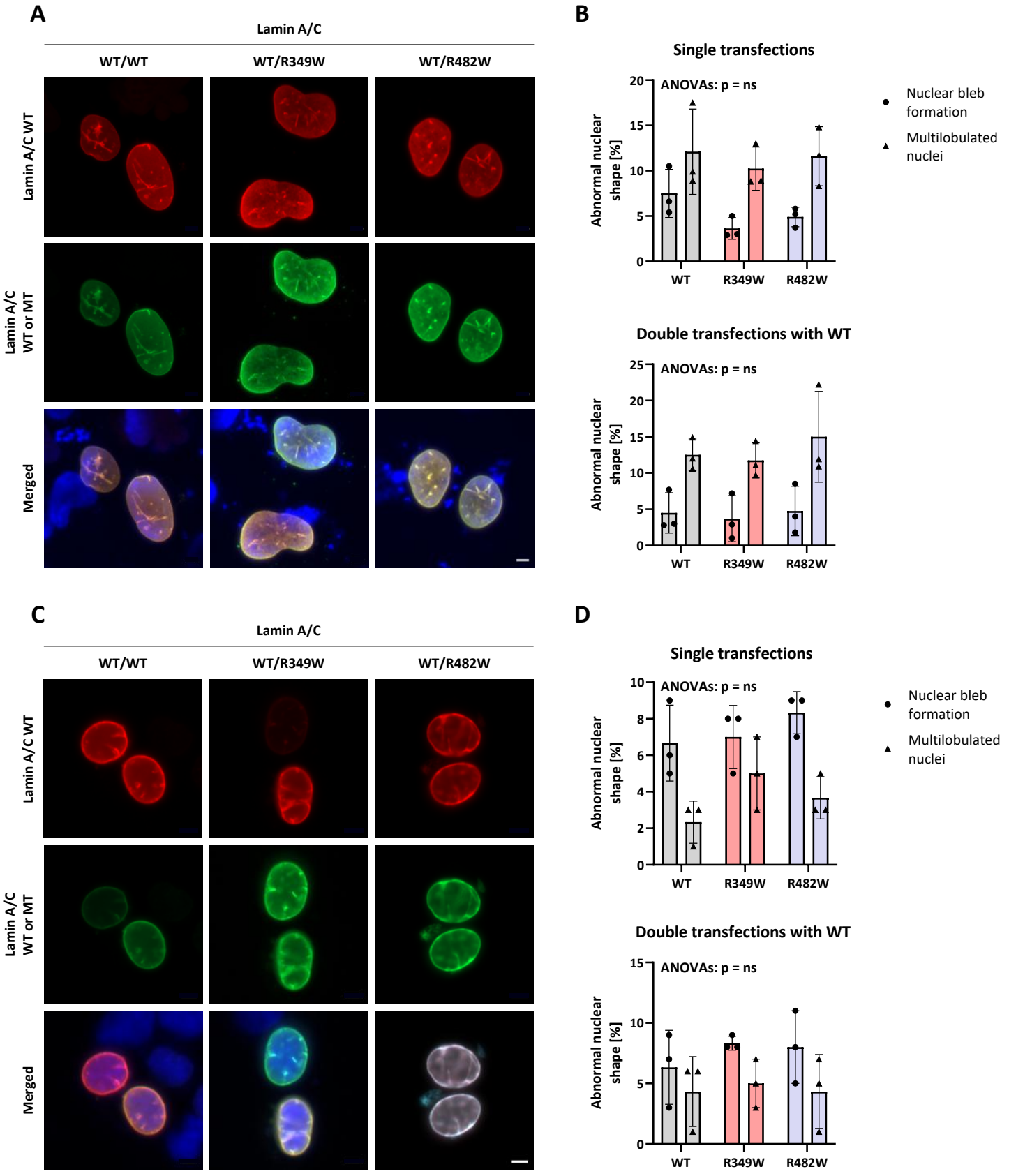
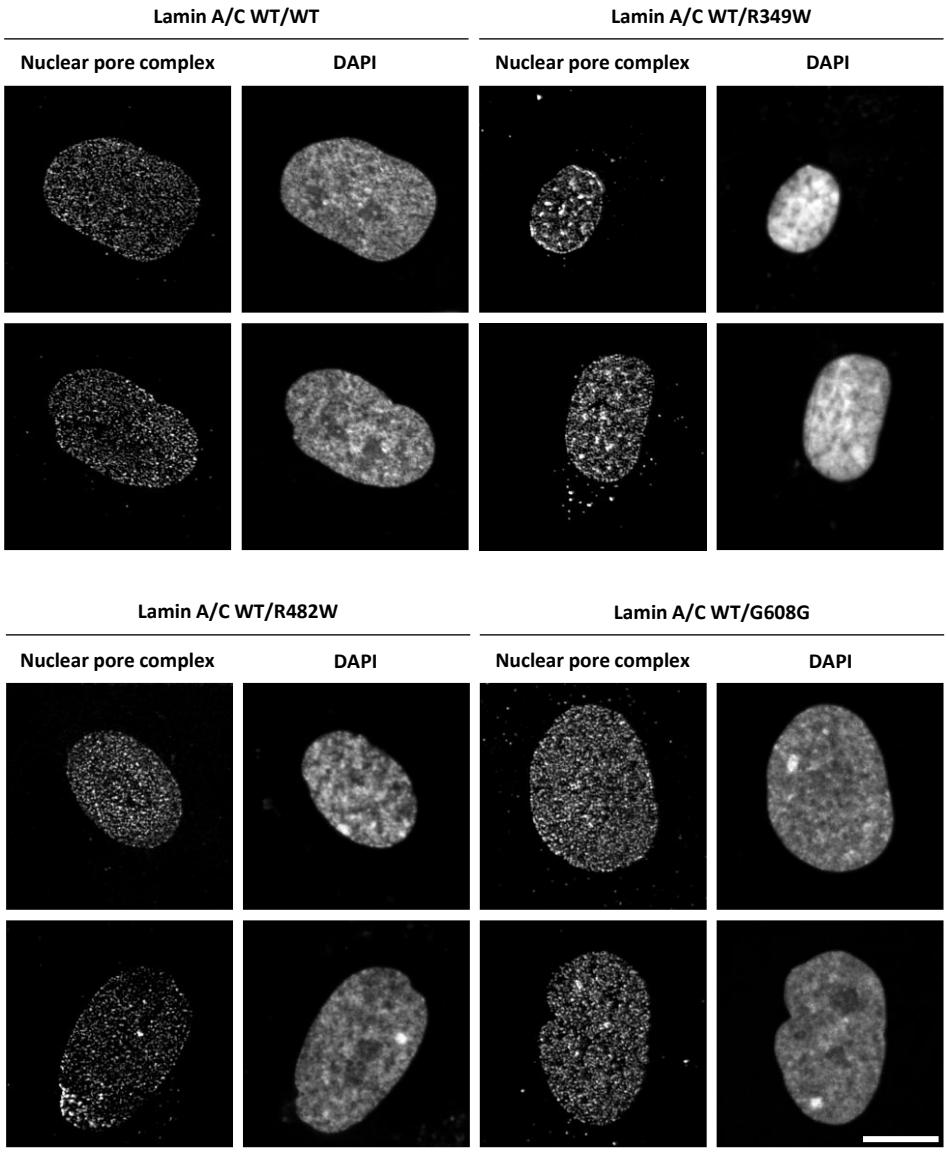
