities associated with secretory carcinomas of the breast. *Hum Pathol* 30:1435–1440. [https://doi.org/10.1016/s0046-8177\(99\)90165-x](https://doi.org/10.1016/s0046-8177(99)90165-x)
 - 38. Alsner J, Yilmaz M, Guldberg P, et al (2000) Heterogeneity in the clinical phenotype of TP53 mutations in breast cancer patients. *Clin cancer Res an Off J Am Assoc Cancer Res* 6:3923–3931. <https://doi.org/10.1186/bcr109>
 - 39. Angelopoulou K, Yu H, Bharaj B, et al (2000) p53 gene mutation, tumor p53 protein overexpression, and serum p53 autoantibody generation in patients with breast cancer. *Clin Biochem* 33:53–62. [https://doi.org/10.1016/s0009-9120\(99\)00084-3](https://doi.org/10.1016/s0009-9120(99)00084-3)
 - 40. Kandioler-Eckersberger D, Ludwig C, Rudas M, et al (2000) TP53 mutation and p53 overexpression for prediction of response to neoadjuvant treatment in breast cancer patients. *Clin cancer Res an Off J Am Assoc Cancer Res* 6:50–56
 - 41. Gudlaugsdottir S, Sigurdardottir V, Snorradottir M, et al (2000) P53 mutations analysis in benign and malignant breast lesions: using needle rinses from fine-needle aspirations. *Diagn Cytopathol* 22:268–274. [https://doi.org/10.1002/\(sici\)1097-0339\(200005\)22:5<268::aid-dc2>3.0.co;2-x](https://doi.org/10.1002/(sici)1097-0339(200005)22:5<268::aid-dc2>3.0.co;2-x)
 - 42. Oh SJ, Jung JY, Shim SS, et al (2000) Identification of p53 gene mutations in breast cancers and

their effects on transcriptional activation function. *Mol Cells* 10:275–280

43. Kannan K, Krishnamurthy J, Feng J, et al (2000) Mutation profile of the p53, fhit, p16INK4a/p19ARF and H-ras genes in Indian breast carcinomas. *Int J Oncol* 17:1031–1035. <https://doi.org/10.3892/ijo.17.5.1031>
44. Kang JH, Kim SJ, Noh DY, et al (2001) The timing and characterization of p53 mutations in progression from atypical ductal hyperplasia to invasive lesions in the breast cancer. *J Mol Med (Berl)* 79:648–655. <https://doi.org/10.1007/s001090100269>
45. Geisler S, Lønning PE, Aas T, et al (2001) Influence of TP53 gene alterations and c-erbB-2 expression on the response to treatment with doxorubicin in locally advanced breast cancer. *Cancer Res* 61:2505–2512
46. Janschek E, Kandioler-Eckersberger D, Ludwig C, et al (2001) Contralateral breast cancer: molecular differentiation between metastasis and second primary cancer. *Breast Cancer Res Treat* 67:1–8. <https://doi.org/10.1023/a:1010661514306>
47. Buzin CH, Tang SH, Cunningham JM, et al (2001) Low frequency of p53 gene mutations in breast cancers of Japanese-American women. *Nutr Cancer* 39:72–77. https://doi.org/10.1207/S15327914nc391_10
48. Kang JH, Kim SJ, Noh DY, et al (2001) Methylation in the p53 promoter is a supplementary route to breast carcinogenesis: correlation between CpG methylation in the p53 promoter and the mutation of the p53 gene in the progression from ductal carcinoma in situ to invasive ductal carcinoma. *Lab Invest* 81:573–579. <https://doi.org/10.1038/labinvest.3780266>
49. Stenmark-Askmalm M, Gentile M, Wingren S, Ståhl O (2001) Protein accumulation and gene mutation of p53 in bilateral breast cancer. South-East Sweden Breast Cancer Group. *Acta Oncol* 40:56–62. <https://doi.org/10.1080/028418601750071064>
50. Wang X, Mori I, Tang W, et al (2001) Metaplastic carcinoma of the breast: p53 analysis identified the same point mutation in the three histologic components. *Mod Pathol: an Off J United States Can Acad Pathol Inc* 14:1183–1186. <https://doi.org/10.1038/modpathol.3880456>
