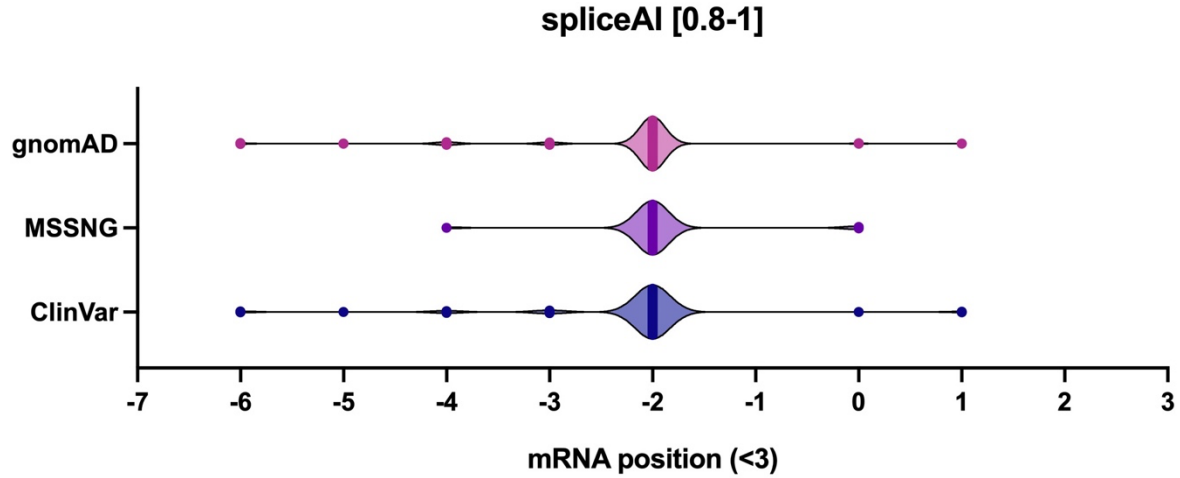


**Supplemental Figure 1. Pre-mRNA positions of DG splice sites with high SpliceAI scores ( $\geq 0.8$ ) created by nonsense variants across gnomAD, MSSNG, and ClinVar.**

Analyses focused on scores with pre-mRNA positions  $< 3$  (i.e., excluding splicing changes downstream of the resulting stop codon). See text for details.



## Supplemental Figure 2. Visualization of a 37 bp window of the MANE Select *TSC2* transcript containing a C>T bp change at cDNA position 4081.

The top strand represents the reference sequence and the bottom strand represented the variant sequence. Highlighted nucleotides indicate the bp change. Blue markers indicate *in silico* prediction scores from SpliceSiteFinder-like, MaxEntScan, NNSPLICE, and GeneSplicer for a donor splice site. See text for details. Image produce by Alamut Visual Plus (v1.7 © 2022 SOPHiA GENETICS).

