

Supplementary Figure 1: Distribution of sequencing coverage by histological subtype There was no difference in the sequencing coverage between samples from different histological subtypes (Wilcoxon-Mann-Whitney, p = 0.08).



Supplementary Figure 2: SV burden associations with BA-SV frequency

(a) There is a strong association between SV burden and BA-SV frequency in acral melanomas (Pearson's r = 0.75, $p = 2.2 \times 10^{-16}$), compared to a (b) moderate association in mucosal melanomas (Pearson's r = 0.57, $p = 8.8 \times 10^{-7}$), and a (c) weak association in cutaneous melanomas (Pearson's r = 0.26, $p = 6.2 \times 10^{-4}$).



B)



Supplementary Figure 3: Functional consequences of highlighted and overlapping SVs in CCLE (a) Percentile gene expressions of cell lines with SVs affecting genes highlighted in Figure 3. (b) Boxplot showing the normalized expression of genes affected by SVs compared to those that are unaffected. The p-value is from performing a Mann-Whitney test on the pan-gene aggregated z-scored (i.e. each gene z-scored separately to put the expression values on the same scale) expression.

SV

No SV



Supplementary Figure 4: Distribution of NHEJ:SSA ratio between signature 3 and non-signature 3 tumors by SV type

The difference between the NHEJ:SSA ratio in SBS3-positive and negative tumors was statistically significant and equally as enriched in SBS3 positive tumors across DUP, INV, and TRA events (Mann-Whitney U, $p < 6.9 \times 10^{-3}$), but not DEL events (Mann-Whitney U, p > 0.05).



11 6

log₂(Geometric Mean of MRN Complex Genes RSEM–UQ Expression)

7 8 9 10 11

6

8 9 10 0.2

0.3

0.4

0.6

0.5 Pearson's Correlation Coefficient

0.7

0.8

0.9

Supplementary Figure 5: Association between ATM and the MRN complex in TWT and non-TWT **Melanomas**

(a) No difference was observed in the association between MRE11A or NBN expression and ATM expression compared to the association between RAD50 and ATM expression in TWT tumors (b) The correlation between ATM expression and MRN complex expression (methods) in non-TWT and TWT cutaneous melanoma tumors. (c) The distribution of Pearson's correlation coefficients from 10,000 randomly sampled simulations where non-TWT cutaneous tumors are downsampled to the number of TWT cutaneous tumors in the cohort.



Supplementary Figure 6: Western Blots for MeWo and A375 melanoma cell lines

Western blots for the MeWo and A375 melanoma cell lines for knockouts of *ATM*, *MRE11*, and *NBN*. Vinculin is used a negative control.