51. Conway K, Edmiston SN, Cui L, et al (2002) Prevalence and spectrum of p53 mutations associated with smoking in breast cancer. *Cancer Res* 62:1987–1995
52. Langerød A, Bukholm IRK, Bregård A, et al (2002) The TP53 codon 72 polymorphism may affect the function of TP53 mutations in breast carcinomas but not in colorectal carcinomas. *Cancer Epidemiol biomarkers Prev: a Publ Am Assoc Cancer Res cosponsored by Am Soc Prev Oncol* 11:1684–1688
53. Tessitore A, Di Rocco ZC, Cannita K, et al (2002) High sensitivity of detection of TP53 somatic mutations by fluorescence-assisted mismatch analysis. *Genes Chromosomes Cancer* 35:86–91. <https://doi.org/10.1002/gcc.10102>
54. Seitz S, Wassmuth P, Fischer J, et al (2002) Mutation analysis and mRNA expression of trail-receptors in human breast cancer. *Int J cancer* 102:117–128. <https://doi.org/10.1002/ijc.10694>
55. Nagai MA, Schaer Barbosa H, Zago MA, et al (2003) TP53 mutations in primary breast carcinomas from white and African-Brazilian patients. *Int J Oncol* 23:189–196

56. Bukholm IRK, Husdal A, Nesland JM, et al (2003) Overexpression of cyclin A overrides the effect of p53 alterations in breast cancer patients with long follow-up time. *Breast Cancer Res Treat* 80:199–206. <https://doi.org/10.1023/A:1024527220362>
57. Geisler S, Børresen-Dale A-L, Johnsen H, et al (2003) TP53 gene mutations predict the response to neoadjuvant treatment with 5-fluorouracil and mitomycin in locally advanced breast cancer. *Clin cancer Res an Off J Am Assoc Cancer Res* 9:5582–5588
58. Sekido Y, Umemura S, Takekoshi S, et al (2003) Heterogeneous gene alterations in primary breast cancer contribute to discordance between primary and asynchronous metastatic/recurrent sites: HER2 gene amplification and p53 mutation. *Int J Oncol* 22:1225–1232
59. Sensi E, Tancredi M, Aretini P, et al (2003) p53 inactivation is a rare event in familial breast tumors negative for BRCA1 and BRCA2 mutations. *Breast Cancer Res Treat* 82:1–9. <https://doi.org/10.1023/B:BREA.0000003836.91844.b5>
60. Reifenberger J, Rauch L, Beckmann MW, et al (2003) Cowden's disease: clinical and molecular genetic findings in a patient with a novel PTEN germline mutation. *Br J Dermatol* 148:1040–1046. <https://doi.org/10.1046/j.1365-2133.2003.05322.x>
61. Chen F-M, Hou M-F, Wang J-Y, et al (2004) High frequency of G/C transversion on p53 gene alterations in breast cancers from Taiwan. *Cancer Lett* 207:59–67. <https://doi.org/10.1016/j.canlet.2003.12.005>
62. Jong Y-J, Li L-H, Tsou M-H, et al (2004) Chromosomal comparative genomic hybridization abnormalities in early- and late-onset human breast cancers: correlation with disease progression and TP53 mutations. *Cancer Genet Cytogenet* 148:55–65. [https://doi.org/10.1016/s0165-4608\(03\)00205-x](https://doi.org/10.1016/s0165-4608(03)00205-x)
63. Lien H-C, Lin C-W, Mao T-L, et al (2004) p53 overexpression and mutation in metaplastic carcinoma of the breast: genetic evidence for a monoclonal origin of both the carcinomatous and the heterogeneous sarcomatous components. *J Pathol* 204:131–139. <https://doi.org/10.1002/path.1624>
64. Hedau S, Jain N, Husain SA, et al (2004) Novel germline mutations in breast cancer susceptibility genes BRCA1, BRCA2 and p53 gene in breast cancer patients from India. *Breast Cancer Res Treat* 88:177–186. <https://doi.org/10.1007/s10549-004-0593-8>
