

Supplementary table 3 Results of the blood p53 functional assay in individuals with wild-type *TP53* genotype or with germline *TP53* variants

Individual (sex, age) <i>TP53</i> variation ^a	Index case / relative	Clinical presentation ^b	Blood p53 functional assay					
			RT-QMPSF		RT-MLPA		Mean values	
			p53 score	mRNA (%)	p53 score	mRNA (%)	p53 score	mRNA (%)
<i>Individuals with wild-type TP53 genotype</i>								
1. (F, 45)	Index case	Bilat. breast cancer (30, 45)	13.9	89	11.1	79	12.5	84
2. (F, 32)	Index case	ACC (31)	10.5	84	10.6	100	10.6	92
3. (F, 31)	Index case	Glioblastoma (31)	13.8	99	10.4	92	12.1	96
4. (F, 34)	Index case	Breast cancer (34)	9.8	94	8.0	80	8.9	87
5. (M, 17)	Relative	Unaffected	11.0	110	10.2	114	10.6	112
6. (F, 61)	Relative	Unaffected	15.5	81	13.7	90	14.6	86
7. (F, 2)	Index case	ACC (2)	12.8	126	12.8	108	12.8	117
8. (F, 46)	Index case	Breast cancer (34)	8.2	114	7.3	85	7.8	100
9. (F, 47)	Index case	RMS (12), Breast cancer (47)	9.8	81	10.2	83	10.0	82
10. (F, 29)	Index case	Breast cancer (27)	12.1	90	12.1	100	12.1	95
11. (H, 63)	Relative	Unaffected	8.4	81	6.5	87	7.5	84
12. (F, 36)	Index case	Breast cancer (34)	11.7	81	8.9	84	10.3	83
13. (F, 44)	Index case	Lung cancer (30,43)	16.6	70	11.5	77	14.1	74
14. (F, 31)	Index case	Lung cancer (31)	22.5	95	10.5	95	16.5	95
15. (M, 8)	Relative	Unaffected	12.7	82	16.5	101	14.6	92
16. (F, 16)	Index case	Lymphoma (7), CNS sarcoma (16)	31.4	111	14.1	110	22.8	111
17. (M, 41)	Index case	Liposarcoma (31)	13.6	88	12.4	89	13.0	89
18. (M, 14)	Relative	Unaffected	18.2	94	12.6	96	15.4	95
19. (F, 66)	Index case	Breast cancer (48), Liposarcoma (65)	9.7	74	7.0	81	8.4	78
20. (F, 34)	Index case	Breast cancer (33)	12.1	78	13.9	93	13.0	86
21. (F, 36)	Index case	Breast cancer (34)	11.5	99	10.0	97	10.8	98
22. (F, 31)	Index case	Breast cancer (31)	14.9	100	10.9	87	12.9	94
23. (F, 68)	Relative	Unaffected	9.4	73	9.3	85	9.4	79
24. (F, 31)	Index case	Breast cancer (31)	13.5	64	9.9	92	11.7	78
25. (M, 18)	Relative	Unaffected	10.1	89	12	105	11.1	97
26. (M,19)	Relative	Unaffected	11	90	8.9	78	10.0	84
27. (F, 57)	Relative	Head Neck cancer (52)	18.2	131	11.2	113	14.7	122
28 (F, 71)	Relative	Lung cancer (71)	10.8	94	19.4	106	15.1	100
29. (F, 34)	Index case	Breast cancer (34)	21.0	81	15.1	96	18.1	89
30. (F, 61)	Index case	Breast cancer (35)	9.4	91	6.6	114	8.0	103
31. (F, 4)	Index case	RMS (8 months)	16.2	118	12.1	113	14.2	116
32. (F, 72)	Relative	Unaffected	9.0	94	7.6	85	8.3	90
33. (F, 46)	Relative	Unaffected	10.3	87	13.6	83	12.0	85
34. (M, 14)	Index case	Medulloblastoma (4)	12.0	89	11.4	90	11.7	90
35. (F, 20)	Index case	Colon cancer (19)	17.3	81	17.4	79	17.4	80
36. (M, 16)	Index case	Sarcoma (15)	10.6	89	11.5	115	11.1	102
37. (M, 13)	Index case	RMS (4)	20.8	81	18.6	91	19.7	86
38. (F, 28)	Index case	Breast cancer (28)	17.0	96	17.3	85	17.2	91
39. (F, 29)	Index case	Breast cancer (28)	10.1	78	12.1	89	11.1	84
40. (F, 24)	Index case	ACC (24)	9.6	77	11.1	80	10.4	79
41. (F, 30)	Index case	Breast cancer (30)	13.1	87	17.1	88	15.1	88
42. (F, 39)	Index case	Breast cancer (31)	8.3	71	9.0	78	8.7	75
43. (F, 33)	Index case	Breast cancer (33)	9.0	75	9.1	92	9.1	84
44. (F, 33)	Index case	Breast cancer (31)	11.7	115	7.8	114	9.8	115
45. (F, 36)	Index case	Breast cancer (29)	20.4	114	18.1	135	19.3	125
46. (F, 47)	Index case	Breast cancer (25)	18.4	105	12.4	93	15.4	99

