



Baricitinib, a JAK-STAT inhibitor, reduces the cellular toxicity of the farnesyltransferase inhibitor lonafarnib in progeria cells

Rouven Arnold ¹, Elena Vehns ¹, Hannah Randl ¹, and Karima Djabali ^{1,*}

¹ Epigenetics of Aging, Department of Dermatology and Allergy, TUM School of Medicine, Technical University of Munich (TUM), 85748 Garching, Germany; rouven.arnold@tum.de (R.A.); elena.vehns@tum.de (E.V.); hannah.randl@tum.de (H.R.)

* Correspondence: djabali@tum.de; Tel.: +49-89-289-10920

Supplementary Figures

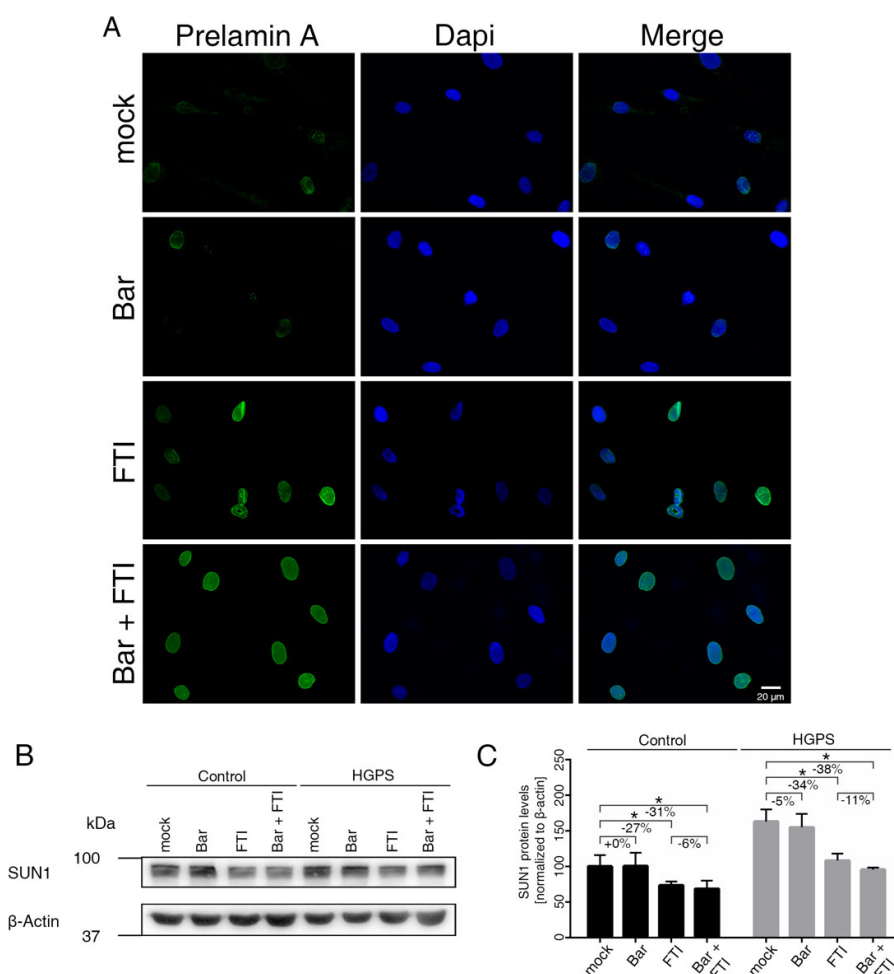


Figure S1. Bar and FTI combination treatment prevents nuclear blebbing in control cells and reduces SUN1 levels. (a) Representative immunofluorescence images of control (GM01651C) fibroblasts treated for nine days as indicated. Antibody against prelamin A (green) was used, and DNA was stained with DAPI. Fluorescence images were taken at 40x magnification. Scale bar 20 μ m. (b) Representative images of western blots for SUN1 and (c) quantification of SUN1. Graphs show mean \pm SD. Representative images are shown (n=3; *p < 0.05)