65. Lord GM, Hollstein M, Arlt VM, et al (2004) DNA adducts and p53 mutations in a patient with aristolochic acid-associated nephropathy. *Am J Kidney Dis Off J Natl Kidney Found* 43:e11–7. <https://doi.org/10.1053/j.ajkd.2003.11.024>
66. Kleivi K, Diep CB, Pandis N, et al (2005) TP53 mutations are associated with a particular pattern of genomic imbalances in breast carcinomas. *J Pathol* 207:14–19. <https://doi.org/10.1002/path.1812>
67. Kalemi TG, Lambropoulos AF, Gueorguiev M, et al (2005) The association of p53 mutations and p53 codon 72, Her 2 codon 655 and MTHFR C677T polymorphisms with breast cancer in Northern Greece. *Cancer Lett* 222:57–65. <https://doi.org/10.1016/j.canlet.2004.11.025>
68. Olivier M, Langerød A, Carrieri P, et al (2006) The clinical value of somatic TP53 gene mutations in 1,794 patients with breast cancer. *Clin Cancer Res*. <https://doi.org/10.1158/1078-0432.CCR-05-1029>

69. Boersma BJ, Howe TM, Goodman JE, et al (2006) Association of breast cancer outcome with status of p53 and MDM2 SNP309. *J Natl Cancer Inst* 98:911–919.
<https://doi.org/10.1093/jnci/djj245>
70. Han B, Mori I, Nakamura M, et al (2006) Myoepithelial carcinoma arising in an adenomyoepithelioma of the breast: case report with immunohistochemical and mutational analysis. *Pathol Int* 56:211–216. <https://doi.org/10.1111/j.1440-1827.2006.01948.x>
71. Langerød A, Zhao H, Borgen Ø, et al (2007) TP53 mutation status and gene expression profiles are powerful prognostic markers of breast cancer. *Breast Cancer Res* 9:R30.
<https://doi.org/10.1186/bcr1675>
72. Ooe A, Kato K, Noguchi S (2007) Possible involvement of CCT5, RGS3, and YKT6 genes up-regulated in p53-mutated tumors in resistance to docetaxel in human breast cancers. *Breast Cancer Res Treat* 101:305–315. <https://doi.org/10.1007/s10549-006-9293-x>
73. Patocs A, Zhang L, Xu Y, et al (2007) Breast-cancer stromal cells with TP53 mutations and nodal metastases. *N Engl J Med* 357:2543–2551. <https://doi.org/10.1056/NEJMoa071825>
74. Eachkoti R, Hussain I, Afrose D, et al (2007) BRCA1 and TP53 mutation spectrum of breast carcinoma in an ethnic population of Kashmir, an emerging high-risk area. *Cancer Lett* 248:308–320. <https://doi.org/10.1016/j.canlet.2006.08.012>
75. Xu Y, Yao L, Zhao A, et al (2008) Effect of p53 codon 72 genotype on breast cancer survival depends on p53 gene status. *Int J Cancer* 122:2761–2766. <https://doi.org/10.1002/ijc.23454>
76. Chrisanthar R, Knappskog S, Løkkevik E, et al (2008) CHEK2 mutations affecting kinase activity together with mutations in TP53 indicate a functional pathway associated with resistance to epirubicin in primary breast cancer. *PLoS One* 3:e3062.
<https://doi.org/10.1371/journal.pone.0003062>
77. Susmitsin EN, Due EU, Vu P, et al (2008) TP53 mutations in synchronous and metachronous bilateral breast carcinomas. *Cancer Genet. Cytogenet.* 184:119–121
78. Colombo M, Giarola M, Mariani L, et al (2008) Cyclin D1 expression analysis in familial breast cancers may discriminate BRCA1 from BRCA2-linked cases. *Mod Pathol* an Off J United States Can Acad Pathol Inc 21:1262–1270. <https://doi.org/10.1038/modpathol.2008.43>
79. Zhou W, Muggerud AA, Vu P, et al (2009) Full sequencing of TP53 identifies identical mutations within in situ and invasive components in breast cancer suggesting clonal evolution. *Mol Oncol* 3:214–219. <https://doi.org/10.1016/j.molonc.2009.03.001>
80. (2012) Comprehensive molecular portraits of human breast tumours. *Nature* 490:61–70.
