



**Supplementary Figure S1. The anti-aging effects of melatonin are not indiscriminate. (a–b)** Treatment of 200  $\mu\text{M}$  melatonin showed upward trend of MTCO-1 in epidermis on day 6. Quantitative (immuno-)histomorphometry and representative pictures of MTCO-1 expression. Mean  $\pm$  SEM;  $n=12$ –17 not consec-utive skin sections from 4 independent donors; Mann-Whitney test, not significant. **(c–d)**  $\gamma\text{H2Ax}$  expression after 6 days of culture in the lower two cell layers of the epidermis after treatment with 100  $\mu\text{M}$  and 200  $\mu\text{M}$  melatonin. Quantitative (immuno-)histomorphometry and representative images of  $\gamma\text{H2Ax}$  expression. Mean  $\pm$  SEM;  $n=13$ –20 non-consecutive skin sections from 4 independent donors; Mann-Whitney test. **(e–f)** Lamin B1 expression after 6 days of culture across the entire epidermis after treatment with 100  $\mu\text{M}$  and 200  $\mu\text{M}$  melatonin. Quantitative (immuno-)histomorphometry and representative images of lamin B1 expression. Mean  $\pm$  SEM;  $n=14$ –18 non-consecutive skin sections from 4 independent donors; Mann-Whitney test. **(g–h)** p16INK4 expression analyzed in the two lower layers of the epidermis after treatment with 100  $\mu\text{M}$  and 200  $\mu\text{M}$  melatonin on day 6. Quantitative (immuno-)histomorphometry and representative images of p16INK4 expression. Mean  $\pm$  SEM;  $n=13$ –20 non-consecutive skin sections from 4 independent donors; Mann-Whitney test. **(i–j)** SIRT-1 expression in the entire epidermis after 6 days of culture treated with 100  $\mu\text{M}$  and 200  $\mu\text{M}$  melatonin. Quantitative (immuno-)histomorphometry and representative images of SIRT-1 expression. Mean  $\pm$  SEM;  $n=16$ –18 non-consecutive skin sections from 4 independent donors; Mann-Whitney test. Epi: epider-mis. Scale bar: 100 $\mu\text{m}$