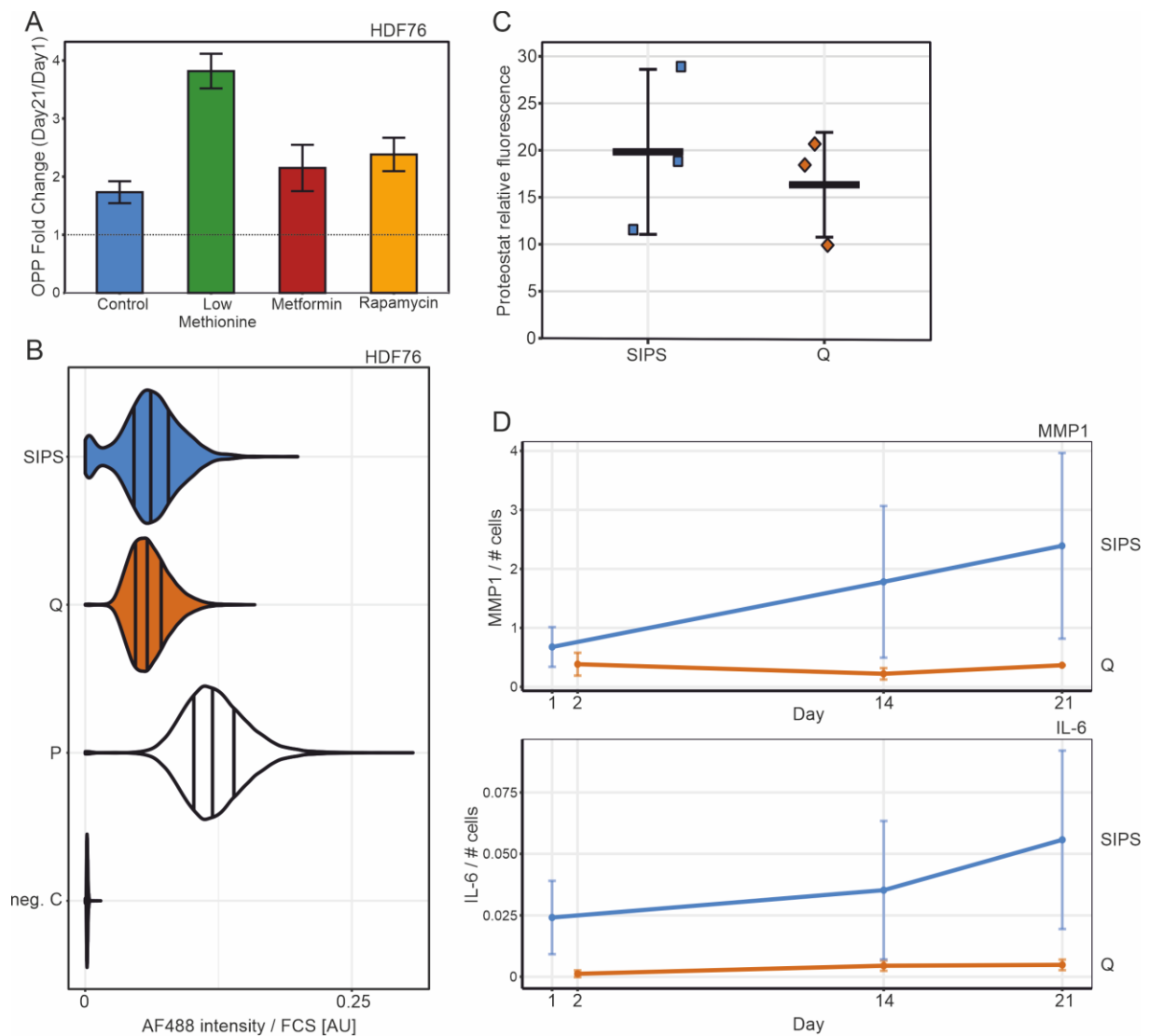
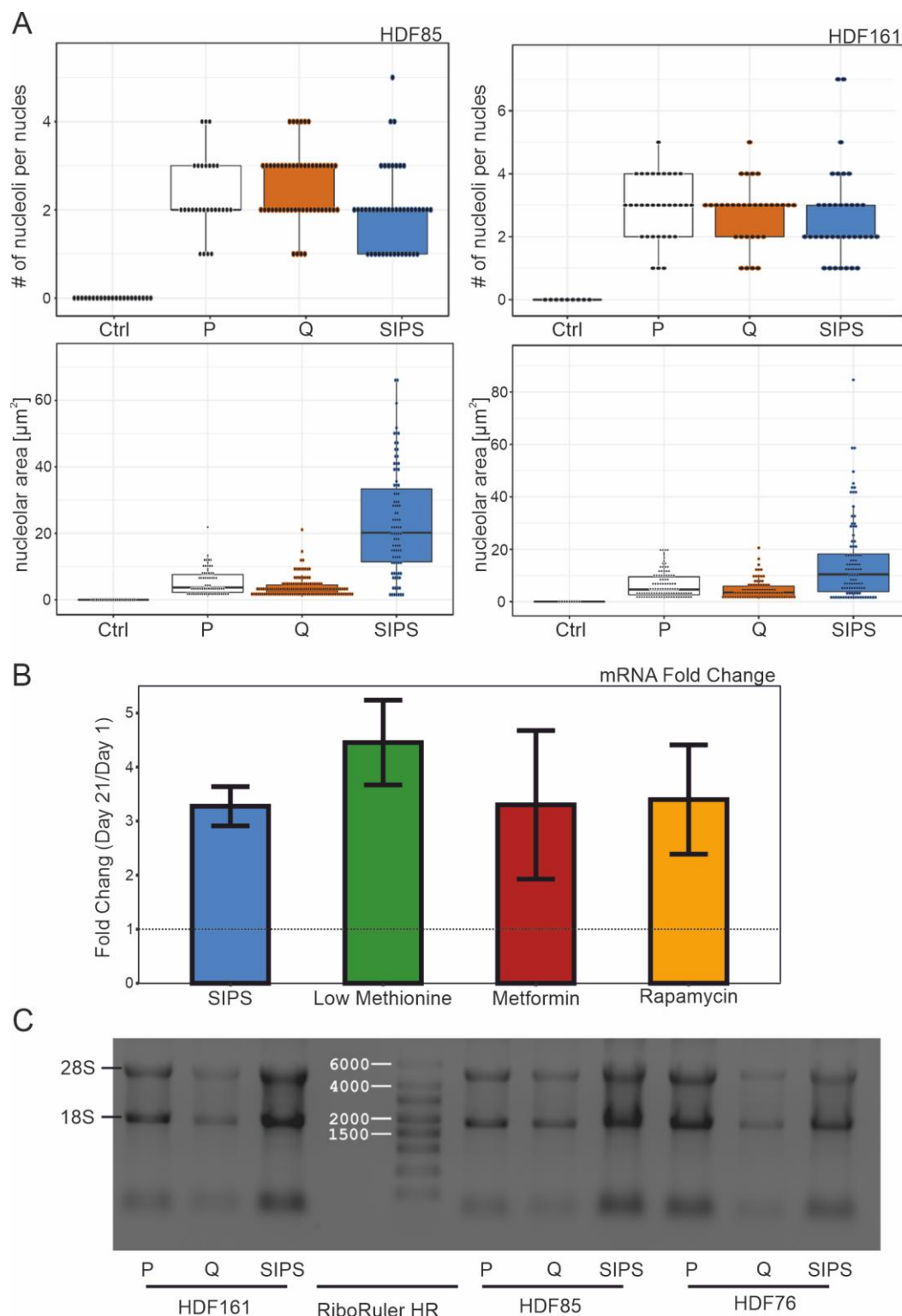