<https://doi.org/10.1038/nature11412>
81. Banerji S, Cibulskis K, Rangel-Escareno C, et al (2012) Sequence analysis of mutations and translocations across breast cancer subtypes. *Nature* 486:405–409.
<https://doi.org/10.1038/nature11154>
82. Stephens PJ, Tarpey PS, Davies H, et al (2012) The landscape of cancer genes and mutational processes in breast cancer. *Nature* 486:400–404. <https://doi.org/10.1038/nature11017>
83. Pereira B, Chin S-F, Rueda OM, et al (2016) The somatic mutation profiles of 2,433 breast cancers

- refines their genomic and transcriptomic landscapes. *Nat Commun* 7:11479. <https://doi.org/10.1038/ncomms11479>
84. Li G, Guo X, Chen M, et al (2018) Prevalence and spectrum of AKT1, PIK3CA, PTEN and TP53 somatic mutations in Chinese breast cancer patients. *PLoS One* 13:e0203495. <https://doi.org/10.1371/journal.pone.0203495>
85. Kan Z, Ding Y, Kim J, et al (2018) Multi-omics profiling of younger Asian breast cancers reveals distinctive molecular signatures. *Nat Commun* 9:1725. <https://doi.org/10.1038/s41467-018-04129-4>
86. Yap Y-S, Singh AP, Lim JHC, et al (2018) Elucidating therapeutic molecular targets in premenopausal Asian women with recurrent breast cancers. *NPJ breast cancer* 4:19. <https://doi.org/10.1038/s41523-018-0070-x>
87. Heong V, Syn NL, Lee XW, et al (2018) Value of a molecular screening program to support clinical trial enrollment in Asian cancer patients: The Integrated Molecular Analysis of Cancer (IMAC) Study. *Int J cancer* 142:1890–1900. <https://doi.org/10.1002/ijc.31091>
88. Zhang G, Wang Y, Chen B, et al (2019) Characterization of frequently mutated cancer genes in Chinese breast tumors: a comparison of Chinese and TCGA cohorts. *Ann Transl Med*. <https://doi.org/10.21037/atm.2019.04.23>
89. Wang S, Pitt JJ, Zheng Y, et al (2019) Germline variants and somatic mutation signatures of breast cancer across populations of African and European ancestry in the US and Nigeria. *Int J cancer* 145:3321–3333. <https://doi.org/10.1002/ijc.32498>
90. Yi D, Xu L, Luo J, et al (2019) Germline TP53 and MSH6 mutations implicated in sporadic triple-negative breast cancer (TNBC): a preliminary study. *Hum Genomics* 13:4. <https://doi.org/10.1186/s40246-018-0186-y>
91. Chang C-S, Kitamura E, Johnson J, et al (2019) Genomic analysis of racial differences in triple negative breast cancer. *Genomics* 111:1529–1542. <https://doi.org/10.1016/j.ygeno.2018.10.010>
92. Powers J, Pinto EM, Barnoud T, et al (2020) A Rare TP53 Mutation Predominant in Ashkenazi Jews Confers Risk of Multiple Cancers. *Cancer Res* 80:3732–3744. <https://doi.org/10.1158/0008-5472.CAN-20-1390>
93. Bouaoun L, Sonkin D, Ardin M, et al (2016) TP53 Variations in Human Cancers: New Lessons from the IARC TP53 Database and Genomics Data. *Hum Mutat*. <https://doi.org/10.1002/humu.23035>
94. Slovackova J, Grochova D, Navratilova J, et al (2010) Transactivation by temperature-dependent p53 mutants in yeast and human cells. *Cell Cycle* 9:2141–2148. <https://doi.org/10.4161/cc.9.11.11808>
95. Jordan JJ, Inga A, Conway K, et al (2010) Altered-function p53 missense mutations identified in breast cancers can have subtle effects on transactivation. *Mol Cancer Res* 8:701–716. <https://doi.org/10.1158/1541-7786.MCR-09-0442>
