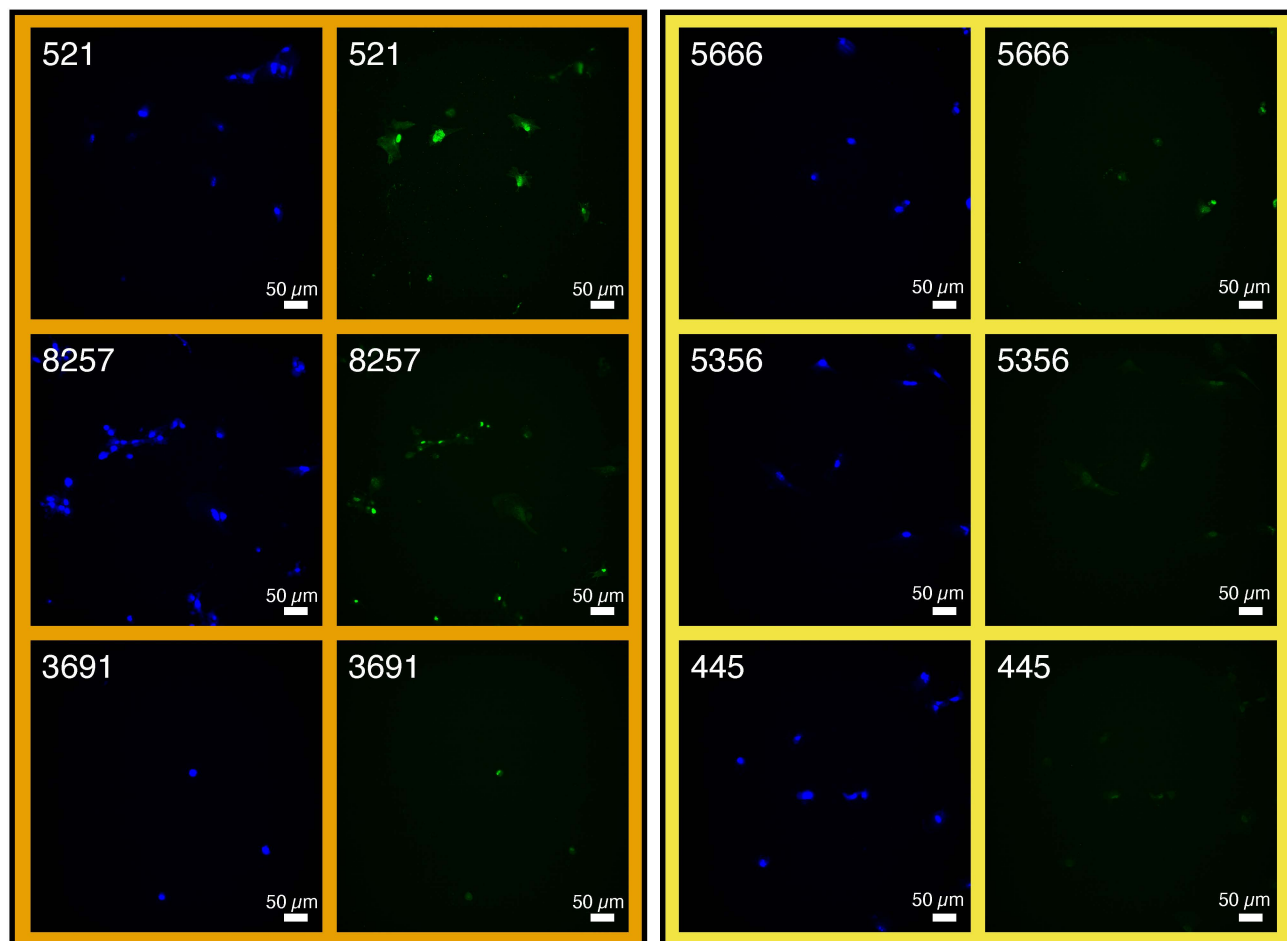


A



B

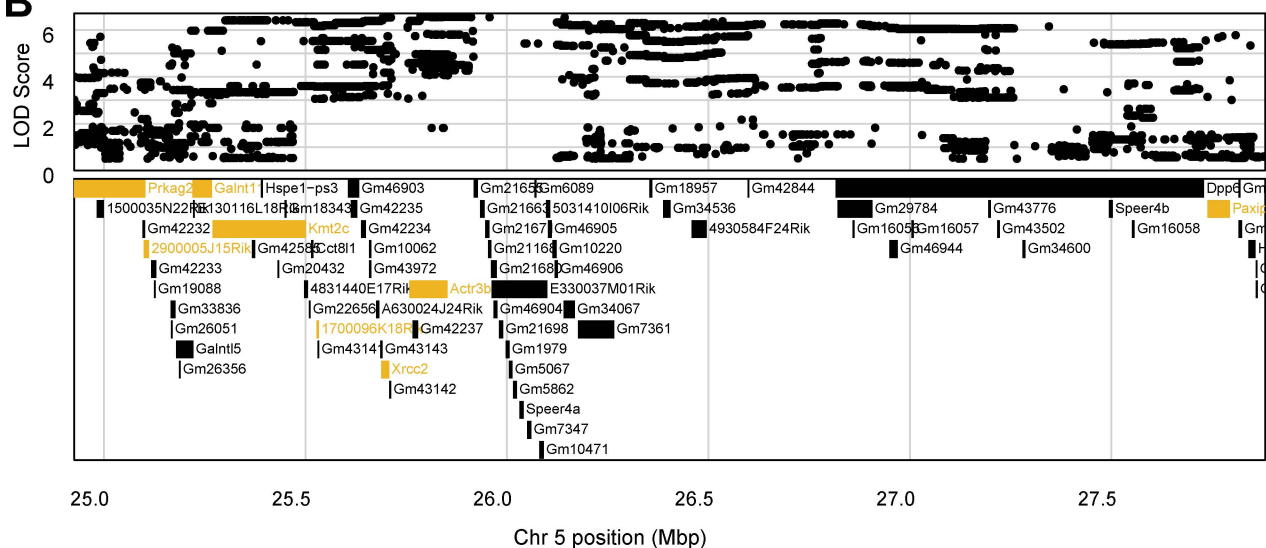


Figure S1: Genetic variation near *Xrcc2* associated with nuclear changes following MMA^{III} exposure

(A) Representative images for the two fibroblast lines at a 1 μ M MMA^{III} concentration with nuclei labeled by Hoechst 33342 (blue) and γ H2AX (Alexa-488 secondary; green) for primary fibroblasts with a 129 allele (orange; n = 3) versus an AJ/B6 allele (yellow; n = 3) at the maximum position for the 'EC90 Hoechst Nucleus Symmetry (02) Hole Mean per Well' cmQTL.

(B) Variant association mapping within the CI the cmQTL 'EC90 Hoechst Nucleus Symmetry (02) Hole Mean per Well'. Top panel shows the LOD scores of the known, segregating variants in the 8 DO founders (GRCm38). Bottom panel shows the gene models within the respective CI. Each point represents a variant. Colors indicate whether a gene is expressed > 0.5 TPM (gold) or < 0.5 TPM (black).

