

Table S1. Genotype and phenotype information for research participants.

Patient No	CC score ^b	Age	Sex	PTEN Genotype	FSIQ	Macrocephaly	Brain MRI Findings	Prior Brain Surgery	Lhermitte-Duclos	Breast-Malignant	Breast-Benign	Thyroid-Malignant	Thyroid-Benign	Trichilemmoma	Acral keratoses	Oral papillomatosis	Lipomas	Fibromas	Penile freckling	AVM/vascular lesion	Glycogenic acanthosis	GI hamartomas	GI polyps-other	Colorectal cancer	Uterine cancer	Uterine fibroids	Renal cell cancer	Other G/U tumor/malformation
1	50	60	M	c.395G>A p.(Gly132Asp)		Y	M					Y	Y	Y	Y		Y			Y	Y	Y					Y-63	Y
2	37	41	F	c.389G>A p.(Arg130Gln)	112	Y				Y-29	Y	Y	Y	Y	Y							Y			Y			Y
3	24	54	F	c.388C>T p.(Arg130Ter)	90	Y	M	Y		Y-50,52	Y	Y			Y	Y						Y			Y			Y
4	38	30	F	c.287C>G p.(Pro96Arg)	112	Y					Y	Y	Y	Y	Y	Y				Y		Y	Y					
5	22	29	F	No mutation	107						Y	Y					Y			Y	Y	Y						Y
6	28	23	M	c.382A>G p.(Lys128Glu)	79	Y	CH					Y			Y	Y				Y		Y						
7	28	44	F	c.634+1G>C	116	Y				Y-43	Y	Y			Y	Y											Y-44	
8	N/A	5	M	c.18_19delAG	80	Y	CH										Y											Y
9	22	44	F	No mutation	135	Y	N			Y-38	Y	Y-27		Y	Y		Y	Y							Y			
10	46	58	F	c.697C>T p.(Arg233Ter)	111	Y				Y-56	Y		Y	Y		Y	Y	Y			Y	Y	Y	Y-34	Y-53			
11	N/A	16	F	c.892C>T p.(Gln298Ter)	85	Y	V,C						Y			Y	Y			Y		Y						
12	18	45	F	c.697C>T p.(Arg233Ter)	65	Y	P	Y	P	Y-44	Y	Y-42	Y			Y	Y											
13	17	58	F	c.1033C>G p.(Leu345Val)	112					Y-46	Y	Y	Y		Y	Y						Y		Y-41	Y			
14	37	46	F	c.401T>C, p.(Met134Thr)	118	Y				Y-43	Y	Y-46	Y	Y	Y	Y		Y		Y	Y	Y	Y		Y			Y
15	25	58	F	Whole gene deletion	107	Y				Y-56	Y	Y	Y	Y	Y	Y	Y			Y		Y	Y			Y		
16	46	44	F	c.734_737del4	103	Y	N				Y	Y-41	Y	Y		Y		Y						Y-38				
17	32	36	F	c.865_871delAAAGTAG	108	Y	V				Y	Y-36	Y			Y				Y		Y						Y
18	N/A	17	F	c.1003C>T p.(Arg335Ter)	113	Y	V,C				Y		Y			Y				Y								
19	62	50	M	c.253+1G>A	78	Y	LD	Y	Y			Y-44	Y		Y	Y	Y				Y	Y	Y					
20	N/A	14	M	c.919G>T p.(Glu307Ter)	94	Y	CH,C	Y					Y					Y			Y	Y						Y
21	N/A	5	M	c.955_958del4	107	Y	PI										Y		Y									Y
22 ^a	44	25	F	c.253+1G>C	116	Y					Y	Y	Y		Y	Y				Y		Y						
23 ^a	44	57	M	c.253+1G>C	133	Y							Y		Y		Y		Y	Y		Y						
24	31	51	F	Exon 2 deletion	101	Y	N			Y-44	Y	Y	Y	Y	Y	Y	Y					Y	Y					
25	27	26	F	c.486_487delCA	95	Y					Y	Y	Y			Y		Y		Y								

^aSubjects related to each other (daughter and father); ^bCleveland Clinic *PTEN* risk score (<http://www.lerner.ccf.org/gmi/ccscore/>) or *PTEN* CC Score calculates a priori likelihood of carrying a germline *PTEN* mutation based on multiple logistic regression approaches, taking into account age of tumor onset and relative prevalence of the component phenotype in the general population²⁴; not applicable (N/A) for pediatric subjects; Y=phenotype present; FSIQ=Full Scale IQ; M=meningioma; CH=Chari I malformation; N=no abnormality; V=venous anomaly/angioma; C=cystic lesion; P=probable presence; LD=Lhermitte-Duclos; PI=perinatal ischemia; numbers signify age at diagnosis

Table S2. Neuropsychological test scores for research participants.

