

Supplementary Table 7. Linear model used for adjusting telomere lengths by cohort.**Call:**

lm(formula = tel ~ cohort, data = full_data, subset = case == control)

Residuals:

Min	1Q	Median	3Q	Max
-301.52	-107.17	-20.56	46.31	814.11

Coefficients

	Estimate	Std. Error	t value	Pr(> t)	
(Intercept)	563.49	24.37	23.12	< 2e-16	***
Cohort: Cambridge	-116.38	32.73	-3.556	0.000542	***
Cohort: WTCCC	-173.1	54.95	-3.15	0.002064	**

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 170.6 on 119 degrees of freedom

(37 observations deleted due to missingness)

Multiple R-squared:

0.1252,

Adjusted R-squared: 0.1105

F-statistic: 8.512 on 2 and 119 DF, p-value: 0.0003506

Supplementary Table 8. Change in interactions with K39N. Residues that showed the greatest differences (K39N – WT) across systems in their total interaction energy with respect to the K39N residue. The average total interaction energy \pm average standard deviation is provided. All values are in kcal mol⁻¹.

	K39N – WT
Ala6	-7.42 \pm 0.01
Lys18	-9.83 \pm 0.02
Lys30	-11.88 \pm 0.02
Lys33	-25.84 \pm 0.11
Pro34	1.05 \pm 0.01
Leu37	2.27 \pm 0.04
Asp42	25.20 \pm 0.02
Asp51	9.96 \pm 0.01
Lys56	-13.17 \pm 0.01
Glu67	13.36 \pm 0.09
Lys74	-10.33 \pm 0.05
Asp77	11.35 \pm 0.04
Arg80	-9.92 \pm 0.01
Arg83	-10.83 \pm 0.03
Lys85	-14.64 \pm 0.04
Lys90	-20.02 \pm 0.04
Lys91	-13.28 \pm 0.08
Glu92	13.97 \pm 0.08
Glu107	9.75 \pm 0.04
Arg117	-10.99 \pm 0.05
Lys121	-9.29 \pm 0.04
Glu128	7.61 \pm 0.01
Asp129	9.00 \pm 0.01
Lys131	-7.24 \pm 0.01

Glu134	7.64 ± 0.01
Arg137	-8.59 ± 0.03
Lys152	-8.87 ± 0.05
Asp155	8.37 ± 0.03
Asp163	12.76 ± 0.05
Lys171	-13.01 ± 0.17
Glu173	14.63 ± 0.24
Asp175	15.10 ± 0.25
Lys182	-9.87 ± 0.08
Asp185	9.23 ± 0.05
Arg188	-7.60 ± 0.04
Arg195	-9.10 ± 0.04
Asp200	8.91 ± 0.08
Glu204	10.90 ± 0.12
Asp206	8.41 ± 0.06
Arg212	-7.42 ± 0.05
Asp219	10.27 ± 0.08
Asp224	25.66 ± 0.78
Arg231	-17.86 ± 0.34
Lys234	-10.94 ± 0.12
Arg240	-11.45 ± 0.08
Lys247	-11.71 ± 0.06
Glu254	7.68 ± 0.09
Glu262	11.20 ± 0.07
Gly268	-1.31 ± 0.04
Arg273	-18.62 ± 0.17
Arg276	-14.51 ± 0.08
Glu280	9.27 ± 0.06
Asp284	9.78 ± 0.04
Asp286	8.08 ± 0.04

Lys289	-8.51 ± 0.05
Lys290	-7.54 ± 0.03
Asp291	8.09 ± 0.04
Glu293	7.17 ± 0.03
Ala299	6.71 ± 0.03
dT1	9.38 ± 0.14
dT2	32.79 ± 0.71
dA3	47.18 ± 1.32
dG4	27.20 ± 0.46
dG5	17.45 ± 0.28
dG6	18.03 ± 0.38
dT7	15.12 ± 0.29
dT8	17.25 ± 0.41
dA9	19.70 ± 0.82
dG10	12.51 ± 0.59

Supplementary Table 9. Change in interactions with D224N. Residues that showed the greatest differences (D224N – WT) across systems in their total interaction energy with respect to the D224N residue. The average total interaction energy \pm average standard deviation is provided. All values are in kcal mol⁻¹.