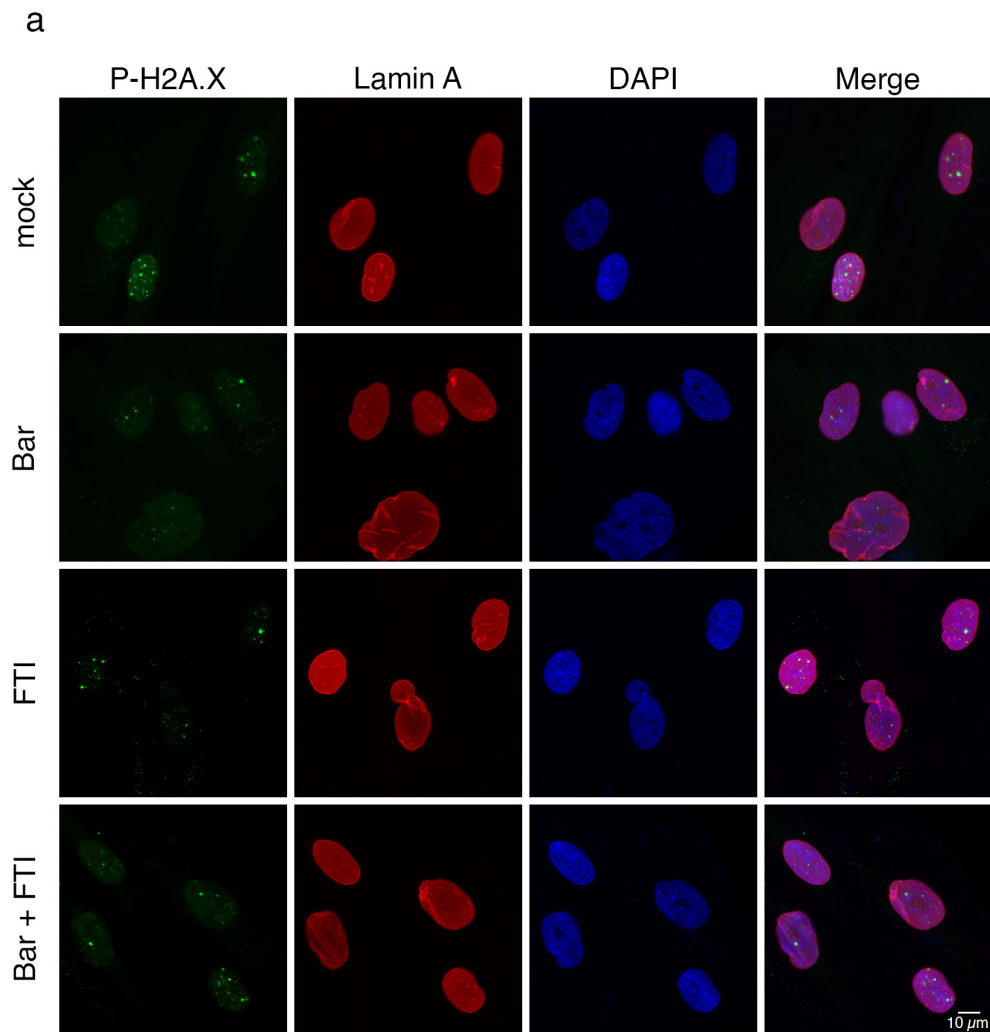


Figure S2. Bar and FTI combination treatment induces no changes in P-H2A.X levels in control cells. (a) Representative immunofluorescence images of control GM01651C fibroblasts treated for nine days as indicated. Antibodies against P-H2A.X (green) and lamin A (red) were used, DNA was stained with DAPI. Fluorescence images were taken at 60x magnification. Scale bar: 10 μ m.

