

SUPPLEMENTARY TABLES

Supplementary Table 1. Telomere length of healthy individuals (controls).

DNA number	relative telomere length	Age (years)	Sex
04P0523	2.16	1	F
04P0862	3.41	1	F
05P0586	1.6	2	M
05P0509	1.12	2	F
04P0535	1.45	3	F
01P0888	0.9	3	M
02P01053	2.25	5	M
04P0216	1.42	9	M
112	1.37	11	F
204	1.29	11	F
166	1.83	12	F
17	1.94	13	F
443	1.93	14	F
444	1.36	15	M
210	0.98	16	F
365	1.51	17	F
247	1.23	18	F
47	1.17	19	F
293	1.58	19	-
193	0.74	20	M
390	1.41	20	M
431	1.25	20	M
423	0.79	20	M
11	1.2	20	M
161	1	20	F
420	0.73	20	F
o2	1	21	M
440	1	21	F
143	1.26	21	F
448	0.83	21	F
129	0.93	21	F
169	1.16	21	F
164	1.18	21	F
13	1.22	21	M
413	0.9	21	F
223	1	22	F
163	0.95	22	M
40	0.91	22	F
188	0.76	22	F
241	1	23	M
246	0.84	23	M
470	1	23	M
280	1.44	23	F
262	0.99	23	F
191	0.89	23	F
328	0.78	24	M
333	1.14	24	F
471	1.39	24	F
464	0.75	24	M
284	1	24	F
150	1	24	F
330	0.85	24	F
292	1.26	24	M
o1	0.97	25	F

425	0.81	25	F
49	1.65	25	F
165	0.99	25	F
189	0.92	25	M
323	1.33	25	M
90	0.84	26	F
320	1.23	26	F
93	1.72	26	F
41	1.52	26	F
388	0.78	27	F
147	0.75	27	F
303	1.34	27	F
445	0.88	27	F
430	0.84	27	F
102	1.3	27	F
32	1	28	M
313	1.54	28	F
160	0.94	28	M
472	0.73	28	F
347	1	28	F
146	0.74	28	M
222	1.1	28	F
Ra	1	28	F
305	1.51	29	F
383	0.92	29	F
207	1	29	F
37	0.81	29	M
73	1.12	29	M
187	0.96	29	M
104	0.74	29	F
23	0.71	29	-
31	0.92	30	F
269	0.84	30	F
1	0.88	30	M
271	1.23	30	F
372	0.93	30	M
27	0.75	30	-
595	1.71	35	M
188	1.21	37	M
596	0.88	38	M
192	0.78	39	M
597	0.94	40	-
194	1	43	F
584	0.79	45	-
591	0.53	60	F
592	0.51	60	M
579	0.4	64	M
590	0.47	66	M
570	0.56	67	M
574	0.5	74	M
588	0.51	75	F
572	0.61	78	F
580	0.61	78	M
587	0.61	80	M

Age group	Number	Mean	SD	Max	Min
1-10	8	1.79	0.80	3.41	0.9
11-20	18	1.30	0.37	1.94	0.73
21-30	65	1.03	0.24	1.72	0.71
31-45	7	1.04	0.33	1.71	0.78
46-80	10	0.53	0.07	0.61	0.4

Supplementary Table 2. Estimation of telomere length of NBS-homozygotes.

DNA number	Relative telomere lengths	Age (years)	Sex
13720	1.62	1	M
12207	1.48	1	M
13424	1.29	1	F
6645	0.3	1	F
5342	0.21	1	M
6018	0.68	2	F
7105	0.44	2	F
3769	0.43	2	M
3772	0.43	2	F
7694	2.1	3	F
11766	2	3	F
8294	2.1	3	F
13607	0.98	5	F
13028	1.55	6	M
3426	1.35	6	F
8165	1	6	M
9990	1.3	6	M
11348	1.17	7	F
5202	0.67	7	F
3201	0.35	7	F
4530	0.22	7	F
8304	0.34	8	M
12557	1.13	8	-
5700	0.99	9	F
11154	1.73	10	M
7822	0.96	10	M
9028	0.78	10	F
5546	0.58	10	M
6023	1.3	12	F
13921	0.76	12	M
2552	0.69	13	M
3197	0.2	13	M
3205	1.3	14	M
3316	0.29	15	M
5567	0.64	15	M
5450	0.56	18	F
10376	0.46	19	F
5431	0.26	20	F

