Poly(ADP-ribose) polymerase-1 activity modulates mitochondrial function following UVB irradiation

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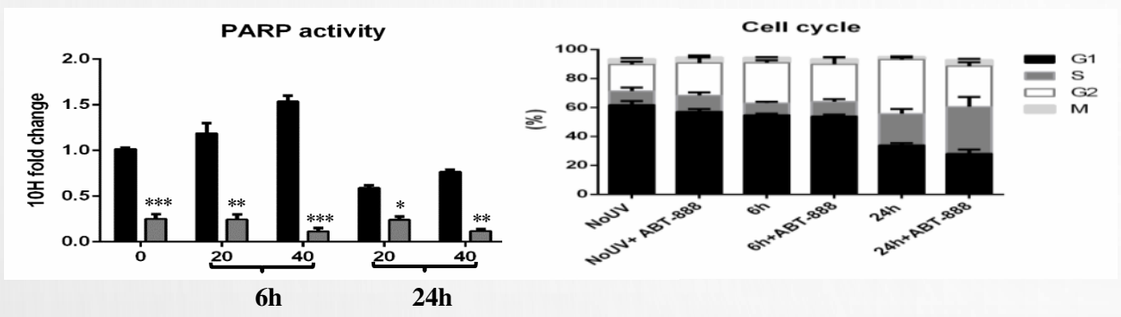
Introduction

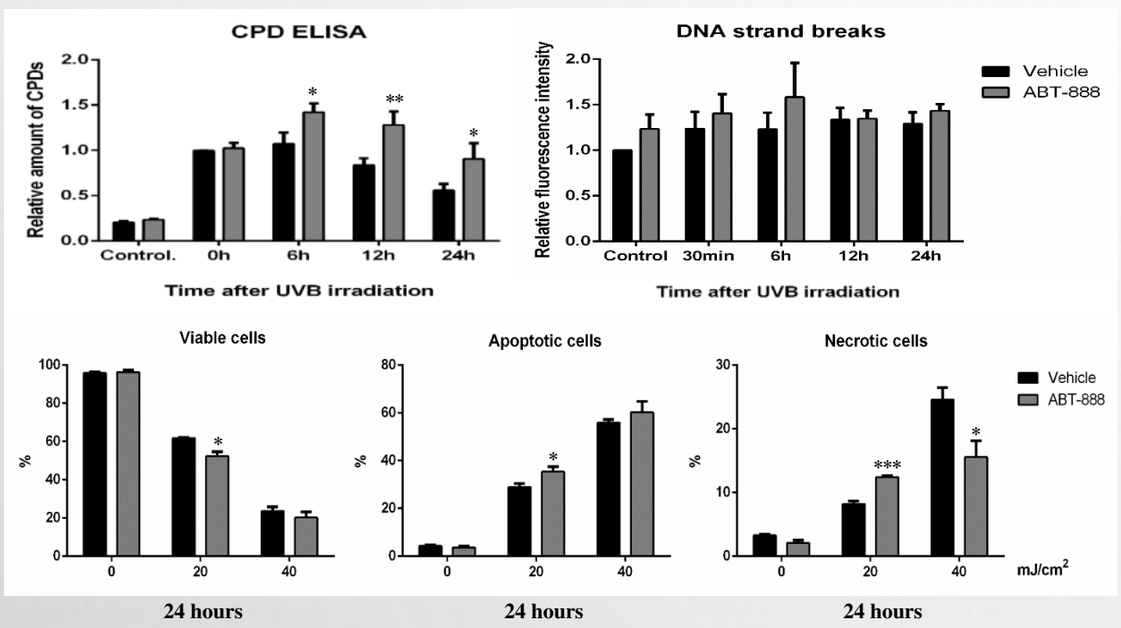
Exposure of skin to ultraviolet radiation is the main cause of skin cancer development. Among UVR, UVB induces diverse cellular function and promotes the formation of DNA helix distorting photolesions such as (6-4) photoproducts and cyclobutane pyrimidine dimers (CPD). Effective repair of such lesions by the nucleotide excision repair pathway is required to prevent DNA damage and mutations. Poly(ADP-ribose) polymerase-1 (PARP-1) is a zinc finger protein and a key mediator in several cellular processes. It rapidly consumes cellular NAD and by that way supresses the activity of mitochondrial regulators ultimately leading to impaired mitochondrial function.