Patient No	Full Scale IQ	Working Memory Index	Processing Speed Index	Trail Making – Part A	Boston Naming Test	Semantic Fluency	Verbal Comprehension Index or VIQ	Controlled Oral Word Association Test	Wisconsin card Sorting Test – Perseverative Errors	Trail Making – Part B	Ruff Figural Fluency Test – Unique Designs	Judgment of Line Orientation	Perceptual Organization Index or PIQ	General Memory Index	Auditory Delayed Recognition Index	Auditory Verbal Learning Test – Immediate Recall	Auditory Verbal Learning Test – Delayed Recall	Auditory Verbal Learning Test – Delayed Recognition	Reading	Spelling	Sentence Comprehension	Math Computation	Finger Tapping – Dominant Hand	Finger Tapping – Non Dominant Hand	Grooved Pegboard – Dominant Hand	Grooved Pegboard – Non Dominant Hand
1	--	--	111	93	80	110	--	83	95	99	102	96	--	111	110	110	101	104	113	109	125	98	94	78	90	72
2	112	111	111	129	94	103	108	102	95	100	105	116	114	96	90	82	84	86	108	124	99	115	94	106	66	90
3	90	82	96	97	57	78	91	58	72	73	78	108	91	78	85	72	87	111	102	109	94	85	85	81	81	58
4	112	92	106	102	117	114	110	83	85	99	93	73	113	96	110	72	78	64	103	100	102	58	88	94	91	75
5	107	94	114	85	106	114	113	93	90	75	87	80	98	95	110	98	99	114	99	100	117	91	84	97	100	94
6	79	73	71	75	63	86	91	74	55	55	67	62	68	75	85	65	68	74	63	65	72	59	60	70	60	55
7	116	124	93	70	102	131	116	113	98	85	99	116	114	122	110	124	120	107	112	117	126	118	84	96	90	82
8	80	--	85	--	--	--	81	--	--	--	--	--	79	77	72	--	--	--	--	--	--	--	--	--	--	--
9	135	117	111	111	117	111	134	110	92	93	--	116	128	118	120	107	114	114	123	111	126	112	--	--	100	90
10	111	115	106	100	116	103	125	114	71	115	103	88	92	96	110	76	91	94	134	138	113	120	81	88	78	81
11	85	84	91	93	100	108	89	99	126	99	71	102	81	109	110	94	119	110	100	101	84	101	84	--	71	--
12	65	75	66	87	<55	61	72	74	--	58	66	--	63	69	65	61	54	80	88	91	71	80	106	96	57	55
13	112	104	106	94	103	77	110	93	100	90	92	116	114	107	115	92	82	105	113	111	100	100	93	94	78	94
14	118	115	120	105	112	103	111	109	69	121	123	108	125	107	115	97	90	86	114	115	125	130	133	117	87	87
15	107	94	91	90	112	95	104	79	106	106	92	102	110	120	110	94	104	116	93	94	104	100	85	93	82	81
16	103	126	111	133	83	106	103	60	72	136	85	88	104	89	95	84	72	66	106	106	104	104	102	102	69	82
17	108	108	103	111	87	86	111	78	101	108	88	96	104	125	130	83	67	103	112	111	126	122	118	118	85	91
18	113	119	120	91	104	95	113	85	111	114	91	96	111	122	110	109	107	103	105	107	101	117	109	116	87	92
19	78	80	76	87	93	72	88	98	75	81	--	--	70	69	75	81	57	76	94	--	--	--	--	--	61	64
20	94	107	97	106	79	82	87	63	80	99	--	--	96	118	115	--	--	--	114	101	102	103	113	117	109	113
21	107	--	110	--	--	--	98	--	--	--	--	--	116	--	94	--	--	--	--	--	--	--	--	--	--	--
22 ^a	116	109	106	105	58	92	119	102	99	106	81	116	110	112	120	101	99	105	105	112	128	107	84	91	72	75
23 ^a	133	124	103	112	119	95	144	124	95	99	133	108	111	127	115	101	97	98	134	120	125	120	94	106	66	100
24	101	97	93	84	90	103	106	85	89	99	85	102	94	95	110	106	109	111	93	109	112	98	87	82	84	78
25	95	106	84	102	84	84	95	71	97	73	86	116	94	101	110	101	99	114	91	91	85	101	93	105	75	88

All scores are reported as standard scores (mean = 100, standard deviation = 15)

Table S3. Performance of individuals with PHTS on individual neuropsychological measures compared to expected proportions and mean scores in normal control samples.