96. Voropaeva EN, Pospelova TI, Voevodina MI, Maksimov VN (2017) [Frequency, spectrum, and functional significance of TP53 mutations in patients with diffuse large B-cell lymphoma]. *Mol Biol (Mosk)* 51:64–72. <https://doi.org/10.7868/S0026898416060227>

97. Li C-L, Yeh K-H, Liu W-H, et al (2015) Elevated p53 promotes the processing of miR-18a to decrease estrogen receptor- α in female hepatocellular carcinoma. *Int J cancer* 136:761–770. <https://doi.org/10.1002/ijc.29052>
98. Gonin-Laurent N, Gibaud A, Huygue M, et al (2006) Specific TP53 mutation pattern in radiation-induced sarcomas. *Carcinogenesis* 27:1266–1272. <https://doi.org/10.1093/carcin/bgi356>
99. O'Farrell TJ, Ghosh P, Dobashi N, et al (2004) Comparison of the effect of mutant and wild-type p53 on global gene expression. *Cancer Res* 64:8199–8207. <https://doi.org/10.1158/0008-5472.CAN-03-3639>
100. Christgen M, Noskowicz M, Heil C, et al (2012) IPH-926 lobular breast cancer cells harbor a p53 mutant with temperature-sensitive functional activity and allow for profiling of p53-responsive genes. *Lab Invest* 92:1635–1647. <https://doi.org/10.1038/labinvest.2012.126>
101. Göhler T, Jäger S, Warnecke G, et al (2005) Mutant p53 proteins bind DNA in a DNA structure-selective mode. *Nucleic Acids Res* 33:1087–1100. <https://doi.org/10.1093/nar/gki252>
102. Bartussek C, Naumann U, Weller M (1999) Accumulation of mutant p53(V143A) modulates the growth, clonogenicity, and radiochemosensitivity of malignant glioma cells independent of endogenous p53 status. *Exp Cell Res* 253:432–439. <https://doi.org/10.1006/excr.1999.4654>
103. Joerger AC, Ang HC, Fersht AR (2006) Structural basis for understanding oncogenic p53 mutations and designing rescue drugs. *Proc Natl Acad Sci U S A* 103:15056–15061. <https://doi.org/10.1073/pnas.0607286103>
104. Kang HJ, Chun S-M, Kim K-R, et al (2013) Clinical relevance of gain-of-function mutations of p53 in high-grade serous ovarian carcinoma. *PLoS One* 8:e72609. <https://doi.org/10.1371/journal.pone.0072609>
105. Monti P, Campomenosi P, Ciribilli Y, et al (2003) Characterization of the p53 mutants ability to inhibit p73 beta transactivation using a yeast-based functional assay. *Oncogene* 22:5252–5260. <https://doi.org/10.1038/sj.onc.1206511>
106. Marutani M, Tonoki H, Tada M, et al (1999) Dominant-negative mutations of the tumor suppressor p53 relating to early onset of glioblastoma multiforme. *Cancer Res* 59:4765–4769
107. Barta JA, Pauley K, Kossenkov A V, McMahon SB (2020) The lung-enriched p53 mutants V157F and R158L/P regulate a gain of function transcriptome in lung cancer. *Carcinogenesis* 41:67–77. <https://doi.org/10.1093/carcin/bgz087>
108. Cardellino U, Ciribilli Y, Andreotti V, et al (2007) Transcriptional properties of feline p53 and its tumour-associated mutants: a yeast-based approach. *Mutagenesis* 22:417–423. <https://doi.org/10.1093/mutage/gem038>
109. Yamamoto S, Iwakuma T (2018) Regulators of Oncogenic Mutant TP53 Gain of Function. *Cancers (Basel)* 11:. <https://doi.org/10.3390/cancers11010004>
110. Berge EO, Huun J, Lillehaug JR, et al (2013) Functional characterisation of p53 mutants identified in breast cancers with suboptimal responses to anthracyclines or mitomycin. *Biochim Biophys Acta* 1830:2790–2797. <https://doi.org/10.1016/j.bbagen.2012.12.004>