To investigate the impact of PARP inhibition on different mitochondrial parameters, human immortalized keratinocytes (HaCaT) were treated with 25 μM ABT-888 and with a single dose of 20 and 40 mJ/cm^2 of UVB.

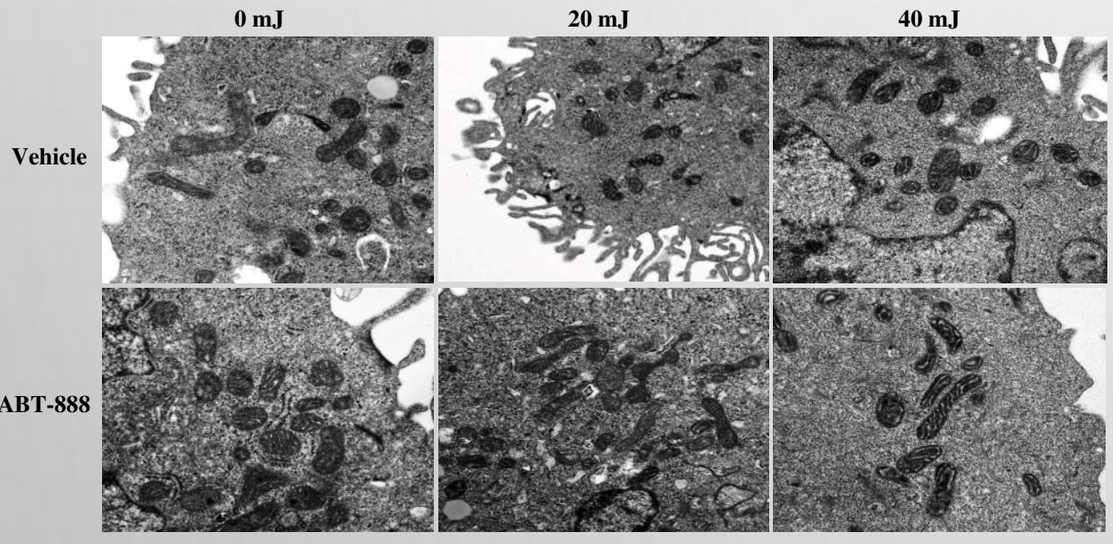
Results

PARP-1 inhibition reduced cell viability coupled with inefficient removal of CPDs and DNA strand breaks (20 mJ/cm^2)