Domain	Test	Measure	N	Above	Avg	Below	χ^2 (p)	M (SD)	t (p)
				Avg	Avg	Avg			
				Observed (Expected)					
Intelligence	Wechsler Scales	Full Scale IQ	24	5 (4)	15 (16)	4 (4)	0.32 (.953)	103.2 (17.2)	0.92 (.370)
Attention/Working Memory	Wechsler Scales	Working Memory Index	22	6 (4)	11 (15)	5 (4)	2.38 (.337)	102.6 (16.4)	0.73 (.474)
Processing Speed	Wechsler Scales	Processing Speed Index	25	2 (4)	19 (17)	4 (4)	1.24 (.652)	99.2 (14.5)	-0.26 (.796)
	Trail Making Test	Part A	23	2 (4)	18 (16)	3 (4)	1.52 (.525)	98.5 (15.1)	-0.48 (.635)
Language	Boston Naming Test	Total Score	25	4 (4)	13 (17)	8 (4)	4.94 (.082)	91.3 (23.7)	-1.77 (.090)
	Semantic Fluency	Total Score	23	1 (4)	16 (16)	6 (4)	3.35 (.193)	96.0 (16.2)	-1.18 (.252)
	Wechsler Scales	Verbal Comprehension Index or VIQ	24	6 (4)	16 (16)	2 (4)	2.10 (.349)	104.96 (16.7)	1.45 (.159)
Executive Functioning	Controlled Oral Word Association	Total Score	23	1 (4)	12 (16)	10 (4)	12.74 (.002)	89.0 (18.3)	1.82 (.083)
	Wisconsin Card Sorting Test	Perseverative Errors	22	1 (4)	14 (15)	7 (4)	4.73 (.094)	89.7 (16.2)	-2.99 (.007)
	Trail Making Test	Part B	23	2 (4)	14 (15)	7 (4)	3.32 (.197)	94.3 (19.6)	-1.41 (.173)
	Ruff Figural Fluency Test	Unique Designs	20	2 (3)	13 (14)	5 (3)	1.74 (.453)	91.8 (16.4)	-2.25 (.036)
Visuospatial	Judgment of Line Orientation	Total Score	20	6 (3)	11 (14)	3 (3)	3.64 (.182)	100.25 (15.6)	0.07 (.944)
	Wechsler Scales	Perceptual Organization Index or PIQ	24	4 (4)	15 (16)	5 (4)	0.31 (.953)	100.00 (17.3)	0.00 (1.000)
Memory Recall	WMS-III or CMS	General Memory Index	24	7 (4)	12 (16)	5 (4)	3.50 (.161)	101.4 (18.1)	0.38 (.705)
	Auditory Verbal Learning Test	Immediate Recall	22	1 (4)	12 (15)	9 (4)	9.47 (.009)	91.3 (16.2)	-2.52 (.020)
		Delayed Recall	22	2 (4)	12 (15)	8 (4)	5.81 (.059)	90.9 (19.0)	-2.26 (.035)
Memory Recognition	WMS-III or CMS	Auditory Delayed Recognition Index	24	3 (4)	18 (16)	3 (4)	.750 (.716)	103.6 (16.5)	1.11 (.280)
	Auditory Verbal Learning Test	Delayed Recognition	22	1 (4)	16 (15)	5 (4)	2.64 (.282)	97.3 (16.5)	-0.78 (.447)
Academic	Wide Range Achievement Test – Fourth Edition	Reading	23	3 (4)	16 (16)	1 (4)	3.15 (.241)	105.2 (15.3)	1.62 (.119)
		Spelling	22	4 (4)	17 (15)	1 (4)	2.59 (.311)	106.5 (14.3)	2.12 (.046)
		Sentence Comprehension	22	8 (4)	11 (15)	3 (4)	5.51 (.073)	106.4 (17.7)	1.70 (.104)
		Math Computation	22	6 (4)	13 (15)	3 (4)	1.54 (.521)	101.8 (18.7)	0.45 (.661)
Motor	Finger Tapping Test	Dominant Hand	21	2 (3)	13 (14)	6 (3)	3.20 (.203)	93.9 (15.6)	-1.81 (.086)
		Non Dominant Hand	21	3 (3)	13 (14)	4 (3)	0.41 (.940)	97.4 (13.7)	-0.86 (.398)
	Grooved Pegboard	Dominant Hand	23	0 (4)	9 (16)	14 (4)	32.57 (.000)	80.0 (13.6)	-7.05 (.000)
		Non Dominant Hand	22	0 (4)	10 (15)	12 (4)	21.54 (.000)	81.7 (14.7)	-5.86 (.000)

Wechsler Scales=Wechsler Adult Intelligence Scale – Third Edition, Wechsler Intelligence Scale for Children – Fourth Edition, or Wechsler Preschool and Primary Scale of Intelligence; WMS-III=Wechsler Memory Scale – Third Edition; CMS=Children’s Memory Scale. Values under each descriptive category (i.e., Above Average, Average, Below Average) represent the number of subjects who scored within that range on that measure. The numbers in parentheses represent the expected number of subjects to fall within that category based on normal control data. All chi-square analyses were conducted by comparing the observed scores within each category to the expected proportions in the normal population based on the normal curve (i.e., 16% Above Average, 68% Average, 16% Below Average).