111. Xie X, Lozano G, Siddik ZH (2016) Heterozygous p53(V172F) mutation in cisplatin-resistant human

- tumor cells promotes MDM4 recruitment and decreases stability and transactivity of p53. *Oncogene* 35:4798–4806. <https://doi.org/10.1038/onc.2016.12>
112. Ryan KM, Vousden KH (1998) Characterization of structural p53 mutants which show selective defects in apoptosis but not cell cycle arrest. *Mol Cell Biol* 18:3692–3698. <https://doi.org/10.1128/mcb.18.7.3692>
 113. Solomon H, Buganim Y, Kogan-Sakin I, et al (2012) Various p53 mutant proteins differently regulate the Ras circuit to induce a cancer-related gene signature. *J Cell Sci* 125:3144–3152. <https://doi.org/10.1242/jcs.099663>
 114. West AN, Ribeiro RC, Jenkins J, et al (2006) Identification of a novel germ line variant hotspot mutant p53-R175L in pediatric adrenal cortical carcinoma. *Cancer Res* 66:5056–5062. <https://doi.org/10.1158/0008-5472.CAN-05-4580>
 115. Xu-Monette ZY, Wu L, Visco C, et al (2012) Mutational profile and prognostic significance of TP53 in diffuse large B-cell lymphoma patients treated with R-CHOP: report from an International DLBCL Rituximab-CHOP Consortium Program Study. *Blood* 120:3986–3996. <https://doi.org/10.1182/blood-2012-05-433334>
 116. Mullany LK, Wong K-K, Marciano DC, et al (2015) Specific TP53 Mutants Overrepresented in Ovarian Cancer Impact CNV, TP53 Activity, Responses to Nutlin-3a, and Cell Survival. *Neoplasia* 17:789–803. <https://doi.org/10.1016/j.neo.2015.10.003>
 117. Kato S, Han S-Y, Liu W, et al (2003) Understanding the function-structure and function-mutation relationships of p53 tumor suppressor protein by high-resolution missense mutation analysis. *Proc Natl Acad Sci U S A* 100:8424–8429. <https://doi.org/10.1073/pnas.1431692100>
 118. Ahn J, Poyurovsky M V, Baptiste N, et al (2009) Dissection of the sequence-specific DNA binding and exonuclease activities reveals a superactive yet apoptotically impaired mutant p53 protein. *Cell Cycle* 8:1603–1615. <https://doi.org/10.4161/cc.8.10.8548>
 119. Martynova E, Pozzi S, Basile V, et al (2012) Gain-of-function p53 mutants have widespread genomic locations partially overlapping with p63. *Oncotarget* 3:132–143. <https://doi.org/10.18632/oncotarget.447>
 120. Suchánková J, Legartová S, Ručková E, et al (2017) Mutations in the TP53 gene affected recruitment of 53BP1 protein to DNA lesions, but level of 53BP1 was stable after γ-irradiation that depleted MDC1 protein in specific TP53 mutants. *Histochem Cell Biol* 148:239–255. <https://doi.org/10.1007/s00418-017-1567-3>
 121. Ticha I, Hojny J, Michalkova R, et al (2019) A comprehensive evaluation of pathogenic mutations in primary cutaneous melanomas, including the identification of novel loss-of-function variants. *Sci Rep* 9:17050. <https://doi.org/10.1038/s41598-019-53636-x>
 122. Lai J-C, Cheng Y-W, Goan Y-G, et al (2008) Promoter methylation of O(6)-methylguanine-DNA-methyltransferase in lung cancer is regulated by p53. *DNA Repair (Amst)* 7:1352–1363. <https://doi.org/10.1016/j.dnarep.2008.04.016>
 123. Friedler A, Veprintsev DB, Hansson LO, Fersht AR (2003) Kinetic instability of p53 core domain mutants: implications for rescue by small molecules. *J Biol Chem* 278:24108–24112. <https://doi.org/10.1074/jbc.M302458200>

