



Supplementary Figure S1. The anti-aging effects of melatonin are not indiscriminate. (a-b) Treatment of 200 μM 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 consecutive skin sections from 4 independent donors; Mann-Whitney test, not significant. **(c-d)** γ H2Ax expression after 6 days of culture in the lower two cell layers of the epidermis after treatment with 100 μM and 200 μM melatonin. Quantitative (immuno-)histomorphometry and representative images of γ 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 μM and 200 μM 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 μM and 200 μM 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 μM and 200 μM 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: epidermis. Scale bar: 100 μm