Figure S1 cassette exon cassette exon retained intron, (NMD-irrelevant) constitutive (NMD-relevant) 10% up = 183 (1.6%)  $N_{\geq 10\% \text{ up}} = 184 (2.2\%)$ down = 256 (3.0%) intron spliced out in S34F (%) inclusion isoform in S34F NMD isoform in S34F NMD isoform in WT (%) intron spliced out in WT (%) inclusion isoform in WT (%) .<sub>10% up</sub> = 113 (1.3%) 10% up = 200 (0.49%) = 166 (1.9%)inclusion isoform in S34Y intron spliced out in S34Y VMD isoform in S34Y O NMD isoform in WT (%) intron spliced out in WT (%) inclusion isoform in WT (%) <sub>10% up</sub> = 117 (0.3%)  $N_{\geq 10\% \text{ up}} = 33 \ (0.39\%)$  $N_{\geq 10\% \text{ up}} = 81 (0.69\%)$  $_{m} = 84 (0.99\%)$ intron spliced out in Q157P inclusion isoform in Q157P NMD isoform in Q157P inclusion isoform in WT (%) NMD isoform in WT (%) intron spliced out in WT (%) 10% up = 63 (0.74%) ≥10% up = 110 (0.94%) = 126 (0.32%)inclusion isoform in Q157R (%) NMD isoform in Q157R (%) ntron spliced out in Q157R NMD isoform in WT (%) intron spliced out in WT (%) inclusion isoform in WT (%) ₹100 <sub>:10% up</sub> = 131 (1.3%) ≥10% up = 186 (1.4%) <del>=</del> 77 (0.17 % down = 96 (0.98% intron spliced out in U2AF1 KD nclusion isoform in U2AF1 KD 1.4X enrichment for exon skipping

NMD isoform in control KD (%)

intron spliced out in control KD (%)

inclusion isoform in control KD (%)