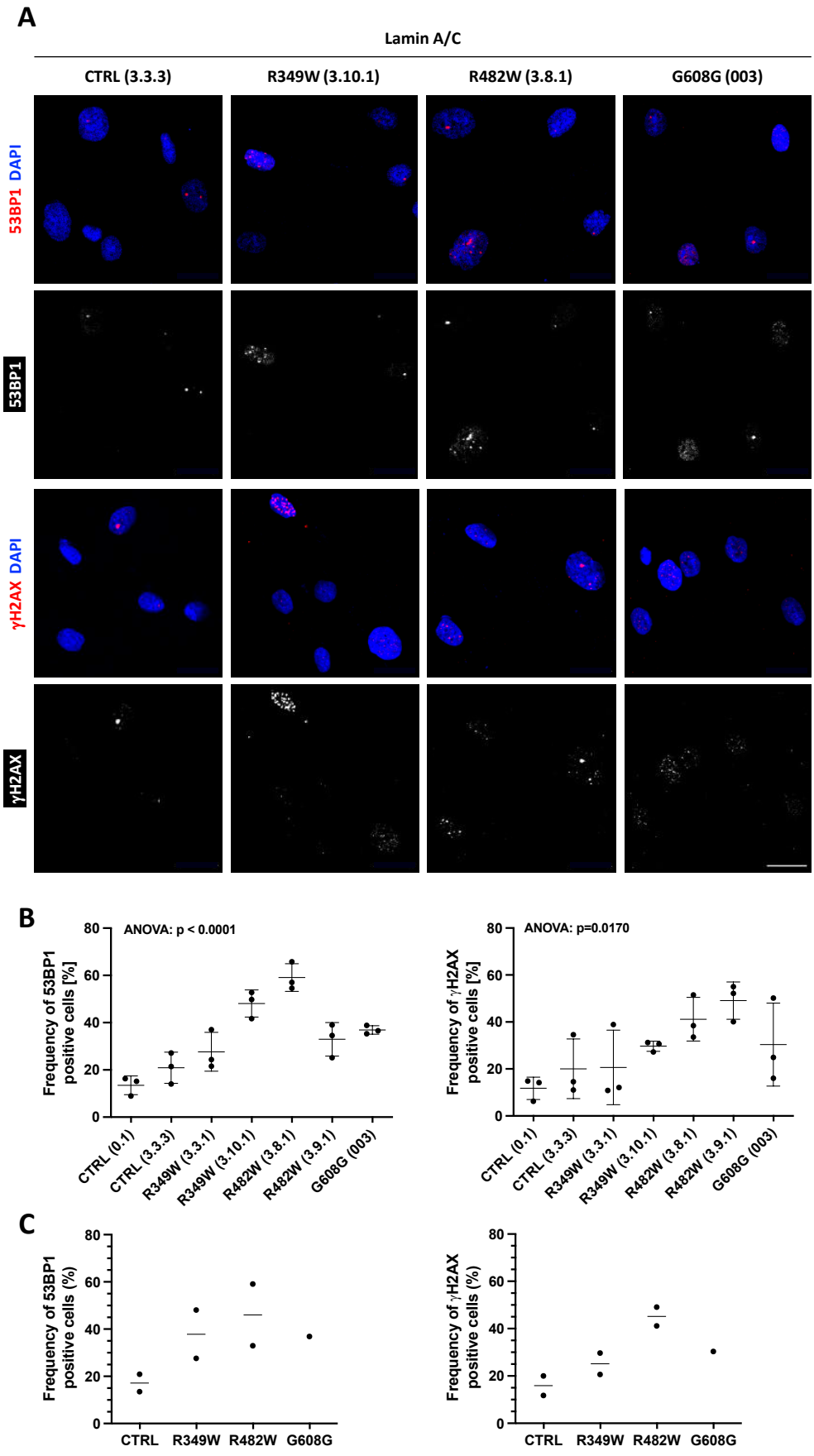


