

Supplementary Information

Genetic variants associated with longer telomere length increase risk of chronic lymphocytic leukemia

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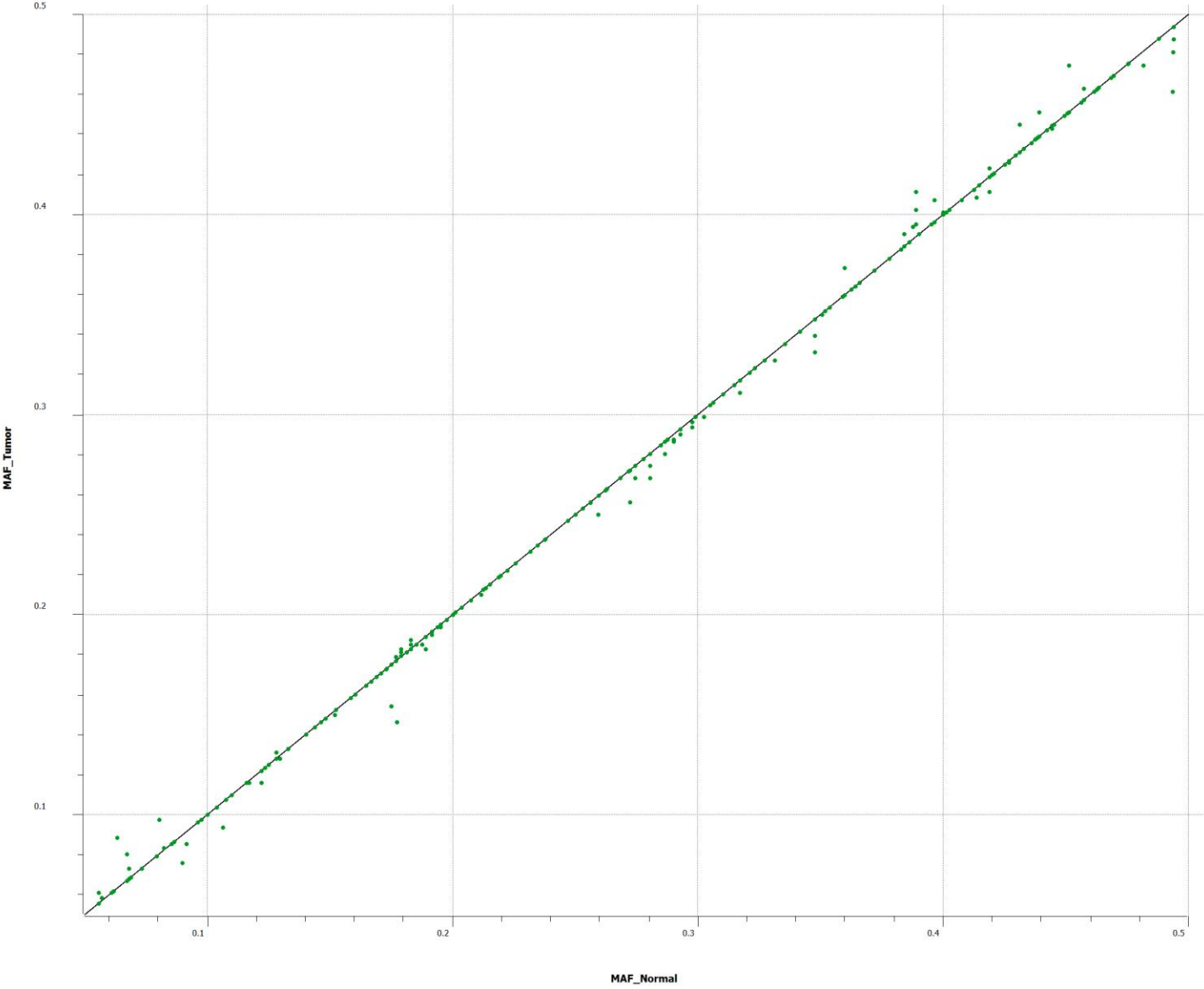
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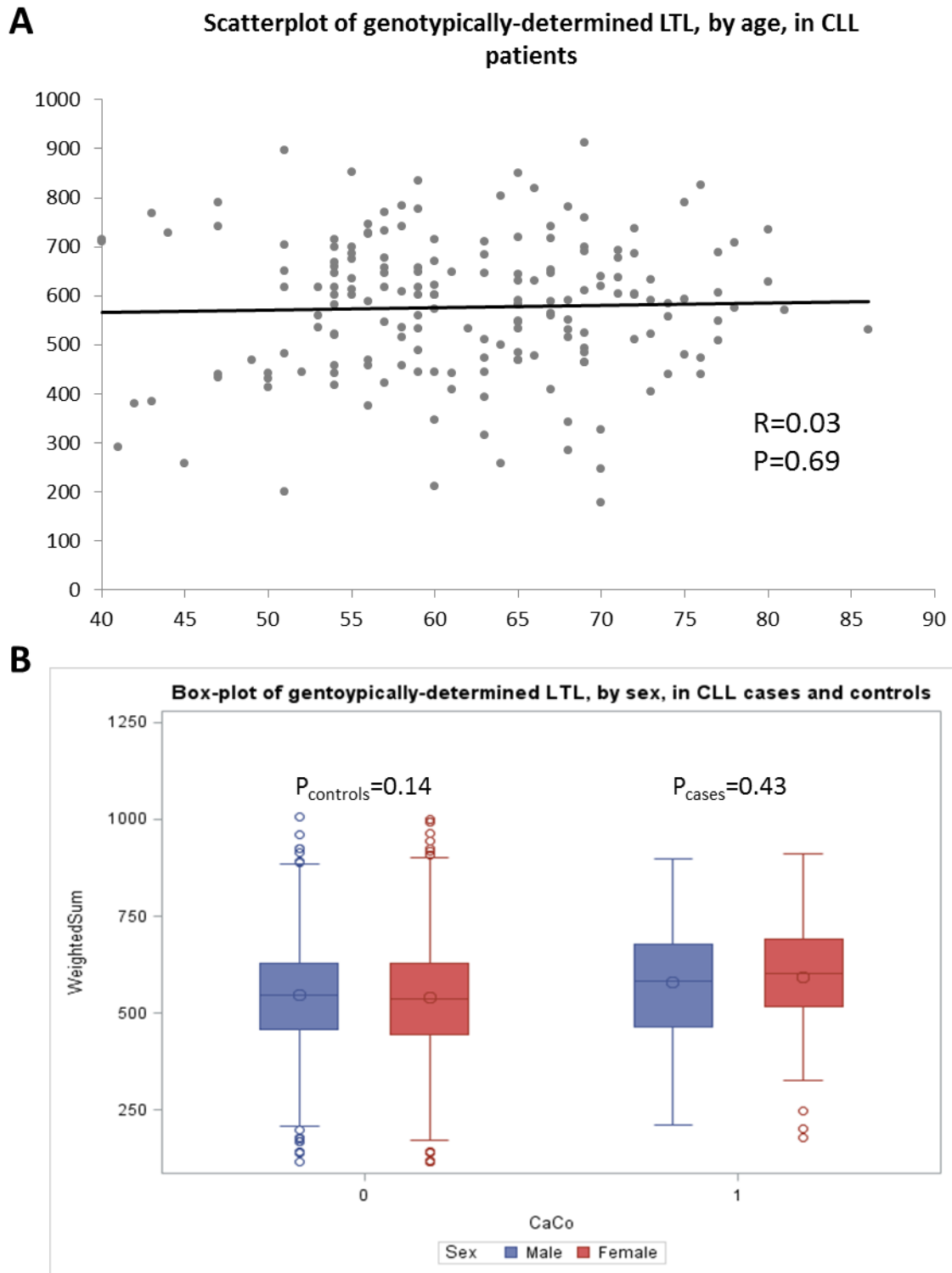
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Supplementary Figure 1: Comparison of allele frequencies in flow-sorted CLL tumor DNA (y-axis) and matched normal DNA (x-axis) among the DFCI subjects. Allele frequencies are plotted for SNPs in eight different 250kb regions containing known LTL-associated genes (*ACYP2*, *TERC*, *NAF1*, *TERT*, *OBFC1*, *CTC1*, *ZNF208*, and *RTEL1*).