124. Tsuchiya K (2000) [Functional restoration of tumor suppressor p53 alters susceptibility of glioblastoma cells to irradiation--analysis using a cell line containing a temperature-sensitive mutant]. *Hokkaido Igaku Zasshi* 75:265–274
125. Dong P, Tada M, Hamada J-I, et al (2007) p53 dominant-negative mutant R273H promotes invasion and migration of human endometrial cancer HHUA cells. *Clin Exp Metastasis* 24:471–483. <https://doi.org/10.1007/s10585-007-9084-8>
126. Jia LQ, Osada M, Ishioka C, et al (1997) Screening the p53 status of human cell lines using a yeast functional assay. *Mol Carcinog* 19:243–253. [https://doi.org/10.1002/\(sici\)1098-2744\(199708\)19:4<243::aid-mc5>3.0.co;2-d](https://doi.org/10.1002/(sici)1098-2744(199708)19:4<243::aid-mc5>3.0.co;2-d)
127. Pavlova S, Mayer J, Koukalova H, Smardova J (2003) High frequency of temperature-sensitive mutations of p53 tumor suppressor in acute myeloid leukemia revealed by functional assay in yeast. *Int J Oncol* 23:121–131
128. Zerdoumi Y, Lanos R, Raad S, et al (2017) Germline TP53 mutations result into a constitutive defect of p53 DNA binding and transcriptional response to DNA damage. *Hum Mol Genet* 26:2591–2602. <https://doi.org/10.1093/hmg/ddx106>
129. Yu X, Blanden AR, Narayanan S, et al (2014) Small molecule restoration of wildtype structure and function of mutant p53 using a novel zinc-metallochaperone based mechanism. *Oncotarget* 5:8879–8892. <https://doi.org/10.18632/oncotarget.2432>
130. Liu S, Kumari S, Hu Q, et al (2017) A comprehensive analysis of coregulator recruitment, androgen receptor function and gene expression in prostate cancer. *eLife* 6:. <https://doi.org/10.7554/eLife.28482>
131. Jia S, Zhao L, Tang W, Luo Y (2012) The gain of function of p53 mutant p53S in promoting tumorigenesis by cross-talking with H-RasV12. *Int J Biol Sci* 8:596–605. <https://doi.org/10.7150/ijbs.4176>
132. Lokshin M, Li Y, Gaiddon C, Prives C (2007) p53 and p73 display common and distinct requirements for sequence specific binding to DNA. *Nucleic Acids Res* 35:340–352. <https://doi.org/10.1093/nar/gkl1047>
133. Davies AJ, Lee AM, Taylor C, et al (2005) A limited role for TP53 mutation in the transformation of follicular lymphoma to diffuse large B-cell lymphoma. *Leukemia* 19:1459–1465. <https://doi.org/10.1038/sj.leu.2403802>
134. Kramer AC, Weber J, Zhang Y, et al (2017) TP53 Modulates Oxidative Stress in Gata1(+) Erythroid Cells. *Stem cell reports* 8:360–372. <https://doi.org/10.1016/j.stemcr.2016.12.025>
135. Quinn EA, Maciaszek JL, Pinto EM, et al (2019) From uncertainty to pathogenicity: clinical and functional interrogation of a rare TP53 in-frame deletion. *Cold Spring Harb Mol case Stud* 5:. <https://doi.org/10.1101/mcs.a003921>
136. Jagosova J, Pitrova L, Slovackova J, et al (2012) Transactivation and reactivation capabilities of temperature-dependent p53 mutants in yeast and human cells. *Int J Oncol* 41:1157–1163. <https://doi.org/10.3892/ijo.2012.1520>
137. Nenutil R, Smardova J, Pavlova S, et al (2005) Discriminating functional and non-functional p53 in human tumours by p53 and MDM2 immunohistochemistry. *J Pathol* 207:251–259.