	D224N – WT
Ala6	6.59 \pm 0.02
Lys18	7.97 \pm 0.05
Lys30	11.83 \pm 0.03
Lys33	23.01 \pm 0.11
Leu37	-1.06 \pm 0.05
Lys39	26.00 \pm 0.79
Asp42	-15.03 \pm 0.19
Asp51	-9.06 \pm 0.02
Lys56	12.19 \pm 0.03
Glu67	-12.81 \pm 0.11
Lys74	11.63 \pm 0.02
Asp77	-11.84 \pm 0.01
Arg80	8.79 \pm 0.02
Arg83	8.53 \pm 0.04
Lys85	9.92 \pm 0.06
Lys90	14.16 \pm 0.11
Lys91	10.66 \pm 0.06
Glu92	-11.49 \pm 0.04
Glu107	-10.35 \pm 0.01
Arg117	11.35 \pm 0.03
Lys121	8.55 \pm 0.05
Glu128	-7.02 \pm 0.01

Asp129	-8.20 ± 0.02
Lys131	6.78 ± 0.01
Glu134	-7.63 ± 0.01
Arg137	8.72 ± 0.01
Lys152	11.27 ± 0.02
Asp155	-10.60 ± 0.03
Asp163	-16.07 ± 0.04
Lys171	18.41 ± 0.02
Glu173	-24.24 ± 0.09
Val174	1.31 ± 0.01
Asp175	-32.49 ± 0.33
Ala177	-4.17 ± 0.21
Ser178	1.19 ± 0.05
Lys182	15.15 ± 0.06
Asp185	-12.22 ± 0.02
Arg188	10.21 ± 0.03
Arg195	13.68 ± 0.08
Asp200	-12.76 ± 0.06
Glu204	-14.84 ± 0.01
Asp206	-11.05 ± 0.01
Arg212	9.52 ± 0.02
Asp219	-16.37 ± 0.08
His226	3.76 ± 0.09
Val227	3.45 ± 0.07
His228	3.29 ± 0.14
Val229	1.34 ± 0.01
Ala230	1.42 ± 0.00

Arg231	29.38 ± 0.11
Lys234	12.94 ± 0.03
Arg240	13.76 ± 0.03
Lys247	19.67 ± 0.21
Glu254	-10.82 ± 0.09
Glu262	-19.03 ± 0.12
Leu265	-1.88 ± 0.03
His266	1.46 ± 0.21
Gly267	5.74 ± 0.12
Arg273	30.99 ± 0.18
Arg276	15.50 ± 0.07
Glu280	-10.55 ± 0.01
Asp284	-11.26 ± 0.01
Asp286	-9.21 ± 0.00
Lys289	9.88 ± 0.00
Lys290	8.73 ± 0.01
Asp291	-9.95 ± 0.02
Glu293	-8.66 ± 0.01
Ala299	-8.51 ± 0.02
dT1	-4.29 ± 0.11
dT2	-14.74 ± 0.37
dA3	-18.74 ± 0.52
dG4	-17.86 ± 0.36
dG5	-14.14 ± 0.21
dG6	-17.65 ± 0.27
dT7	-17.94 ± 0.21
dT8	-24.81 ± 0.39

dA9	-28.25 ± 0.53
dG10	-10.10 ± 1.25

Supplementary Table 10. Change in interactions with dG6 for K39N. Residues that showed the greatest differences (K39N – WT) across systems in their total interaction energy with respect to the dG6 residue. The average total interaction energy \pm average standard deviation is provided. All values are in kcal mol⁻¹.

	K39N – WT
Lys30	2.41 \pm 0.76
Lys33	11.95 \pm 3.73
Lys39	18.03 \pm 0.38
Lys56	4.10 \pm 1.02
Lys74	1.11 \pm 0.35
Asp77	-1.26 \pm 0.37
Lys91	1.13 \pm 0.69
Glu92	4.95 \pm 0.75
Asp163	-2.28 \pm 0.56
Arg240	2.04 \pm 0.43
Thr269	-1.25 \pm 0.23
Ser270	1.06 \pm 0.75
Tyr271	1.59 \pm 0.51
Gly272	1.14 \pm 0.18
Arg273	2.47 \pm 1.10
Asp284	-1.07 \pm 0.25
dA9	-2.43 \pm 0.39

Supplementary Table 11. Change in interactions with dG6 for C59Y. Residues that showed the greatest differences (C59Y – WT) across systems in their total interaction energy with respect to the dG6 residue. The average total interaction energy \pm average standard deviation is provided. All values are in kcal mol⁻¹.

