

1	F - Osteosarcoma (17), breast (32), breast (37), stomach (42)	Choroid plexus (23), leukemia (37), hepatocellular (55), thyroid (60)
2	F - Breast (28), breast (32), sarcoma (41)	Hypophysis, breast (40), central nervous system (6)
3	M - Glioblastoma (20)	F - Breast (59)*, F - mucinous adenocarcinoma of the appendix, low grade glioma (34, 38)*, lung (45), stomach (50)
4	F - Breast (26), sarcoma (38)	F - Breast (45, 54)*, colorectal (48), pancreas (54), oligodendroglioma (20), sarcoma (4), central nervous system (5), breast bilateral (26, 38)
5	F - Bilateral breast (30)	Central nervous system (32), lung (51)
6	F - Breast (28)	Stomach (29)
7	M - Rhabdomyosarcoma (1), osteosarcoma (15)	Lung (52)
8	F - Bilateral breast (28), sarcoma (34)	Stomach (34), stomach, lung (64, 65), pancreas (65), lung (38)
9	F - Breast (28), breast (41)	-
10	F - Breast (24)	Breast (35), breast (40), breast (40), breast (42), breast (50)
11	F - Bilateral breast (34, 40)	Lymphoma (81)
12	F - Chondrosarcoma (15), breast (50), sarcoma (51, 53)	Leukemia (61), ovary (60)
13	F - Breast (59), melanoma (62)	Central nervous system (55), stomach (57), breast (60), leukemia (52)
14	F - Melanoma (32), breast (35)	Ovary (40), breast, sarcoma (30,53)
15	M - Hodgkin lymphoma (11), osteosarcoma (14, 24), colorectal (39)	-
16	F - Breast (34), squamous cell carcinoma (44)	Bilateral breast (31,35), sarcoma (15), leiomyosarcoma (38)
17	F - Bilateral breast (37, 38), lung adenocarcinoma (44)	Breast (36), breast (73), colorectal (78)
18	F - Breast (31), kidney (31)	F - Breast (19)*, osteosarcoma (36), central nervous system (11), rhabdomyosarcoma (1)
19	F - Breast (48), endometrial serous carcinoma (58)	Breast (29), pancreas (61), melanoma (41)
20	M - Leiomyosarcoma (53)	Sarcoma (20)
21	F - Breast (21)	-
22	F - Fallopian tube endometrioid carcinoma (57)	-

F - female, M - male, \*relatives also confirmed to be carriers

**Molecular characterization:** Twenty different TP53 P/LPVs were identified in this cohort (Figure 2), including one not previously described [c.242del p.(Thr81Asnfs\*42)]. Two recurrent variants were diagnosed in unrelated families: the missense c.799C>T p.(Arg267Trp) in Families 13 and 14 and the nonsense c.1024C>T p.(Arg342\*) in Families 20 and 21. Most of the observed TP53 P/LPV were missense (n=10), 8

of which located in the DNA Binding Domain. The remaining variants were frameshifts (n=4), nonsense (n=3), and splicing (n=3). We were able to confirm two de novo cases by negative tests in both parents (Families 15 and 21). Regarding LAF variants, the nonsense c.1024C>T p.(Arg342\*) variant was identified with an allele frequency of 34% in two different samples from the peripheral blood DNA of a

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**J Elliott**



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