Supplementary Figures 1–3

Supplementary Figure 1. **A)** O-propargyl-puromycin (OPP) measurement of the protein production rate in cells treated with metformin (1 mM), rapamycin (12.5 nM), and low methionine. N = 3. **B)** Normalization of the OPP signal to forward scatter (cell size) indicated that an increase in cell volume does not explain the increase in the protein production rate. **C)** Measurement of unfolded protein in human dermal fibroblasts (HDFs) from HDF76 using the PROTEOSTAT assay kit between SIPS and quiescent controls revealed no statistically significant difference. Unpaired *t*-test: $p = 0.5913$, N = 3. **D)** Concentration of the senescence-associated secretory phenotype factors MMP1 and IL-6 in the media of quiescent and SIPS HDFs. MMP1 and IL-6 levels were measured using ELISA and normalized to the cell count. N = 3. P = proliferating, Q = quiescent, SIPS = stress-induced premature senescence, neg. C = unstained control. Error bars represent the standard deviation.



Supplementary Figure 2. A) Quantification of nucleolar number and size after fluorescence staining of human dermal fibroblasts from HDF85 and HDF161. **B)** Fold change of mRNA content compared with proliferating controls measured through MeTaFlow staining and subsequent flow cytometry. Stress-induced premature senescence cells from HDF76 exhibited increased mRNA content, which was not reversed by treatment with metformin (1 mM), rapamycin (12.5 nM), or low methionine. N = 3. **C)** Agarose gel of RNA. Quantified in Figure 3D. Error bars represent the standard deviation.



Supplementary Figure 3. A) Top 15 enriched Gene Ontology (GO) terms in stress-induced premature senescence (SIPS) cells compared with quiescent cells on a total mRNA level. **B)** Top 15 enriched GO terms in SIPS cells compared with quiescent cells on a buffering level. **C–F)** Percentages of adenine (**C**), cytosine (**D**), thymine (**E**), and guanine (**F**) in the 5'-untranslated regions (5'-UTRs) of SIPS cells compared with quiescent cells among all detected mRNAs (background) and translationally up- and downregulated mRNAs. Wilcoxon's rank-sum test + Bonferroni's correction.