	C59Y – WT
Lys18	-1.01 \pm 0.19
Lys33	8.00 \pm 2.67
Asp51	1.28 \pm 0.20
Lys56	-10.02 \pm 0.80
Lys90	-2.62 \pm 0.66
Glu92	5.88 \pm 0.76
Asp163	1.31 \pm 0.36
Asp224	1.13 \pm 0.41
Lys247	-1.43 \pm 0.23
Thr269	-1.09 \pm 0.27
Ser270	-1.09 \pm 0.50
Arg273	-1.88 \pm 0.83
Arg276	-1.37 \pm 0.25
dA3	-1.31 \pm 0.29
dG4	-3.12 \pm 0.70
dT8	1.02 \pm 0.38
dA9	-1.94 \pm 0.40

Supplementary Table 12. Change in interactions with dG6 for D224N. Residues that showed the greatest differences (D224N – WT) across systems in their total interaction energy with respect to the dG6 residue. The average total interaction energy \pm average standard deviation is provided. All values are in kcal mol⁻¹.

	D224N – WT
Lys30	1.71 \pm 0.94
Lys33	11.17 \pm 3.92
Lys39	2.07 \pm 3.92
Asp42	-1.02 \pm 0.49
Lys56	3.74 \pm 1.13
Glu67	-1.26 \pm 0.33
Lys74	1.13 \pm 0.41
Asp77	-1.21 \pm 0.45
Lys90	1.76 \pm 0.63
Lys91	2.06 \pm 0.85
Glu92	4.17 \pm 1.03
Asp163	-1.70 \pm 0.77
Asp224	-17.65 \pm 0.27
Arg240	1.72 \pm 0.54
Tyr271	1.78 \pm 0.49
Gly272	1.26 \pm 0.18
Arg273	2.96 \pm 1.27
dA3	-1.56 \pm 0.43
dG4	-5.10 \pm 0.99
dT8	1.11 \pm 0.33

Supplementary Table 13. Samples included in this study. The list shows all 6,226 samples in this study, with their ID, proportion of high-quality bases sequenced in the 1st sequencing round, case/control status and cohort of origin.

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Case_2419		1	Case	SEARCH
Case_2420		1	Case	SEARCH
Case_2421	0.998950131		Case	SEARCH

Case_2422		1	Case	SEARCH
Case_2423		1	Case	SEARCH
Case_2424	0.998950131		Case	SEARCH
Case_2425		1	Case	SEARCH
Case_2426	0.997375328		Case	SEARCH
Case_2427		1	Case	SEARCH
PD30700a	0.940682415		Case	SEARCH
Case_2428		1	Case	SEARCH
Case_2429	0.999475066		Case	SEARCH
Case_2430		1	Case	SEARCH
PD30722a		1	Case	SEARCH
Case_2431		1	Case	SEARCH
Case_2432		1	Case	SEARCH
Case_2433		1	Case	SEARCH
Case_2434		1	Case	SEARCH
Case_2435		1	Case	SEARCH
Case_2436		1	Case	SEARCH
Case_2437		1	Case	SEARCH
Case_2438		1	Case	SEARCH
Case_2439		1	Case	SEARCH
Case_2440		1	Case	SEARCH
Case_2441		1	Case	SEARCH
Case_2442	0.94488189		Case	SEARCH
Case_2443		1	Case	SEARCH
Case_2444		1	Case	SEARCH
Case_2445		1	Case	SEARCH
Case_2446	0.999475066		Case	SEARCH
Case_2447	0.999475066		Case	SEARCH
Case_2448		1	Case	SEARCH
Case_2449		1	Case	SEARCH
Case_2450		1	Case	SEARCH
Case_2451		1	Case	SEARCH
Case_2452		1	Case	SEARCH
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Case_2454		1	Case	SEARCH
Case_2455		1	Case	SEARCH
Case_2456		1	Case	SEARCH
Case_2457		1	Case	SEARCH
Case_2458	0.998425197		Case	SEARCH
Case_2459		1	Case	SEARCH