<https://doi.org/10.1002/path.1838>

138. Fulci G, Ishii N, Maurici D, et al (2002) Initiation of human astrocytoma by clonal evolution of cells with progressive loss of p53 functions in a patient with a 283H TP53 germ-line mutation: evidence for a precursor lesion. *Cancer Res* 62:2897–2905
139. Vaughan CA, Frum R, Pearsall I, et al (2012) Allele specific gain-of-function activity of p53 mutants in lung cancer cells. *Biochem Biophys Res Commun* 428:6–10.
<https://doi.org/10.1016/j.bbrc.2012.09.029>
140. Dearth LR, Qian H, Wang T, et al (2007) Inactive full-length p53 mutants lacking dominant wild-type p53 inhibition highlight loss of heterozygosity as an important aspect of p53 status in human cancers. *Carcinogenesis* 28:289–298. <https://doi.org/10.1093/carcin/bgl132>
141. Li J, Yang L, Gaur S, et al (2014) Mutants TP53 p.R273H and p.R273C but not p.R273G enhance cancer cell malignancy. *Hum Mutat* 35:575–584. <https://doi.org/10.1002/humu.22528>
142. Ko J-L, Chiao M-C, Chang S-L, et al (2002) A novel p53 mutant retained functional activity in lung carcinomas. *DNA Repair (Amst)* 1:755–762. [https://doi.org/10.1016/s1568-7864\(02\)00094-0](https://doi.org/10.1016/s1568-7864(02)00094-0)
143. Di Como CJ, Prives C (1998) Human tumor-derived p53 proteins exhibit binding site selectivity and temperature sensitivity for transactivation in a yeast-based assay. *Oncogene* 16:2527–2539. <https://doi.org/10.1038/sj.onc.1202041>
144. Buzek J, Latonen L, Kurki S, et al (2002) Redox state of tumor suppressor p53 regulates its sequence-specific DNA binding in DNA-damaged cells by cysteine 277. *Nucleic Acids Res* 30:2340–2348. <https://doi.org/10.1093/nar/30.11.2340>
145. Noureddine MA, Menendez D, Campbell MR, et al (2009) Probing the functional impact of sequence variation on p53-DNA interactions using a novel microsphere assay for protein-DNA binding with human cell extracts. *PLoS Genet* 5:e1000462.
<https://doi.org/10.1371/journal.pgen.1000462>
146. Wang B, Niu D, Lam TH, et al (2014) Mapping the p53 transcriptome universe using p53 natural polymorphs. *Cell Death Differ* 21:521–532. <https://doi.org/10.1038/cdd.2013.132>
147. Menendez D, Inga A, Resnick MA (2006) The biological impact of the human master regulator p53 can be altered by mutations that change the spectrum and expression of its target genes. *Mol Cell Biol* 26:2297–2308. <https://doi.org/10.1128/MCB.26.6.2297-2308.2006>
148. Zhou R, Xu A, Wang D, et al (2018) A homozygous p53 R282W mutant human embryonic stem cell line generated using TALEN-mediated precise gene editing. *Stem Cell Res* 27:131–135.
<https://doi.org/10.1016/j.scr.2018.01.035>
149. Lang V, Pallara C, Zabala A, et al (2014) Tetramerization-defects of p53 result in aberrant ubiquitylation and transcriptional activity. *Mol Oncol* 8:1026–1042.
<https://doi.org/10.1016/j.molonc.2014.04.002>
150. Kamada R, Nomura T, Anderson CW, Sakaguchi K (2011) Cancer-associated p53 tetramerization domain mutants: quantitative analysis reveals a low threshold for tumor suppressor inactivation. *J Biol Chem* 286:252–258. <https://doi.org/10.1074/jbc.M110.174698>
151. Kawaguchi T, Kato S, Otsuka K, et al (2005) The relationship among p53 oligomer formation,

structure and transcriptional activity using a comprehensive missense mutation library.
Oncogene 24:6976–6981. <https://doi.org/10.1038/sj.onc.1208839>