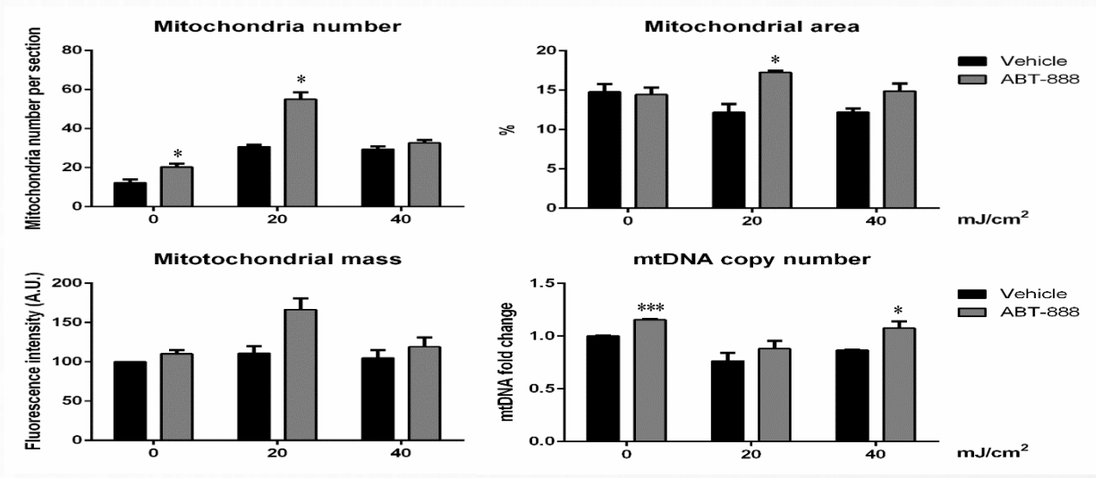




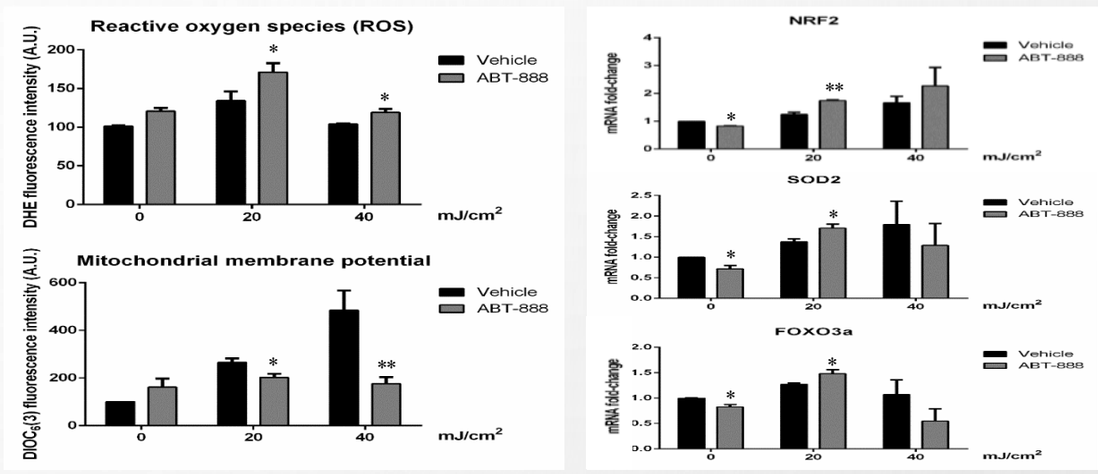
PARP inhibition and UVB induces mitochondrial morphological changes (24h)



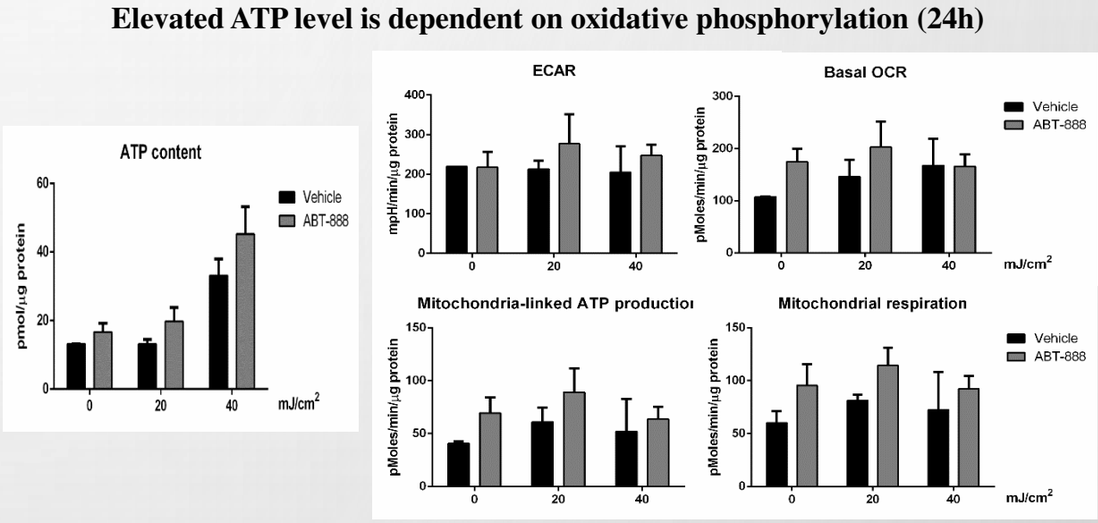
PARP-1 regulates mitochondrial number, area, mass and mtDNA content (24h)