Case_2460		1	Case	SEARCH
Case_2461	0.996850394		Case	SEARCH
Case_2462		1	Case	SEARCH
Case_2463		1	Case	SEARCH
Case_2464		1	Case	SEARCH
Case_2465		1	Case	SEARCH
Case_2466	0.999475066		Case	SEARCH
Case_2467		1	Case	SEARCH
Case_2468		1	Case	SEARCH
Case_2469		1	Case	SEARCH
Case_2470		1	Case	SEARCH
PD30701a	0.999475066		Case	SEARCH
Case_2471		1	Case	SEARCH
Case_2472		1	Case	SEARCH
Case_2473		1	Case	SEARCH
Case_2474		1	Case	SEARCH
Case_2475		1	Case	SEARCH
Case_2476		1	Case	SEARCH
Case_2477		1	Case	SEARCH
Case_2478		1	Case	SEARCH
Case_2479		1	Case	SEARCH
Case_2480	0.999475066		Case	SEARCH
Case_2481		1	Case	SEARCH
Case_2482		1	Case	SEARCH
Case_2483		1	Case	SEARCH
Case_2484		1	Case	SEARCH
Case_2485	0.998425197		Case	SEARCH
Case_2486		1	Case	SEARCH
Case_2487		1	Case	SEARCH
Case_2488		1	Case	SEARCH
Case_2489		1	Case	SEARCH
Case_2490	0.996325459		Case	SEARCH
Case_2491		1	Case	SEARCH
Case_2492		1	Case	SEARCH
Case_2493		1	Case	SEARCH
Case_2494		1	Case	SEARCH
Case_2495		1	Case	SEARCH
Case_2496		1	Case	SEARCH
Case_2497	0.999475066		Case	SEARCH
Case_2498		1	Case	SEARCH

Case_2499		1	Case	SEARCH
Case_2500		1	Case	SEARCH
Case_2501		1	Case	SEARCH
Case_2502		1	Case	SEARCH
Case_2503		1	Case	SEARCH
Case_2504		1	Case	SEARCH
Case_2505		1	Case	SEARCH
Case_2506		1	Case	SEARCH
Case_2507	0.998950131		Case	SEARCH
Case_2508		1	Case	SEARCH
Case_2509		1	Case	SEARCH
Case_2510		1	Case	SEARCH
Case_2511	0.999475066		Case	SEARCH
Case_2512		1	Case	SEARCH
Case_2513	0.945931759		Case	SEARCH
Case_2514		1	Case	SEARCH
Case_2515		1	Case	SEARCH
Case_2516		1	Case	SEARCH
Case_2517		1	Case	SEARCH
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Case_2519		1	Case	SEARCH
Case_2520		1	Case	SEARCH
Case_2521		1	Case	SEARCH
Case_2522		1	Case	SEARCH
Case_2523	0.998950131		Case	SEARCH
Case_2524		1	Case	SEARCH
Case_2525		1	Case	SEARCH
Case_2526		1	Case	SEARCH
Case_2527	0.994225722		Case	SEARCH
Case_2528		1	Case	SEARCH
Case_2529		1	Case	SEARCH
Case_2530		1	Case	SEARCH
PD30725a	0.984776903		Case	SEARCH
Case_2531		1	Case	SEARCH
Case_2532		1	Case	SEARCH
Case_2533		1	Case	SEARCH
Case_2534		1	Case	SEARCH
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Case_2536	0.96167979		Case	SEARCH
Case_2537		1	Case	SEARCH

Case_2538		1	Case	SEARCH
Case_2539	0.998425197		Case	SEARCH
Case_2540		1	Case	SEARCH
Case_2541		1	Case	SEARCH
Case_2542	0.972703412		Case	SEARCH
Case_2543		1	Case	SEARCH
Case_2544		1	Case	SEARCH
Case_2545		1	Case	SEARCH
Case_2546		1	Case	SEARCH
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Case_2548		1	Case	SEARCH
PD30723a		1	Case	SEARCH
Case_2549		1	Case	SEARCH
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Case_2555		1	Case	SEARCH
Case_2556		1	Case	SEARCH
Case_2557		1	Case	SEARCH
Case_2558		1	Case	SEARCH
Case_2559	0.940682415		Case	SEARCH
Case_2560	0.999475066		Case	SEARCH
Case_2561		1	Case	SEARCH
Case_2562		1	Case	SEARCH
Case_2563		1	Case	SEARCH
Case_2564		1	Case	SEARCH
Case_2565	0.998425197		Case	SEARCH
Case_2566		1	Case	SEARCH
Case_2567		1	Case	SEARCH
Case_2568		1	Case	SEARCH
Case_2569		1	Case	SEARCH
Case_2570	0.996325459		Case	SEARCH
Case_2571		1	Case	SEARCH
Case_2572		1	Case	SEARCH
Case_2573		1	Case	SEARCH
Case_2574		1	Case	SEARCH
Case_2575		1	Case	SEARCH
Case_2576		1	Case	SEARCH