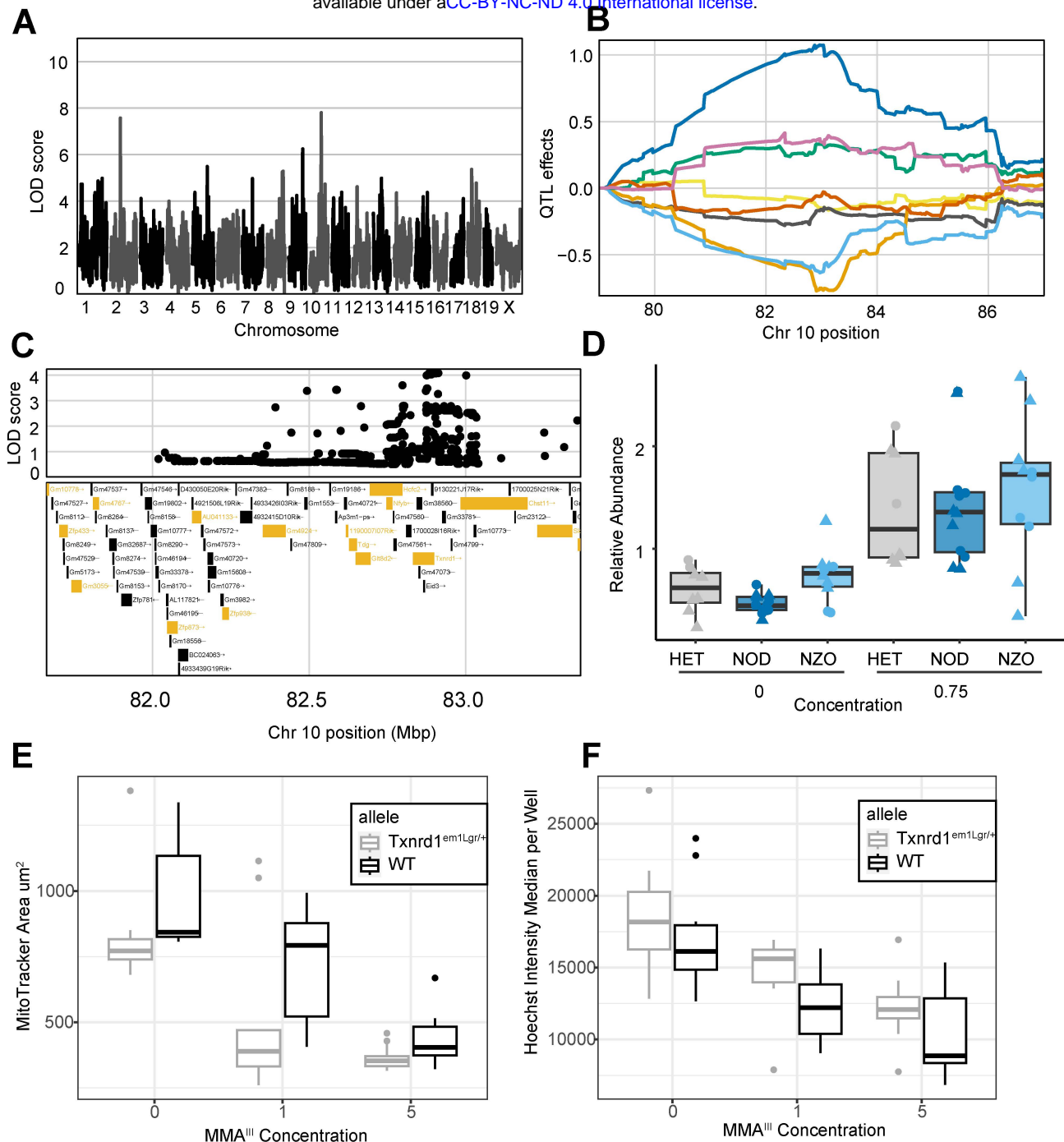


Figure S2: Heterozygous SECIS-Knockout in Txnrd1 Recapitulates Cell Area Phenotype

(A) QTL scan for the `EC90 Mitosmooth Symmetry (3) Texture Edge Mean per Well` cmQTL with the maximum peak at chromosome 10: 82,967,807 bp (m38) and a LOD score of 7.64.

(B) Allele effects plot showing the eight DO founders (colors, see Methods) for the `EC90 Mitosmooth Symmetry (3) Texture Edge Mean per Well` cmQTL across the surrounding region on chromosome 10 (Mbp).

(C) Variant association mapping within the CI the cmQTL `H2AX-negative cells slope Cell Area μm^2 mean per well`. Top panel shows the LOD scores of the known, segregating variants in the 8 DO founders (m38). Bottom panel shows the gene models within the respective CI. Each point represents a variant. Colors indicate whether a gene is expressed > 0.5 TPM (gold) or < 0.5 TPM (black). The arrow indicates the direction of transcription.

(D) Relative abundance of TXNRD1 compared between DO fibroblast lines with NOD (n=6), NZO (n=5), and NOD/NZO (n=4) alleles at the chromosome 10 locus. Significance testing was performed using permutations testing (n = 1000). Star (*) represents p-value < .05.

(E) MitoTracker Deep Red Cell Area across increasing MMA^{III} concentration for Txnrd1^{em1Lgr/+} (n=3) compared to B6 control (n=3) primary fibroblasts. Colors indicate wild-type (black) compared to Txnrd1^{em1Lgr/+} (gray) primary fibroblast lines.

(F) `Hoechst 33342 intensity` across increasing MMA^{III} concentration for Sec^{-/-} (n=3) compared to B6 control (n=3) primary fibroblasts. Colors indicate wild-type (black) compared to Txnrd1^{em1Lgr/+} (gray) primary fibroblast lines.