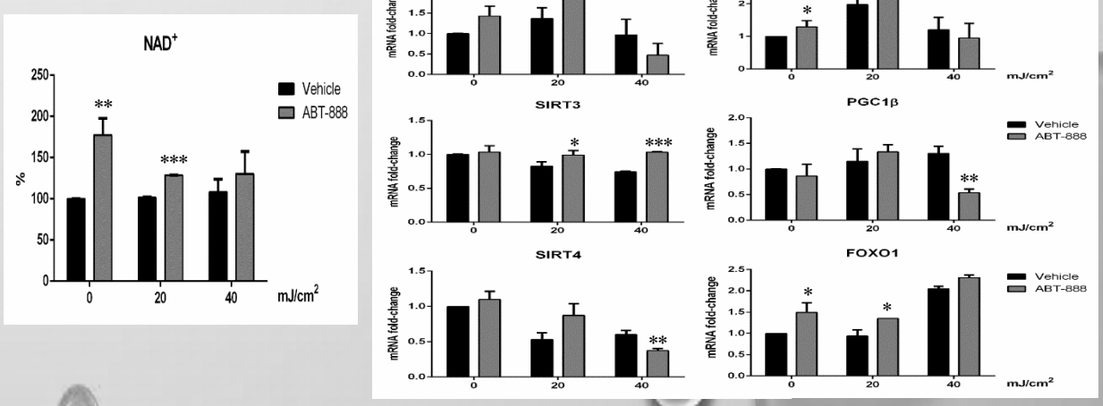
PARP inhibition induces mitochondrial depolarization and late increase in ROS production (24h)



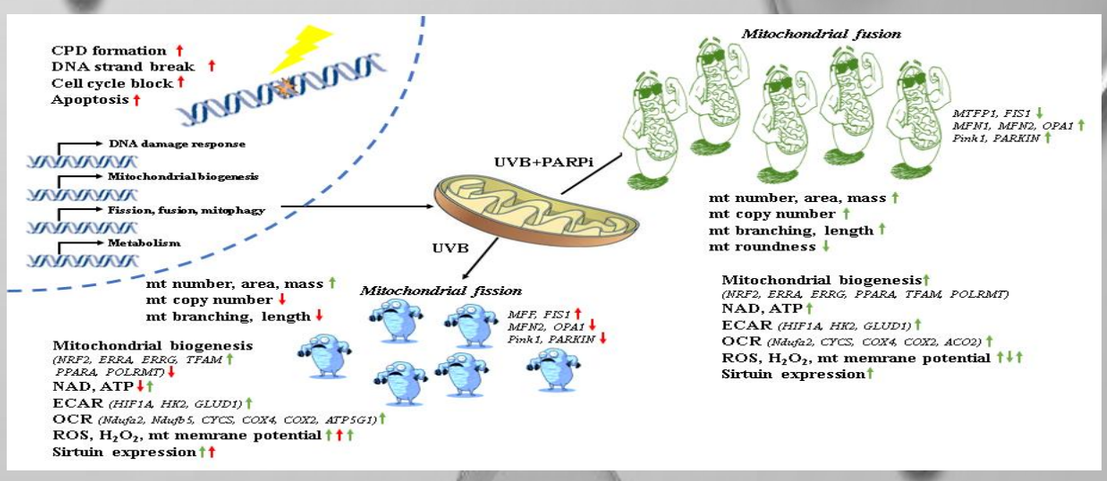
Elevated ATP level is dependent on oxidative phosphorylation (24h)



Cellular NAD$^+$ contributes to gene expression changes of mitochondrial regulators (24h)



Conclusion



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