Case_2577		1 Case	SEARCH
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Case_2579		1 Case	SEARCH
Case_2580		1 Case	SEARCH
Case_2581		1 Case	SEARCH
Case_2582		1 Case	SEARCH
Case_2583		1 Case	SEARCH
Case_2584	0.999475066	Case	SEARCH
Case_2585		1 Case	SEARCH
Case_2586		1 Case	SEARCH
Case_2587	0.998950131	Case	SEARCH
Case_2588		1 Case	SEARCH
Case_2589		1 Case	SEARCH
Case_2590		1 Case	SEARCH
Case_2591		1 Case	SEARCH
Case_2592		1 Case	SEARCH
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Case_2601		1 Case	SEARCH
Case_2602		1 Case	SEARCH
Case_2603		1 Case	SEARCH
Case_2604		1 Case	SEARCH
Case_2605		1 Case	SEARCH
Case_2606		1 Case	SEARCH
Case_2607		1 Case	SEARCH
PD30736a		1 Case	SEARCH
Case_2608		1 Case	SEARCH
Case_2609		1 Case	SEARCH
Case_2610		1 Case	SEARCH
Case_2611		1 Case	SEARCH
Case_2612		1 Case	SEARCH
Case_2613		1 Case	SEARCH
Case_2614		1 Case	SEARCH
Case_2615		1 Case	SEARCH

Case_2616		1	Case	SEARCH
Case_2617		1	Case	SEARCH
Case_2618	0.998950131		Case	SEARCH
Case_2619		1	Case	SEARCH
Case_2620	0.998950131		Case	SEARCH
Case_2621		1	Case	SEARCH
Case_2622	0.998950131		Case	SEARCH
Case_2623	0.986351706		Case	SEARCH
Case_2624	0.999475066		Case	SEARCH
Case_2625		1	Case	SEARCH
Case_2626		1	Case	SEARCH
Case_2627		1	Case	SEARCH
Case_2628		1	Case	SEARCH
Case_2629		1	Case	SEARCH
Case_2630		1	Case	SEARCH
Case_2631		1	Case	SEARCH
Case_2632		1	Case	SEARCH
Case_2633	0.999475066		Case	SEARCH
Case_2634		1	Case	SEARCH
Case_2635		1	Case	SEARCH
Case_2636		1	Case	SEARCH
Case_2637		1	Case	SEARCH
Case_2638		1	Case	SEARCH
Case_2639		1	Case	SEARCH
Case_2640		1	Case	SEARCH
Case_2641		1	Case	SEARCH
Case_2642		1	Case	SEARCH
PD30726a	0.998425197		Case	SEARCH
Case_2643		1	Case	SEARCH
Case_2644		1	Case	SEARCH
Case_2645		1	Case	SEARCH
Case_2646		1	Case	SEARCH
Case_2647		1	Case	SEARCH
Case_2648		1	Case	SEARCH
Case_2649		1	Case	SEARCH
Case_2650	0.940682415		Case	SEARCH
Case_2651		1	Case	SEARCH
Case_2652		1	Case	SEARCH
Case_2653	0.999475066		Case	SEARCH
Case_2654		1	Case	SEARCH

