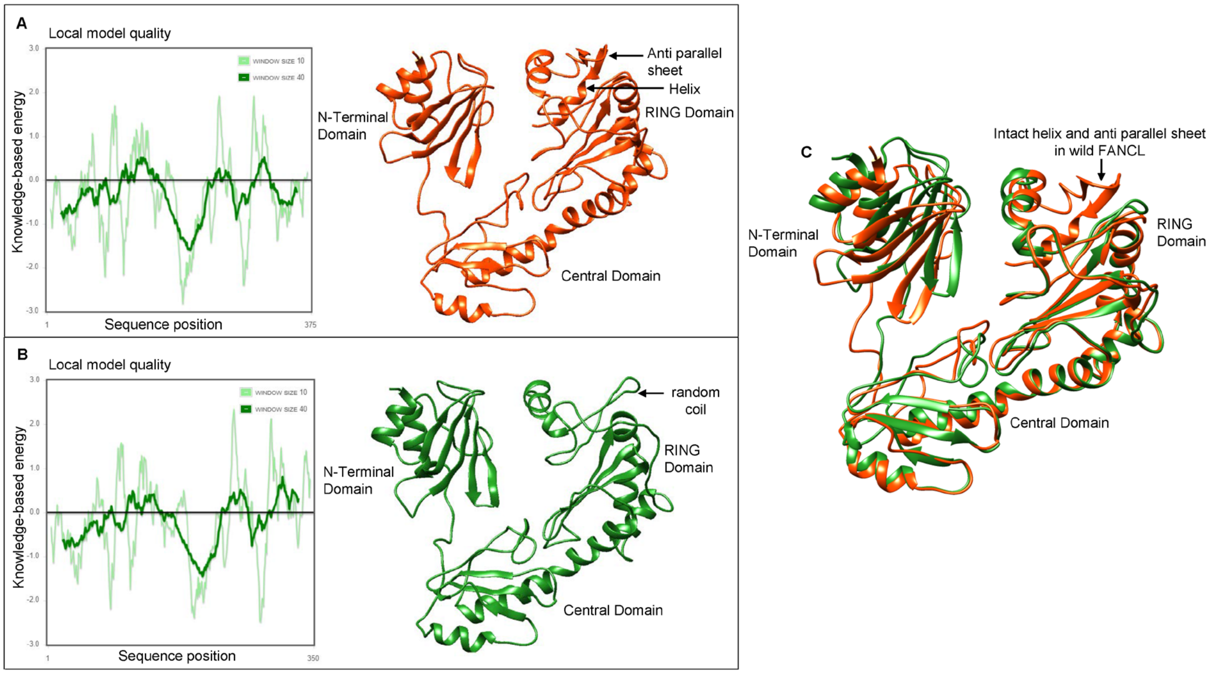
Supplemental Figure S1.



PROSA based local model quality analysis to estimate the overall knowledge-based energy [Left] and structures generated using GenTHREADER [Right]. (A) wild-type FANCL and (B) mutant FANCL p.W341_K364del. (C) Structural superimposition of wild-type FANCL with mutant FANCL p.W341_K364del. The wild-type is shown in orange color and the mutant in green color.

Supplemental Figure S2.

Population stratification *via* multi-dimensional scaling analysis of the fourteen genotyped individuals from our study (FANCL_c.1092G>A) and the 2,501 individuals from the 1000 Genomes Project Phase 3 cohort. AFR – African; AMR – Ad Mixed American; EAS – East Asian; EUR – European; SAS – South Asian.

Supplemental Table S1. Summary of chromosome breakage test results.

Individuals	With MMC					Without MMC		
	No. of metaphases	No. of breaks	Breaks/ metaphase	Metaphases with breaks	No. of breaks/ metaphase with breaks	No. of metaphases	No. of breaks	Breaks/ metaphase
IN01	52	85	1.6	19	4.47	25	5	0.2
IN02	48	112	2.33	23	4.86	20	16	0.8
IN03	45	113	2.5	34	3.32	22	11	0.5
IN04	50	72	1.44	32	2.25	33	7	0.2
IN05	45	53	1.18	20	2.65	30	3	0.1
IN06	54	141	2.6	25	5.64	28	18	0.6
IN07	50	185	3.7	23	8	25	26	1.0
IN08	50	155	3.1	25	6.2	27	20	0.7
IN09	51	53	1.03	19	2.78	23	3	0.1
IN10	54	135	2.5	25	5.4	32	22	0.6
TKFA33*	100	70	0.7	28	2.5	100	6	0.06
FA17*	30	60	2	5	12	50	7	0.14
FA91*	20	161	8.1	18	8.9	50	21	0.42

*DEB (0.1ug/ml) was used, instead of MMC, as the crosslinking agent to induce chromosomal breakage in these three samples.

Supplemental Table S2. In silico prediction results for the effect on mRNA splicing from the *FANCL* chr2:58387243C>T variant.

Prediction Method	Predicted Effect/Score
Human Splicing Finder	Broken Donor Site: “most probably affecting splicing”
MaxEnt	Score difference of 2.91 (decreased from 10.22 (ref score) to 7.31 (mut score))
SpliceAI	Delta score of 0.76 for Donor Loss (Probability that chr2:58387243 is used as a donor site decreases by 0.76)
CADD	PHRED-scaled value of 23.8