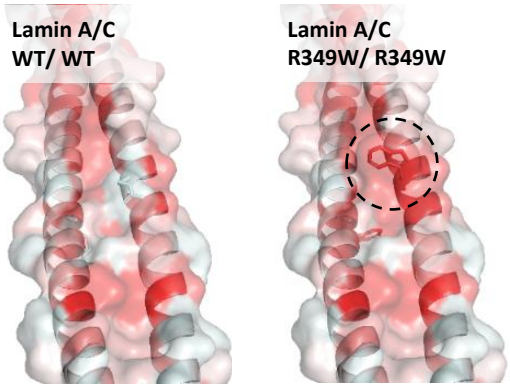
Supplemental Figure 1. Lamin A/C Arg349Trp localizes to the nuclear envelope and does not alter nuclear morphology in immortalized human podocytes and HEK293T cells. Immortalized human podocytes or HEK293T cells were transiently co-transfected with wild-type mCherry-tagged *LMNA* and wild-type or mutant EmGFP-tagged *LMNA* constructs as indicated. (**A**) In podocytes, wild-type and mutant lamin A/C colocalize at the nuclear envelope. Nuclei are stained with DAPI (blue). Scale bar, 5 µm. (**B**) In podocytes, the amount of abnormally shaped nuclei does not significantly differ between genotypes. Data from one of two observers; one-way ANOVAs; number of nuclei analyzed, n = 99-121. Mean ± SD. (**C**) In HEK293T cells, wild-type and mutant lamin A/C colocalize at the nuclear envelope. Nuclei are stained with DAPI (blue). Scale bar, 5 µm. (**D**) In HEK293T cells, the amount of abnormally shaped nuclei does not significantly differ between genotypes (data from one of two observers; one-way ANOVAs; number of nuclei analyzed, n = 100-104). Mean ± SD. WT, wild-type; MT, mutant.