47. (F, 6)	Relative	Unaffected	18.3	94	14.2	95	16.3	95
48. (M, 54)	Index case	Leiomyosarcoma (34)	11.8	91	11.8	84	11.8	88
49. (F, 32)	Index case	Breast cancer (32)	12.7	82	11.9	88	12.3	85
50. F, 26)	Index case	Breast cancer (26)	16.9	87	15.0	122	16.0	105
51. (F, 42)	Index case	ACC (42)	16.0	75	13.3	128	14.7	102
<i>Individuals with pathogenic/likely pathogenic TP53 variants</i>								
52. (F, 15) c.524G>A, p.(Arg175His)	Index case	Osteosarcoma (14)	3.1	88	3.2	103	3.2	96
53. (F, 65) c.542G>A, p.(Arg181His)	Index case	Breast cancer (65)	3.7	80	3.8	81	3.8	81
54. (M, 6) c.844C>T, p.(Arg282Trp)	Relative	Unaffected	4.7	92	4.9	112	4.8	102
55. (F, 44) c.844C>T, p.(Arg282Trp)	Relative	Bilat. breast cancer (32, 33)	6.2	100	3.7	95	5.0	98
56. (F, 58) c.1010G>A, p.(Arg337His)	Relative	Unaffected	5.0	103	5.8	99	5.4	101
57. (M, 62) c.375G>A, p.? Splicing alteration	Relative	Unaffected	3.2	60	2.9	61	3.1	61
58. (M, 37) c.723del, p.(Cys242Alafs*5) S1 S2	Relative	Unaffected	7.7 6.0	51 49	6.4 5.9	60 55	7.1 6.0	56 52
59. (M, 29) c.770del, p.(Leu257Argfs*88)	Relative	Leiomyosarcoma (29)	4.9	52	4.5	72	4.7	62
<i>Individual with a benign TP53 variant</i>								
60. (F, 14) c.704A>G, p.(Asn235Ser)	Index case	Medulloblastoma	14.5	118	11.4	118	12.9	118
<i>Individuals with unclassified rare TP53 variants</i>								
61. (F, 73) c.215C>A, p.(Pro72His)	Index case	Breast cancer (72)	6.1	83	6.1	89	6.1	86
62. (M, 75) c.314G>A, p.(Gly105Asp)	Relative	Unaffected	2.9	84	2.8	79	2.9	82
63. (M, 28) c.329G>A, p.(Arg110His)	Index case	Ependymoma (2) Multiple meningioma, BCC (23)	3.1	81	5.1	85	4.1	83
64. (F, 39) c.402T>G, p.(Phe134Leu)	Index case	Bilat. breast cancer (27, 36) 2 BCC	3.2	75	3.8	81	3.5	78
65. (F, 45) c.472C>T, p.(Arg158Cys)	Index case	Leiomyosarcoma (42)	3.7	81	2.6	90	3.2	86
66. (F, 44) c.572C>G, p.(Pro191Arg)	Relative	Unaffected	17.7	99	16.4	80	17.1	90
67. (M, 19) c.833C>G, p.(Pro278Arg)	Index case	Osteosarcoma (7, 19, 19)	4.9	63	5.3	92	5.1	78
68. (F, 45) c.847C>T, p.(Arg283Cys)	Index case	Breast cancer (39)	6.0	77	4.6	81	5.3	79
69. (F, 65) c.847C>T, p.(Arg283Cys)	Index case	Breast cancer (46)	6.7	85	6.1	91	6.4	88
70. (F, 29) c.1043T>C, p.(Leu348Ser) S1 S2	Index case	Breast cancer (29)	6.0 6.7	82 84	5.5 5.4	95 96	5.8 6.1	89 90

71. (F, 15) [◇] c.1054G>T, p.(Asp352Tyr) S1	Relative	Unaffected	3.5	110	4.5	92	4.0	101
			4.9	103	5.0	108	5.0	106
72. (H, 31) c.323_235del p.(Gly108_Phe109delinsVal)	Index case	Osteosarcoma (31)	2.9	88	4.7	100	3.8	94
73. (F, 22) c.393_395del, p.(Asn131del) S1	Relative	Unaffected	2.2	81	3.0	78	2.6	80
			4.3	97	5.2	100	4.8	99
74. (F, 22) c.792_794del, p.(Leu265del)	Index case	Breast cancer (31)	3.6	98	3.2	91	3.4	95
75. (F, 32) c.-117G>T (5'UTR)	Index case	Breast cancer (32)	23.7	102	17.3	97	20.5	100
<i>Individual with the homozygous c.*1175A>C polymorphic variant</i>								
76. (F, 35) c.*1175A>C (homozygous) S1	Relative	Unaffected	5.1	61	5.8	76	5.5	69
			6.1	67	5.2	78	5.7	73
<i>Individual with a pathogenic TP53 variant and the c.*1175A>C polymorphic variant</i>								
77. (F, 6) c.723del p.(Cys242Alafs*5) c.*1175A>C (heterozygous)	Index case	Glioma (5)	2.4	47	3.8	56	3.1	52

^aFor each individual, the identification number is indicated. For some individuals, two blood samples (S1 and S2) were collected. In brackets are indicated the sex (M, male; F, female) and age (in years) at blood sampling. *TP53* variation is indicated for carriers: cDNA numbering is given with the first nucleotide corresponding to the A of the ATG translation initiation codon in the reference sequence (GenBank RefSeq-file accession number NM_000546.5) and protein numbering with the initiation codon numbered as codon 1 (accession number NP_000537.3).^bAge at diagnosis is indicated in years, if not specified. [◇]For this individual, a second *TP53* variant was identified in *cis*: c.1021T>A, p.(Phe341Ile), which is classified as benign. ACC: Adrenocortical carcinoma; BCC: basocellular carcinoma; Bilat.: bilateral; CNS: central nervous system; RMS: rhabdomyosarcoma. Results in bold are suggestive of a deleterious effect of the variant.