Supplemental section

Supplementary Figure 1. UV sensitivity of NER deficient primary MDFs. Two independent primary MDF lines of each genotype and wt littermate control primary MDFs at early passage were treated with indicated UV doses and cells counted 72 hrs post treatment (100%=non-treated cells of respective cell line, error bars = SD).

Supplementary Figure 2. A) Q-PCR verification of microarray expression profiles. Twenty randomly picked genes whose expression was change ±1.2 fold, $p<0.05$, on the microarrays were evaluated by qPCR, thus verifying the accuracy of both methods (FC = fold change compared to untreated controls; error bars = SD, n=4). IGF-1R and GHR repression is not dependent on IGF-1R or GHR signaling: Primary MDFs (B) or chondrocytes (C) were treated either with DMSO or with indicated doses of PI3K inhibitor LY294,002, MAPK inhibitor U-0126 (25μM), or JAK inhibitor AG490 (50μM) for one hour prior to UV treatment and then left until samples were taken 6 hrs post UV treatment. IGF-1R/GHR expression levels were normalized to B2M, gTUB, and Hprt levels and compared to untreated samples. (FC = fold change compared to untreated controls; *=$p<0.05$, **=$p<0.01$, two-tailed t-test, error bars = SD, n=4)

Supplementary Figure 3. ATM, ATR or p53 are not required for UV-induced IGF-1R and GHR repression. (A) Primary human fibroblasts from AT patient (ATRO), Atr deficient Seckel patient (ATR-Seckel) and control (C5RO) were UV-treated and IGF-1R and GHR expression levels were determined 6 hours later and normalized to Gapdh and B2M. To exclude redundancy of ATR and CHK1 kinases were downregulated by siRNA in ATM deficient cells (B) or ATM was inhibited with indicated doses of the ATM specific inhibitor KU-99533 in ATR deficient cells (C) and assays performed as in (A).

(D) Primary MDFs were derived from p53 deletion animals and littermate controls and expression levels determined 6 h post UV treatment and normalized to B2M and gTUB (FC = fold change compared to untreated controls; error bars = SD, n=4).

Supplementary Figure 4. Other growth-associated genes are also repressed in response to UV-damage in quiescent cells. C5RO primary human fibroblasts were treated 6 days after having grown to confluence and transferred to 1% FCS medium (A) and primary neurons derived from the hippocampus of rats (B) and samples taken 6hrs post UV treatment. IGF-1, FGF1, EGFR and PDGFb expression levels were normalized to Gapdh and gTUB (A) or Gapdh and Hprt (B) (FC = fold change compared to untreated controls; *=$p<0.05$, **=$p<0.01$, two-tailed t-test, error bars = SD, n=4). Primary MDFs were treated with mitomycin C (C) or 4-NQO (D) and IGF-1R and GHR expression levels were evaluated after 6 h by qPCR and normalized to gTUB and B2M. p21 expression was included as control for DNA damage response (FC = fold change compared to untreated controls; **=$p<0.01$, two-tailed t-test, error bars = SD; n=4). E) Transcriptional inhibition does not lead to IGF-1R or GHR repression. Quiescent primary human fibroblasts were treated with either α-amanitin or actinomycin D continuously for 6 hours when expression levels were determined by qPCR and normalized to Gapdh, Hprt and B2M (FC = fold change compared to untreated controls; error bars SD, n=4). De novo RNA synthesis was determined by counting autoradiographic grains after labeling with [3H]uridine during a pulse-labeling period of 1 h.

Supplementary Figure 5. Uncropped Western blots for Figure 2C showing endogenous protein levels, Figure 2E endogenous protein levels after IGF-1R siRNA, and Figure 2G

endogenous protein levels upon IGF-1 treatments. Figure 7A shows RNAPIIo ChIP (* indicates cross-reacting bands).

Supplementary Tables.

Gene expression changes in response to UV damage: The transcriptional response to UV was readily seen even in wt MDFs that were exposed to 0.6 J/m^2 of UV irradiation (two-sided ANOVA/t-test, p-value <0.05, ±1.2-fold change; Supplementary Table 1; 998 genes), greatly pronounced at 4 J/m^2 UV (2360 genes, Supplementary Table 2) and was even further enhanced in *Csb*$^{m/m}$*/Xpa*$^{-/-}$ cells irradiated with only 0.6 J/m^2 of UV (2646 genes, Supplementary Tables 3-5).

Supplementary Table 1. List of significant expression profiles of wt cells irradiated with 0.6J/m2 of UV (gray color) as compared to non-irradiated wt cells.

Supplementary Table 2. List of significant expression profiles of wt cells irradiated with 4 J/m2 of UV (gray color) as compared to non-irradiated wt cells.

Supplementary Table 3. List of significant expression profiles of XPA cells irradiated with 0.6 J/m2 of UV (gray color) as compared to non-irradiated XPA controls

Supplementary Table 4. List of significant expression profiles of CSB cells irradiated with 0.6 J/m2 of UV (gray color) as compared to non-irradiated CSB cells

Supplementary Table 5. List of significant expression profiles of DKO cells irradiated with 0.6 J/m2 of UV (gray color) as compared to non-irradiated DKO cells

Supplementary Table 6. Expression profiles of genes (red and green color indicate up- and down-regulated genes respectively) associated with over-represented biological processes in irradiated cells and with natural aging in the four organs (as indicated) as compared to corresponding controls.

Supplementary Table 7. Significantly overrepresented gene ontology (GO) categories of upregulated genes in UV treated cells and in mice with extended longevity

Supplementary Table 8. Oxidative damage does not result in somatotropic attenuation. Primary MDFs were treated with either low (10μM) or high (50μM) doses of hydrogen peroxide and RNA samples were taken 6h later. Gene expression changes in treated as compared to non-treated cells are shown within biological processes oxidative stress response, DNA repair and genes involved in GH/IGF-1 axis and other growth stimuli.