Case_2655		1	Case	SEARCH
Case_2656		1	Case	SEARCH
Case_2657		1	Case	SEARCH
Case_2658	0.998950131		Case	SEARCH
Case_2659	0.998950131		Case	SEARCH
Case_2660		1	Case	SEARCH
Case_2661	0.984251969		Case	SEARCH
Case_2662		1	Case	SEARCH
Case_2663	0.999475066		Case	SEARCH
Case_2664		1	Case	SEARCH
Case_2665		1	Case	SEARCH
Case_2666		1	Case	SEARCH
Case_2667		1	Case	SEARCH
Case_2668		1	Case	SEARCH
Case_2669		1	Case	SEARCH
Case_2670		1	Case	SEARCH
Case_2671		1	Case	SEARCH
Case_2672		1	Case	SEARCH
Case_2673	0.999475066		Case	SEARCH
Case_2674		1	Case	SEARCH
Case_2675		1	Case	SEARCH
Case_2676		1	Case	SEARCH
Case_2677		1	Case	SEARCH
Case_2678		1	Case	SEARCH
Case_2679		1	Case	SEARCH
PD30710a		1	Case	SEARCH
Case_2680		1	Case	SEARCH
Case_2681		1	Case	SEARCH
Case_2682		1	Case	SEARCH
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Case_2685		1	Case	SEARCH
Case_2686		1	Case	SEARCH
Case_2687		1	Case	SEARCH
Case_2688		1	Case	SEARCH
Case_2689		1	Case	SEARCH
Case_2690		1	Case	SEARCH
Case_2691	0.998425197		Case	SEARCH
Case_2692		1	Case	SEARCH
PD30695a		1	Case	SEARCH

Case_2693		1	Case	SEARCH
Case_2694		1	Case	SEARCH
Case_2695	0.999475066		Case	SEARCH
Case_2696		1	Case	SEARCH
Case_2697		1	Case	SEARCH
Case_2698		1	Case	SEARCH
Case_2699		1	Case	SEARCH
Case_2700	0.998950131		Case	SEARCH
Case_2701		1	Case	SEARCH
Case_2702	0.996325459		Case	SEARCH
Case_2703		1	Case	SEARCH
Case_2704		1	Case	SEARCH
Case_2705		1	Case	SEARCH
Case_2706		1	Case	SEARCH
Case_2707		1	Case	SEARCH
Case_2708		1	Case	SEARCH
Case_2709		1	Case	SEARCH
Case_2710		1	Case	SEARCH
Case_2711		1	Case	SEARCH
Case_2712		1	Case	SEARCH
Case_2713		1	Case	SEARCH
Case_2714		1	Case	SEARCH
Case_2715	0.999475066		Case	SEARCH
Case_2716	0.998950131		Case	SEARCH
Case_2717	0.981627297		Case	SEARCH
Case_2718		1	Case	SEARCH
Case_2719		1	Case	SEARCH
Case_2720		1	Case	SEARCH
Case_2721		1	Case	SEARCH
Case_2722		1	Case	SEARCH
Case_2723		1	Case	SEARCH
Case_2724		1	Case	SEARCH
Case_2725		1	Case	SEARCH
Case_2726		1	Case	SEARCH
Case_2727		1	Case	SEARCH
Case_2728		1	Case	SEARCH
Case_2729		1	Case	SEARCH
Case_2730		1	Case	SEARCH
Case_2731		1	Case	SEARCH
Case_2732		1	Case	SEARCH

Case_2733		1	Case	SEARCH
Case_2734		1	Case	SEARCH
Case_2735	0.993700787		Case	SEARCH
Case_2736		1	Case	SEARCH
Case_2737		1	Case	SEARCH
Case_2738		1	Case	SEARCH
Case_2739		1	Case	SEARCH
Case_2740		1	Case	SEARCH
Case_2741	0.997900262		Case	SEARCH
Case_2742		1	Case	SEARCH
Case_2743		1	Case	SEARCH
Case_2744		1	Case	SEARCH
Case_2745		1	Case	SEARCH
Case_2746		1	Case	SEARCH
Case_2747		1	Case	SEARCH
Case_2748	0.998950131		Case	SEARCH
Case_2749		1	Case	SEARCH
PD30734a		1	Case	SEARCH
Case_2750		1	Case	SEARCH
Case_2751		1	Case	SEARCH
Case_2752		1	Case	SEARCH
Case_2753		1	Case	SEARCH
Case_2754		1	Case	SEARCH
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Case_2761		1	Case	SEARCH
Case_2762		1	Case	SEARCH
Case_2763		1	Case	SEARCH
Case_2764		1	Case	SEARCH
Case_2765		1	Case	SEARCH
Case_2766		1	Case	SEARCH
Case_2767	0.962729659		Case	SEARCH
Case_2768	0.999475066		Case	SEARCH
Case_2769	0.999475066		Case	SEARCH
Case_2770		1	Case	SEARCH
Case_2771		1	Case	SEARCH