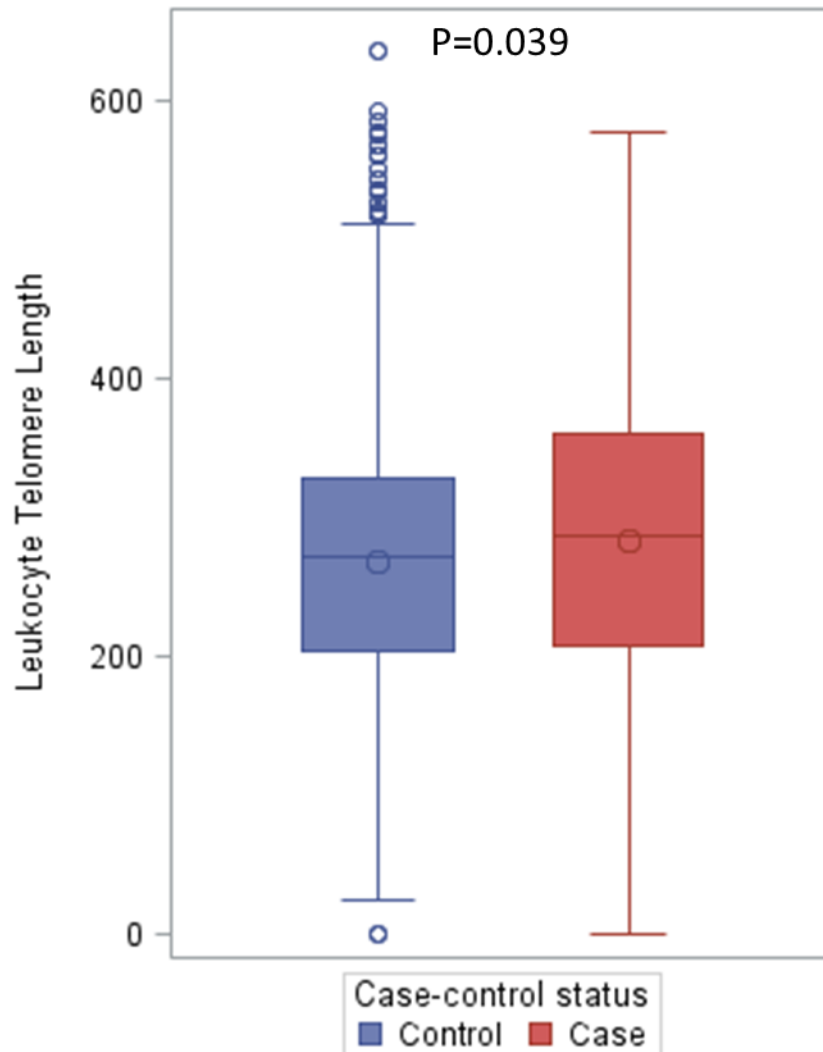


Supplementary Figure 2: Genotypically-estimated leukocyte telomere length (LTL) is not associated with subject age or sex. (A) Scatter-plot of genotypically-estimated LTL and subject age in CLL patients. (B) Boxplots comparing genotypically-estimated LTL in females (blue) and males (red), stratified by CLL case-control status.



Supplementary Figure 3: Boxplot comparing genotypically-estimated leukocyte telomere length (LTL) in 273 CLL patients and 5725 controls, after excluding contributions from known CLL risk genes (*TERC*, *TERT*) and retaining contributions from *ACYP2*, *NAF1*, *OBFC1*, *CTC1*, *ZNF208* and *RTEL1*. P-values are adjusted for the first two ancestry-informative principal components and for genotyping platform.

Comparison of genotypically-estimated LTL by CLL case-control status, excluding contributions from *TERC* and *TERT*



Supplementary Table 1. Subject characteristics of CLL patients and controls: Eastern Cooperative Oncology Group (ECOG) 2997 trial CLL patients, Illumina iControls, Dana-Farber Cancer Institute (DFCI) CLL patients, and Wellcome Trust (WTCCC) controls.

Populations	N (cases/controls)	Genotyping array	Ethnicity	% Female (cases/controls)	Median Age (cases/controls)
<u>Discovery</u>					
ECOG CLL patients	215 / 0	Illumina 550k	Caucasian	32% / -	61 / -
Illumina iControls	0 / 3390	Illumina 370k/550k	Caucasian	- / 63%	- / 31
<u>Validation</u>					
DFCI CLL patients	101 / 0	Affymetrix 6.0	Caucasian	38% / -	55 / -
Wellcome Trust controls	0 / 2603	Affymetrix 6.0	Caucasian	- / 48%	- / ^a

^a Precise age data were unavailable, but >50% of the included samples were members of the 1958 UK Birth Cohort.