



BAICALEIN ATTENUATES ADENINE-INDUCED FERROPTOSIS IN HUMAN KIDNEY PRIMARY PROXIMAL TUBULAR EPITHELIAL CELLS (PTEC) VIA INDUCTION OF ANTIOXIDANT PATHWAYS

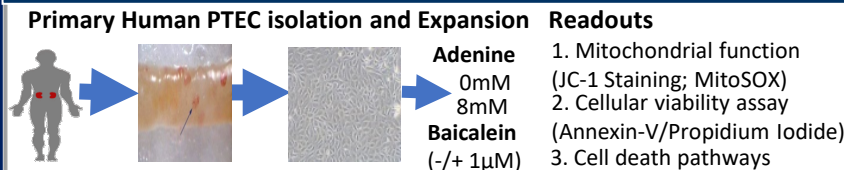
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Background

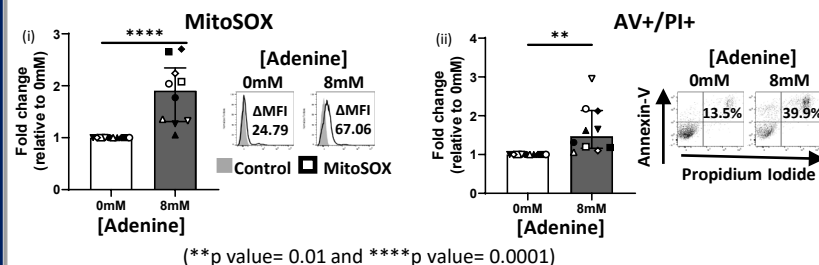
- Chronic kidney disease (CKD) is a global health burden, increasing in incidence in developed and developing countries.
- Adenine diet-induced CKD is a tubular crystalline nephropathy that is a well-accepted pre-clinical model of CKD.
- Adenine-induced PTEC injury and loss are believed to be related to oxidative stress.
- However little is known regarding the mechanisms of injury that cause PTEC loss.
- In this study, modes of adenine-induced cell death were investigated in human primary PTEC.

Methods



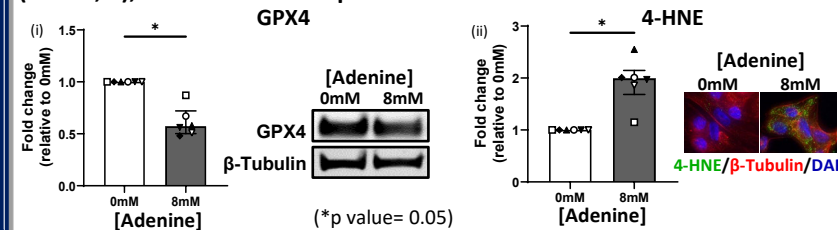
Results

1. Adenine significantly increases production of mitochondrial superoxide (MitoSOX, i) and PTEC necrosis (AV+/PI+, ii)

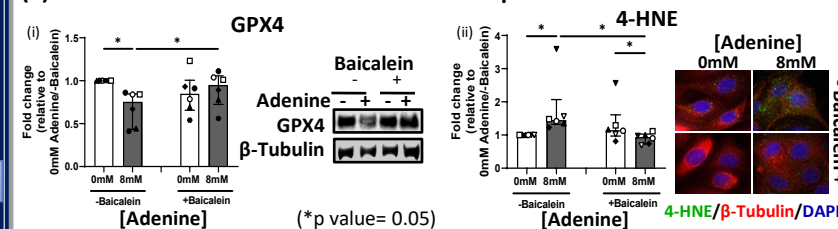


Results

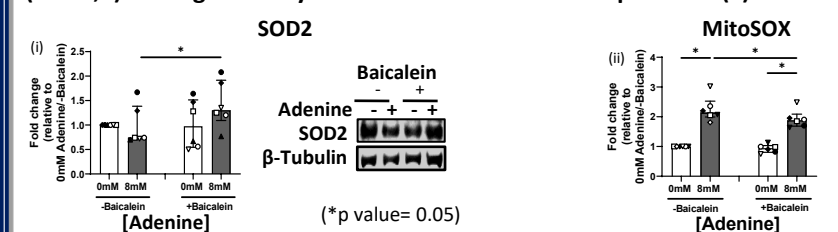
2. Adenine significantly decreases lipid repair enzyme GPX4 (i), significantly increases lipid peroxidation biomarker 4-hydroxyl-non-enal (4-HNE, ii), and induces ferroptotic PTEC death



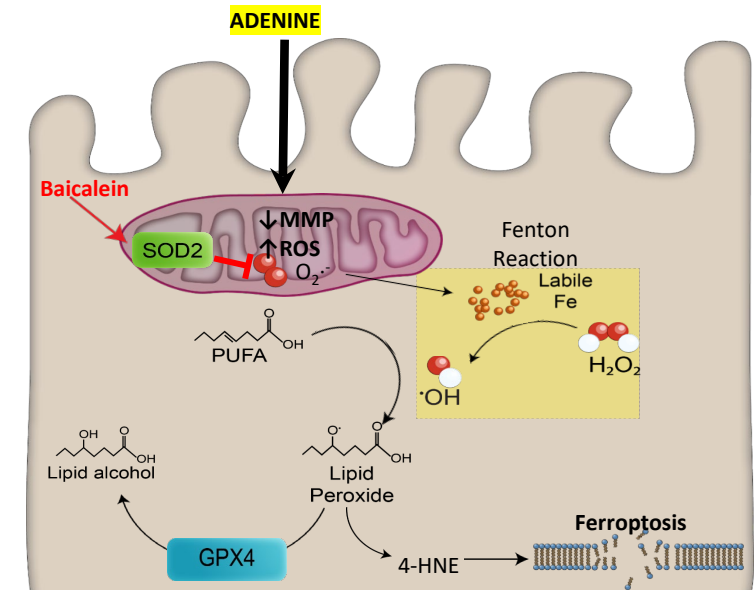
3. Baicalein significantly restores GPX4 (i), significantly decreases 4-HNE (ii) and inhibits adenine-induced PTEC ferroptotic death



4. Baicalein significantly induces expression of superoxide dismutase-2 (SOD2, i) and significantly decreases mitochondrial superoxide (ii)



Summary and Conclusions



- Adenine induces PTEC oxidative stress
- Ferroptosis – A key PTEC cell death pathway
- Baicalein inhibits ferroptosis via the SOD2 signalling pathway
- Baicalein - A potential therapeutic agent in human CKD**

Acknowledgements

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