Case_2772		1	Case	SEARCH
Case_2773		1	Case	SEARCH
Case_2774		1	Case	SEARCH
Case_2775		1	Case	SEARCH
Case_2776		1	Case	SEARCH
Case_2777		1	Case	SEARCH
Case_2778		1	Case	SEARCH
Case_2779	0.98687664	1	Case	SEARCH
Case_2780		1	Case	SEARCH
Case_2781		1	Case	SEARCH
PD30715a		1	Case	SEARCH
Case_2782		1	Case	SEARCH
Case_2783		1	Case	SEARCH
Case_2784		1	Case	SEARCH
Case_2785		1	Case	SEARCH
Case_2786		1	Case	SEARCH
Case_2787		1	Case	SEARCH
Case_2788	0.994225722	1	Case	SEARCH
Case_2789		1	Case	SEARCH
PD30730a		1	Case	SEARCH
Case_2790	0.981102362	1	Case	SEARCH
Case_2791		1	Case	SEARCH
Case_2792		1	Case	SEARCH
Case_2793		1	Case	SEARCH
Case_2794	0.999475066	1	Case	SEARCH
Case_2795		1	Case	SEARCH
Case_2796	0.999475066	1	Case	SEARCH
Case_2797		1	Case	SEARCH
Case_2798		1	Case	SEARCH
Case_2799		1	Case	SEARCH
Case_2800		1	Case	SEARCH
Case_2801		1	Case	SEARCH
Case_2802		1	Case	SEARCH

Supplementary Table 15. List of samples that were re-sequenced by Illumina for confirmation. The average coverage of coding *POT1* exons is included. In red, samples with a coverage lower than 10.

Sample	Average coverage
PD30545a	287.8183206
PD30546a	288.3867684
PD30547a	316.0020356
PD30548a	261.8880407
PD30549a	270.092112
PD30550a	276.5094148
PD30551a	233.7791349
PD30552a	280.6137405
PD30553a	213.3725191
PD30554a	222.3903308
PD30555a	251.7562341
PD30556a	274.5073791
PD30557a	232.5338422
PD30558a	258.5124682
PD30559a	238.7760814
PD30560a	272.6096692
PD30561a	222.6605598
PD30562a	219.8117048
PD30563a	199.8819338
PD30564a	205.2101781
PD30565a	207.2946565
PD30566a	162.3760814
PD30567a	179.4575064
PD30568a	242.4076336
PD30569a	221.9236641
PD30570a	192.2992366
PD30571a	203.7043257
PD30572a	200.3638677
PD30573a	240.3857506
PD30574a	176.0834606
PD30575a	171.8956743
PD30576a	283.5114504

PD30577a	39.16132316
PD30578a	197.389313
PD30580a	210.7857506
PD30581a	198.3964377
PD30583a	46.1821883
PD30584a	297.8717557
PD30585a	249.1292621
PD30586a	226.3501272
PD30587a	193.0188295
PD30588a	202.0259542
PD30589a	172.4081425
PD30590a	209.4025445
PD30591a	217.8610687
PD30592a	151.3547074
PD30593a	258.092112
PD30594a	254.4625954
PD30595a	277.8605598
PD30596a	370.070229
PD30597a	255.5842239
PD30598a	282.1699746
PD30599a	621.8208651
PD30600a	327.9231552
PD30602a	388.0508906
PD30603a	353.3725191
PD30605a	138.205598
PD30606a	254.4748092
PD30607a	95.09363868
PD30609a	194.2732824
PD30611a	15.45343511
PD30612a	35.04529262
PD30616a	21.76743003
PD30619a	17.80050891
PD30621a	9.415776081
PD30625a	50.44732824
PD30627a	113.9089059
PD30628a	21.96234097
PD30629a	3.165903308
PD30630a	45.34249364
PD30632a	36.01475827