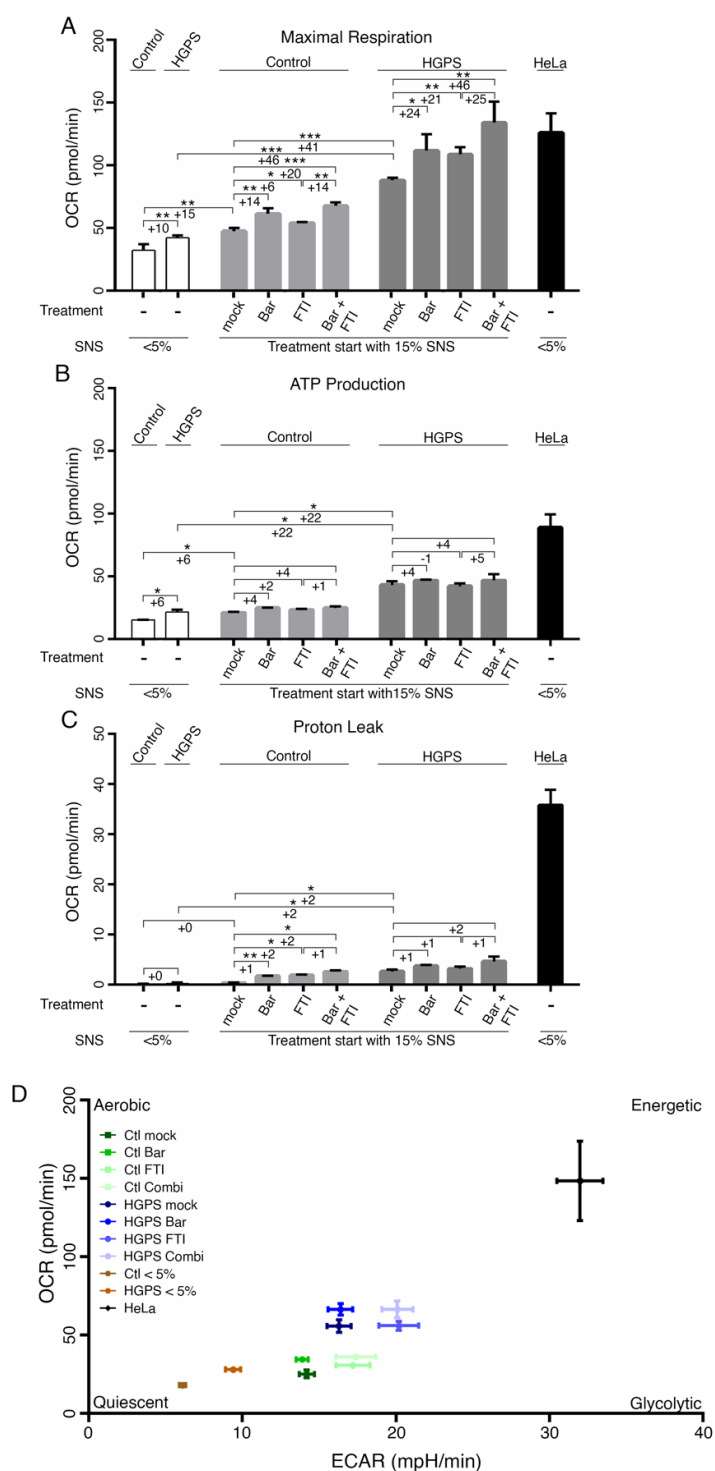
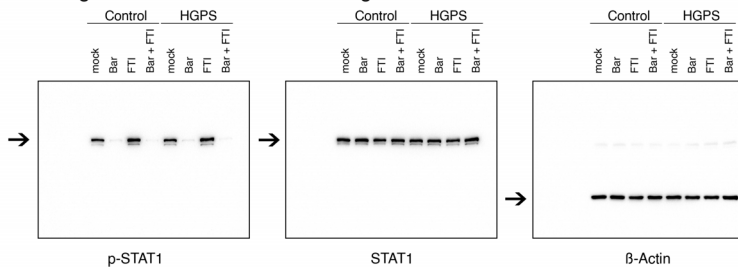
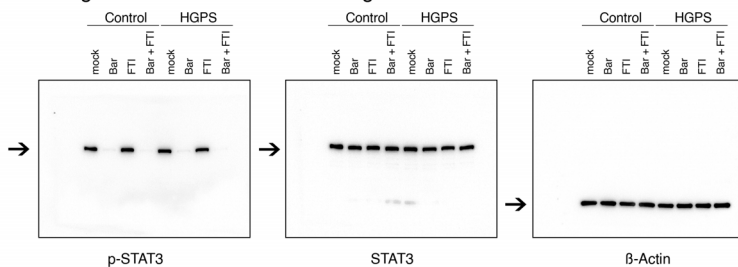