1-10 years:					
Category	Number	Mean	SD	Max	Min
Control	8	1.79	0.80	3.41	0.90
NBS-Homozygote	28	1.01	0.58	2.10	0.21

11-20 years					
Category	Number	Mean	SD	Max	Min
Control	18	1.30	0.37	1.94	0.73
NBS-Homozygote	10	0.65	0.39	1.30	0.20

Supplementary Table 3. Estimation of telomere length of NBS-heterozygotes.

DNA number	Relative telomere lengths	Age (years)	Sex
5343	2	1	F
10130	1.51	2	M
4328	0.89	3	M
8296	1.68	3	M
3221	1	4	M
3223	2	5	F
10133	1.38	5	F
10131	0.99	5	M
10123	2.35	7	M
7234	1.56	8	F
6017	1.77	8	M
3224	1.49	10	M
10120	0.71	12	F
4787	1.31	19	M
8295	0.71	22	F
3222	1	25	F
10124	2	25	M
508	1	27	F
6024	1.3	30	F
466	1.3	30	M
7235	0.79	30	M
7824	0.75	33	M
7823	0.78	35	M
6025	0.32	40	M
4786	0.25	40	M
464	0.6	50	F
463	0.27	54	M

Age	Category	Number	Mean	SD	Max	Min
1 -- 10	Control	8	1.79	0.80	3.41	0.90
	NBS-Heterozygote	12	1.55	0.45	2.35	0.89
11 -- 30	Control	83	1.08	0.29	1.94	0.71
	NBS-Heterozygote	9	1.12	0.41	2.00	0.71
>30	Control	17	0.74	0.33	1.71	0.40
	NBS-Heterozygote	6	0.50	0.24	0.78	0.25

Supplementary Table 4. Analysis of chromosome fragility after irradiation in six NBS lymphoblastoid cell lines with the absolute longest (above) and absolute shortest (below) telomere lengths.

	Survival (y)	Aberrant mitoses (%)			Breaks (%)		
		0 Gy	0,5 Gy	1,0 Gy	0 Gy	0,5 Gy	1,0 Gy
89P0319 ♀	0	14	69	88	0.16	1.42	2.2
96P0616 ♀	0,2	2	38	42	0.02	0.54	0.68
95P0182 ♀	2,8	0	42	100	0	1.18	3.5
Mean ± SD		5 ± 8	50 ± 7	77 ± 31	0.16 ± 0,02	1.05 ± 0,45	2.13 ± 1,41
97P0614 ♂	>12	2	40	42	0.04	0.52	0.66
RoZd ♀	>12	0	39	59	0	0.48	0.71
94P0307 ♂	>12	0	42	72	0	1.16	1.58
		1 ± 1	40 ± 2	58 ± 15	0.01 ± 0.02	0.72 ± 0.38	0.98 ± 0.52
Control		0	16	10	0	0.2	0.14

Chromatid breaks were distinguished from chromatid translocations. Since the latter are due to two breakage events, they were counted twice for the calculation of the total break events. Dicentric chromosomes were not scored because they cannot be induced in the G2 phase and apparently are due to telomere fusions.

Supplementary Table 5. T/C-FISH data on telomere lengths of NBS-LCL 94P0307.