PD30633a	15.52875318
PD30634a	9.458015267
PD30635a	32.99592875
PD30636a	26.81017812
PD30637a	15.63206107
PD30638a	15.51094148
PD30639a	9.541984733
PD30642a	59.01577608
PD30643a	60.43613232
PD30644a	44.78015267
PD30646a	74.86310433
PD30647a	16.94045802
PD30648a	38.43358779
PD30650a	33.04478372
PD30651a	26.5129771
PD30652a	36.93180662
PD30654a	79.25292621
PD30655a	11.03918575
PD30656a	4.024936387
PD30657a	17.70585242
PD30659a	14.7216285
PD30660a	12.85496183
PD30661a	20.13231552
PD30662a	194.1725191
PD30663a	27.2783715
PD30664a	220.9577608
PD30665a	197.2371501
PD30668a	16.32315522
PD30682a	15.10025445
PD30683a	72.46412214
PD30684a	7.121119593
PD30689a	10.51501272
PD30693a	42.9740458
PD30695a	194.9338422
PD30697a	83.20101781
PD30698a	73.72315522
PD30699a	179.6483461
PD30700a	206.3348601
PD30701a	139.0452926

PD30702a	170.1180662
PD30705a	167.4447837
PD30707a	167.2417303
PD30708a	124.3145038
PD30710a	156.3195929
PD30711a	18.57201018
PD30712a	180.1597964
PD30713a	206.6977099
PD30714a	200.1389313
PD30715a	250.7633588
PD30716a	184.5175573
PD30717a	198.6508906
PD30718a	217.8335878
PD30719a	262.378117
PD30720a	291.1007634
PD30721a	198.0447837
PD30722a	235.4697201
PD30723a	266.5867684
PD30725a	172.2631043
PD30727a	287.464631
PD30728a	237.1211196
PD30729a	188.5796438
PD30730a	260.6300254
PD30731a	247.113486
PD30732a	199.1058524
PD30733a	261.3852417
PD30735a	362.6697201
PD30736a	349.4178117
PD30737a	269.4223919
PD30738a	332.5206107
PD30739a	393.026972
PD30740a	343.0900763
PD30741a	419.5821883
PD30742a	367.9903308
PD30743a	314.8748092
PD30744a	377.329771
PD30745a	358.3201018
PD30746a	382.1913486
PD30747a	357.1867684

PD30748a	313.3450382
PD30749a	368.9536896
PD30750a	420.6681934
PD30751a	320.8229008
PD30752a	444.4320611
PD30753a	380.2483461
PD30754a	331.4610687
PD30755a	480.23257
PD30756a	442.5760814
PD30757a	376.9058524
PD30758a	444.9033079
PD30759a	429.3709924
PD30760a	359.3750636
PD30761a	419.8956743
PD30762a	417.4147583

Supplementary Table 16. List of samples that were re-sequenced by capillary. Information about the variants re-sequenced and the result of the experiment is included. In green, samples and variants that were confirmed.

Sample	Variant tested	Result
PD30582a	p.Cys307Arg	Not present
PD30601a	p.Arg117His	Present
PD30604a	p.His393Arg	Present
PD30608a	p.Ile22Val	Present
PD30610a	p.Pro601Leu	Not present
PD30624a	p.Glu92Lys, p.Arg83Gly	Not present
PD30681a	p.Val391Ile	Not present
PD30687a	p.Gln376Ter	Not present
PD30692a	p.Trp194Ter	Not present
PD30696a	p.Pro34Ser	Not present
Case_2636	p.Asp617GlufsTer9	Present
Ctrl_1401	p.Asp617GlufsTer9	Present
Ctrl_3151	p.Asp617GlufsTer9	Present
Case_1755	p.Gln358SerfsTer13	Present
Ctrl_2641	p.Glu204Ter	Not present
Ctrl_2500	p.Asp200Asn	Not present
Case_2329	p.Asp185Glu	Not present
Ctrl_2165	p.Asp185Glu	Not present
Case_1223	p.Asp175Ter	Not present

Supplementary Table 17. List of samples with variants in known melanoma predisposition genes. Genes *CDK4*, *CDKN2A* and *BAP1* were checked for variants. Only samples that were resequenced by Illumina (Supplementary Table 15) were assessed.

Sample	POT1 variant	Variant in pathogenic gene
PD30744a	p.Gln376Arg	<i>CDKN2A</i> Ala148Thr
PD30549a	p.Gly404Val	<i>CDKN2A</i> Ala148Thr
PD30730a	p.Gly404Val & p.Tyr419Cys	<i>CDKN2A</i> Ala60Thr