Supplemental Figure 2. Lamin A/C Arg349Trp associates with nuclear pore complex aggregation. Stimulated emission depletion (STED) micrographs of nuclei from patient-derived dermal fibroblasts harboring wild-type or mutant lamin A/C as indicated. Nuclear pore complex aggregation is only evident in cells with lamin A/C Arg349Trp. In addition to the nuclei shown in **Figure 3A**, two more nuclei per condition are presented here. Scale bar, 10 µm. WT, wild-type.

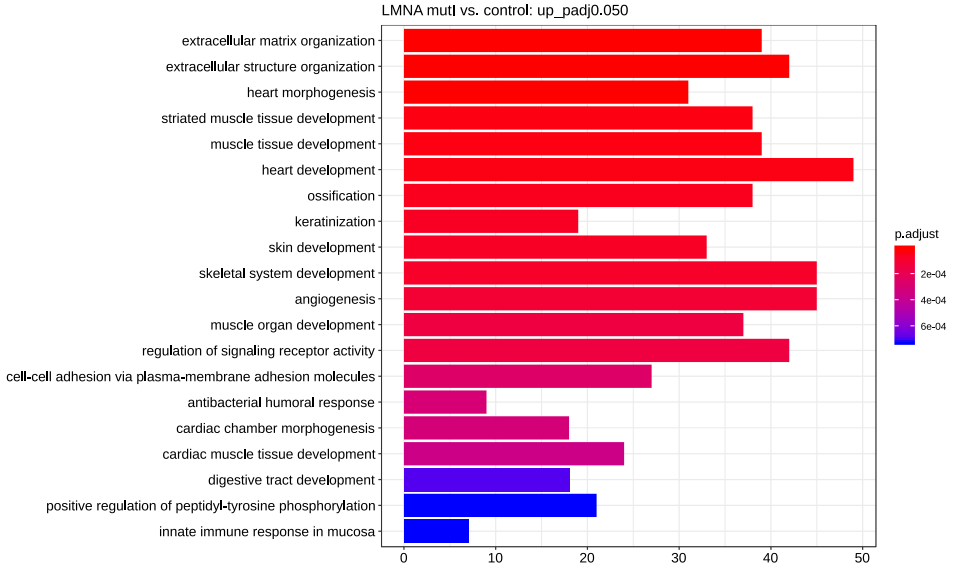


Supplemental Figure 3. (**A**) Immunofluorescence staining of DNA damage response markers (53BP1 and gH2AX, red) in nuclei (blue) from patient-derived dermal fibroblasts harboring wild-type or mutant lamin A/C as indicated. Scale bar, 25µm. (**B**) Patient-derived fibroblasts with heterozygous lamin A/C Arg349Trp show similar DNA damage response activation as control and lamin A/C Gly608Gly fibroblasts (one-way ANOVAs; number of nuclei analyzed, n = 107-425). Mean ± SD. (**C**) Lamin A/C Arg349Trp fibroblasts show a trend towards an increase in DNA damage response activation compared to control fibroblasts (triplicates were analyzed for each patient sample; the average of each triplicate is plotted for each sample). CTRL, control; (·), (subject identifier).

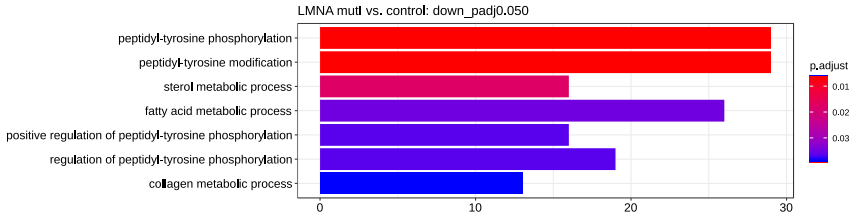


Supplemental Figure 4. Part of lamin A/C dimer structure (PDB ID 1X8Y, Strelkov et al. *J Mol Biol* 2004) with cartoon and surface colored according to hydrophobicity (red), PyMol script Color h.

A



B



Supplemental Figure 5. Enrichment analysis of gene ontology biological processes in the set of significantly differentially expressed genes between lamin A/C Arg349Trp harboring patient-derived fibroblasts and control lines ($p_{adj} < 0.05$). (**A**) The first 20 of the 297 significantly enriched biological processes in genes significantly differentially upregulated in lamin A/C Arg349Trp positive cells. (**B**) All seven biological processes significantly enriched in genes significantly differentially downregulated in lamin A/C Arg349Trp harboring cells.