Figure S3. Mitochondrial function and glycolysis are altered in HGPS fibroblasts. Oxygen consumption rates (OCR) and extracellular acidification (ECAR) were determined with a Seahorse XF Flux Analyzer in basal and stimulated conditions (n=3). Maximal respiration (a), ATP production (b), and proton leak (c) were calculated with Wave software v2.6.1.53 (Agilent Technologies). (d) Plotting basal ECAR and OCR levels provides a snap-shot of the bioenergetics profiles. Graphs show mean \pm SD. (*p < 0.05, **p < 0.01, ***p < 0.001).

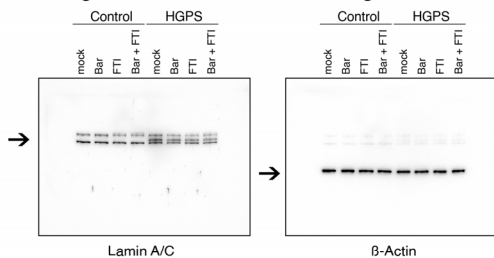
Full-length scans of western blots in figure 1f



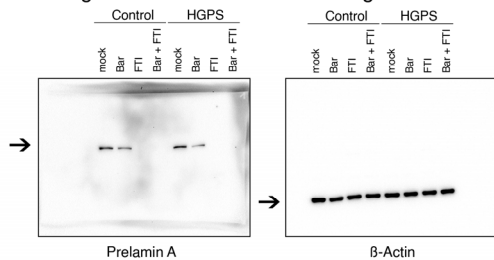
Full-length scans of western blots in figure 1i



Full-length scans of western blots in figure 4a



Full-length scans of western blots in figure 4c



Full-length scans of western blots in figure S1b

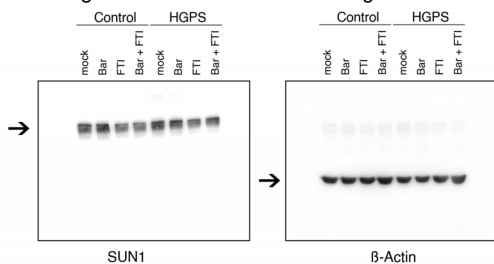


Figure S4. Full-length scan of western blots from Figures 1f, i, Figure 4a, c, Figure S1b.

Table S1. Primers used for real-time quantitative PCR analysis

| Primer sequence | Target Gene | Product size (bp) | Melting Temp | Info |
|--|---------------|-------------------|----------------------|---|
| FW:5'-GCTTGGATTCTACAAAGAAGCA-3' REV:5'-ATAGATGGTCAATGCGGCGTC-3' | IFN- β | 166 | 59.24 °C 60.87 °C | |
| FW:5'-CGCCAATGACTCAGAGGAAGA-3' REV:5'-AGGGCGTCATTGAGGATGAA-3' | IL-1 α | 120 | 59.79 °C 59.09 °C | doi.org/10.1371/journal.pone.0002301 |
| FW:5'-AGCATGAAAGTCTCTGCCGC-3' REV:5'-GGCATTGATTGCATCTGGCTG-3' | CCL2 | 93 | 62.9 °C 66.0 °C | doi.org/10.1172/jci.insight.87023 |
| FW:5'-GGTACATCCTCGACGGCATCT-3' REV:5'-GTGCCTCTTTGCTGCTTTCAC-3' | IL-6 | 81 | 63.6 °C 62.4 °C | doi.org/10.1152/ajpendo.00255.2002 |
| FW:5'-CTGGCCGTGGCTCTCTTG-3' REV:5'-CCTTGGCAAACTGCACCTT-3' | CXCL8 | 69 | 63.2 °C 62.5 °C | doi.org/10.1172/jci.insight.87023 |