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Supplemental Data

Mutations in *TOP3A* Cause a Bloom Syndrome-like Disorder

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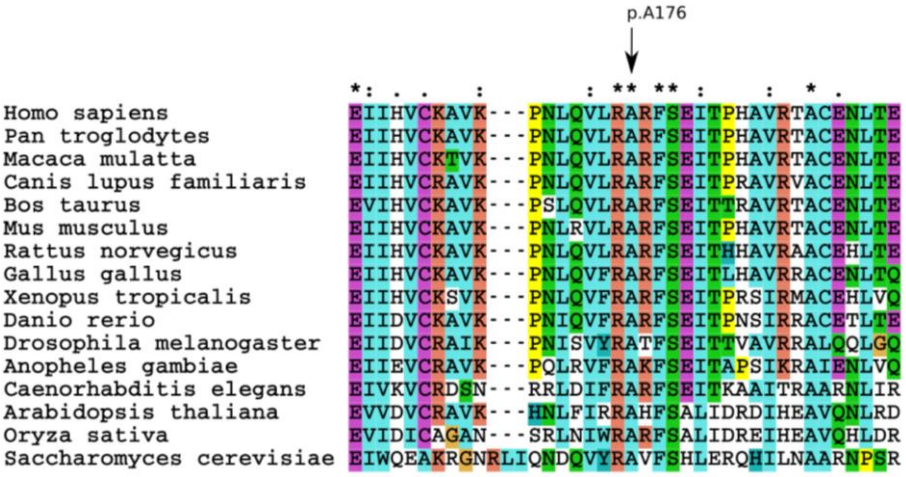

Figure S1. Ala176 in TopIIIα is conserved in eukaryotes.

Refseq sequences from NCBI were aligned using ClustalOmega. For *Saccharomyces cerevisiae*, Top3 aligned.

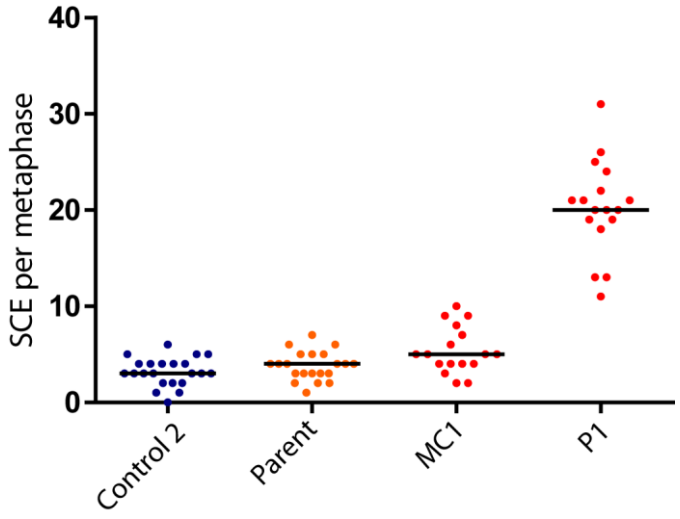

Figure S2. The *TOP3A* MC1 fibroblast cell line does not demonstrate elevated SCEs similar to those seen in patient P1-10.

Quantification of BrdU strand specific labelling of sister chromatids from *TOP3A* MC1 primary fibroblast cells compared to control 2, P1 and P1 parent cells. Median value plotted, n>15 metaphase spreads counted per patient. Data from C2, Parent and P1 reproduced from main figure 3C for comparison.

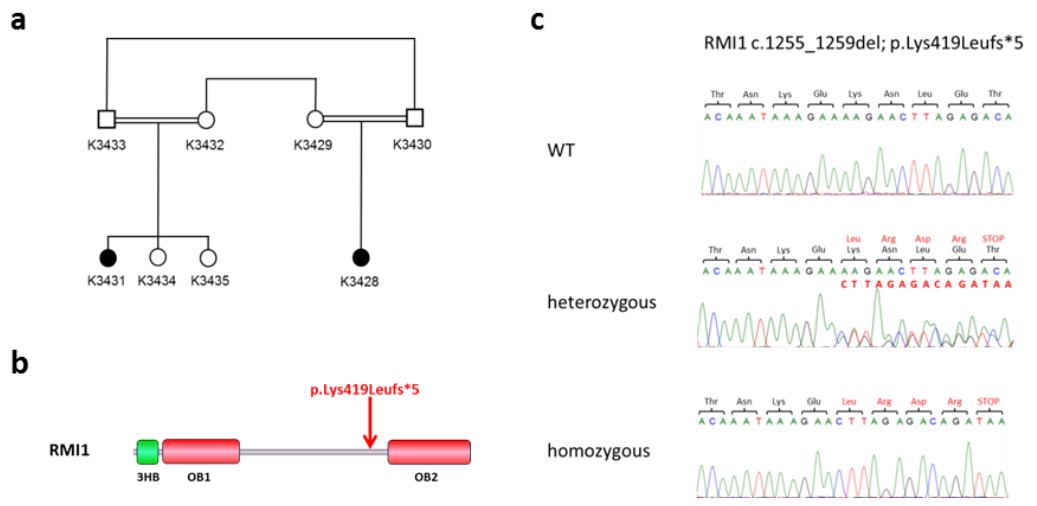

Figure S3: Identification of a homozygous variant in *RMI1* associated with microcephalic dwarfism. (a) Pedigree of the family. **(b)** Position of *RMI1* truncating variant (red) relative to a schematic representation of RMI1 protein structure: RMI1 c.1255_1259del; p.Lys419Leufs*5. 3HB=three-helix bundle; OB=oligonucleotide-binding domain. **(c)** Chromatograms of the novel homozygous variant in *RMI1*.

Table S1. Summary of features of *BLM*, *TOP3A* and *RMI1* individuals.

Key features	*BLM*	*TOP3A*	*RMI1*
Growth restriction	+	+	+
Microcephaly	+	+	+
Malar rash	+	-	-
Cancer predisposition	+	unknown	unknown
Cardiomyopathy	-	+	N/A
Elevated SCE	+	+	N/A