Chromosome	Median (\pm SD) of p-arm	Median (\pm SD) of q-arm
1	8.7 (\pm 4.8)	8 (\pm 5.9)
2	5.2 (\pm 4.5)	5.1(\pm 8.3)
3	9.0 (\pm 9.3)	9.9 (\pm 6.1)
4	11.2(\pm 10.1)	7.2(\pm 10.5)
5	9.1(\pm 5.7)	11.4(\pm 11.1)
6	9.1(\pm 7.1)	7.8(\pm 4.8)
7	10.6(\pm 6.1)	4.9(\pm 6.7)
8	9.3 (\pm 6.3)	7.1(\pm 6.6)
9	10.7(\pm 5.9)	7.3(\pm 5.5)
10	10.2(\pm 9.4)	17.4(\pm 11.1)
11	9.5(\pm 6.5)	7 (\pm 5.6)
12	8.9(\pm 5.2)	7.5(\pm 5.4)
13	5.6(\pm 6.1)	8.6(\pm 7.3)
14	6.4(\pm 7.3)	9.8(\pm 6.9)
15	5.5(\pm 4.5)	9.7(\pm 4.9)
16	7.5(\pm 6.5)	8.1(\pm 5.1)
17	5 (\pm 4.6)	6.1(\pm 5.7)
18	6.9(\pm 6.2)	5.8(\pm 6.6)
19	13.2(\pm 36.6)	6.2(\pm 5.9)
20	5.3(\pm 4.2)	6.7(\pm 4.1)
21	4.6(\pm 3.2)	6.2(\pm 6.1)
22	5.7(\pm 3.5)	4.9(\pm 3.3)
X	6.6(\pm 7.1)	6.1(\pm 7.9)
Y	6.3(\pm 3.3)	4.5(\pm 5.1)

Supplementary Table 6. Q-FISH analysis of telomere lengths of the p arm of chromosome 19 in 11 metaphases of the NBS lymphoblastoid cell line 94P0307. T/C values are presented for the highly and weakly fluorescent chromosome 19.

Metaphase	1	2	3	4	5	6	7	8	9	10	11	Ø
T/C value: high	85.2	52.6	47.1	44.1	60.5	33.4	79.4	60.2	32.9	68.3	58.6	56.6
T/C value: low	3.2	12.6	2.0	2.1	8.2	1.1	2.1	6.3	2.2	3.5	9.6	4.8

Supplementary Table 8. Regulation of telomeric 19p genes in normal and NBS fibroblasts with short telomeres (relative to cells with long telomeres).

Gene	Functions in senescence and/or cell growth	Reference	Distance to telomere [Mbp]	Differential gene expression, Affymetrix data	Differential gene expression, qPCR data Control fibroblasts	Differential gene expression, qPCR data NBS fibroblasts	TPE-OLD Effect
					[fold-change]		
BSG	MMP and cytokine production	[32]	0.6	+2.8	+3.2	+2.4	(N)
GAMT	ATP production (SASP?)	[33, 34]	1.4	+2.0	+5.6	+1.9	(N)
SCAMP4	player in SASP	[35]	1.9	+2.3	+1.9	+1.6	(N)
OLFM2	cell differentiation	[36]	9.9	+3.8	+50	+3.3	(N)
UHRF1	neg. regulator of senescence	[40]	4.9	-2.7	-5.0	+1.7	R
COL5A3	age-dependent tissue remodel.	[37]	10.0	+2.4	+25.0	+4.0	(N)
RNASEH2A	migration and invasion	[41]	12.8	-2.1	-4.5	+1.2	R
CACNA1A	calcium entry; nerve function	[38]	13.6	+2.1	+1.3	-1.5	R
DDX39A	role in cancer and longevity	[42]	14.6	-2.0	-2.2	+1.7	R
NOTCH3	pos. regulator of senescence (p21)	[39]	15.2	+4.1	+100.0	+58.0	(N)

BSG, basigin; GAMT, guanidinoacetate methyl-transferase; SCAMP4, secretory carrier membrane protein 4; OLFM2, olfactomedin 2; UHRF1, Ubiquitin like with PHD and ring finger domain 1; COL5A3, collagen type V alpha 3 chain; RNASEH2A, ribonuclease H2 subunit A; CACNA1A, calcium voltage-gated channel subunit alpha1 A; DDX39A, DExD-box helicase 39A; NOTCH3, Notch Receptor 3; SASP, senescence associated secretory phenotype; MMP, matrix metalloproteinases; (N), TPE-OLD: normal but attenuated regulation; R, TPE-OLD: reversed regulation, compared to regulation (mRNA) in healthy control fibroblasts; grey overlay: upregulation in pre-senescent cells; green overlay, down regulation in pre-senescent cells.

Supplementary Table 9. Correlation between telomere length and clinical data of 21 NBS homozygotes.

Telomere length	Age at cancer manifestation		Age at death	
		p		p
Long vs. median		0.07		0.50
Median vs. short		0.52		0.54
Long vs. short		0.41		0.99

The p values are based on the unpaired T- test.