



Medical School, University of Crete, Greece
Molecular and Cellular Pneumonology Laboratory

Mitochondrial homeostasis in IPF alveolar macrophages: Increased levels of mitochondrial ROS and possible link with mitophagy and autophagy.

Eirini Vasarmidi, Eliza Tsitoura, Chara Koutoulaki, Eleni Bibaki, George Margaritopoulos, Nikolaos Tzanakis and Katerina Antoniou

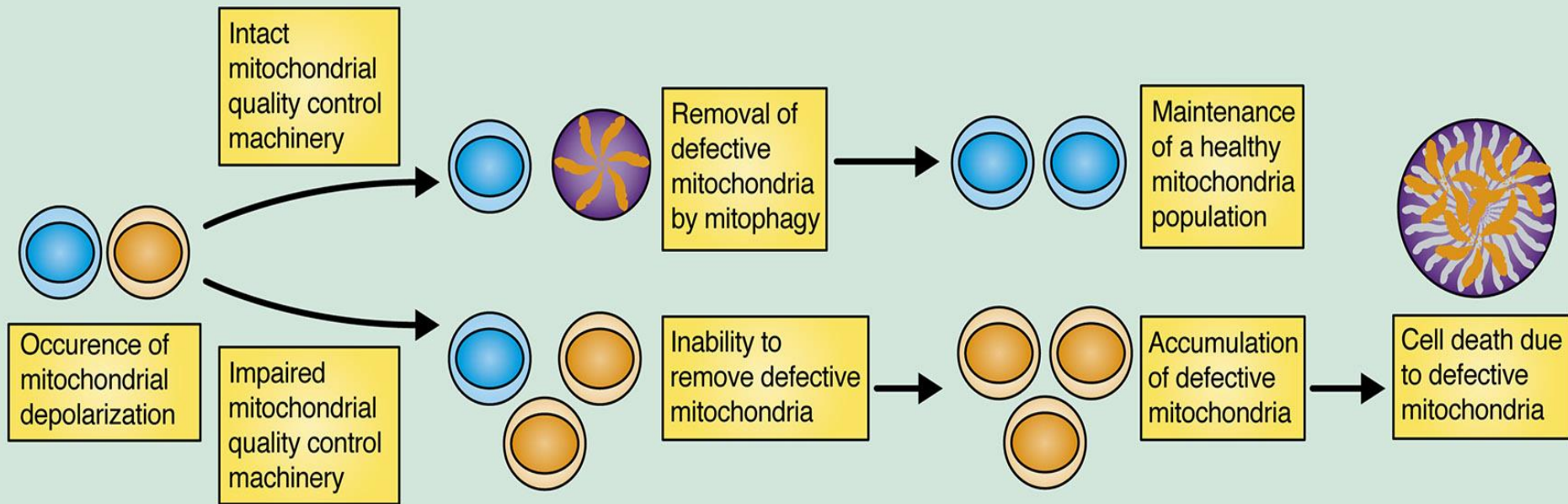


MILANO – ITALY
FEBRUARY
24 - 25, 2017



DEFECTIVE MITOPHAGY

Pathogenesis caused by defective mitochondrial quality control systems



PINK1 deficiency in IPF

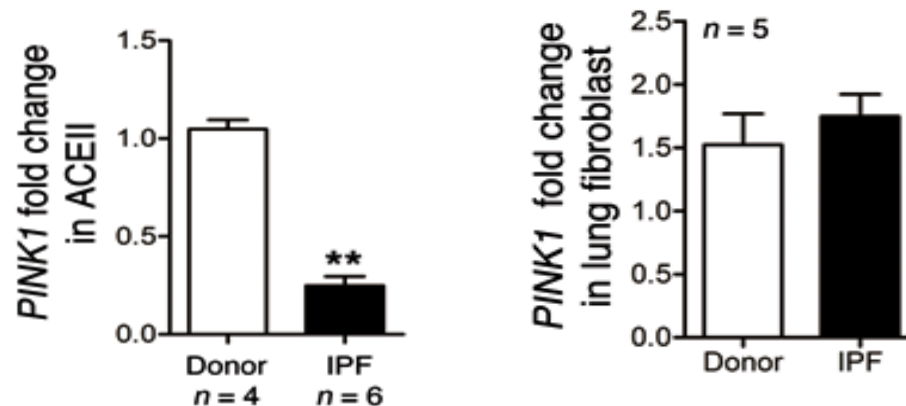
The Journal of Clinical Investigation

RESEARCH ARTICLE

PINK1 deficiency impairs mitochondrial homeostasis and promotes lung fibrosis

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PINK1 downregulation in AECIIs but not in IPF fibroblasts



Aim of the study

Alveolar macrophages play an important role in the pathogenesis of IPF:

- Apoptosis resistant
- Initiate immune responses
- Generate reactive oxygen species
- Secrete growth factors and cytokines - TGF β 1

The aim of our study was to evaluate:

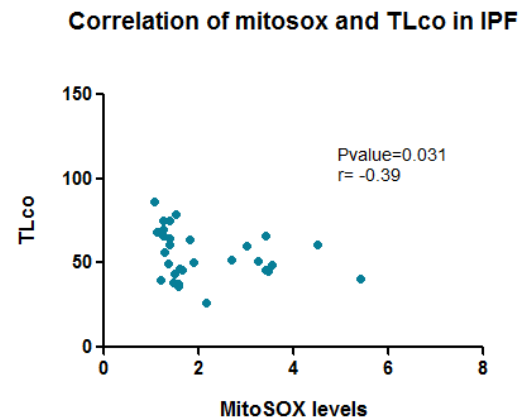
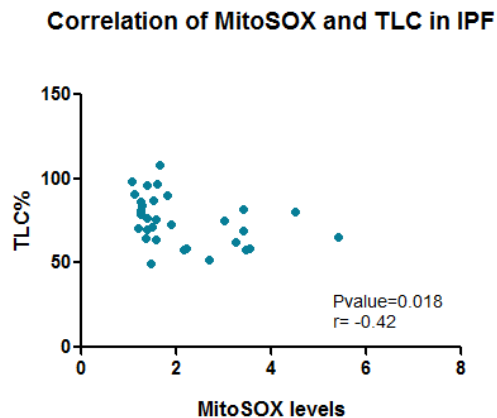
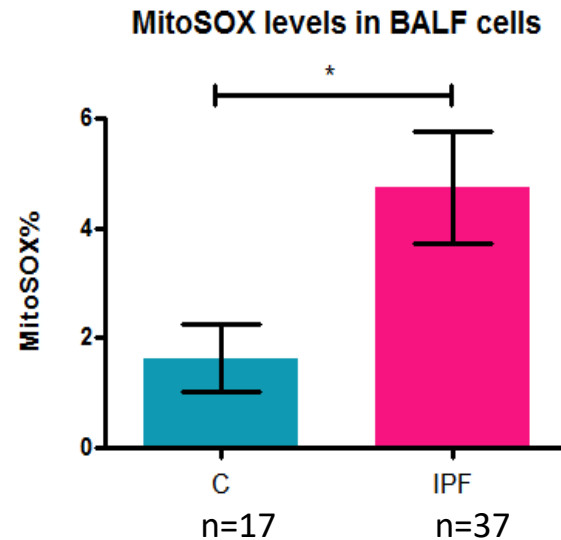
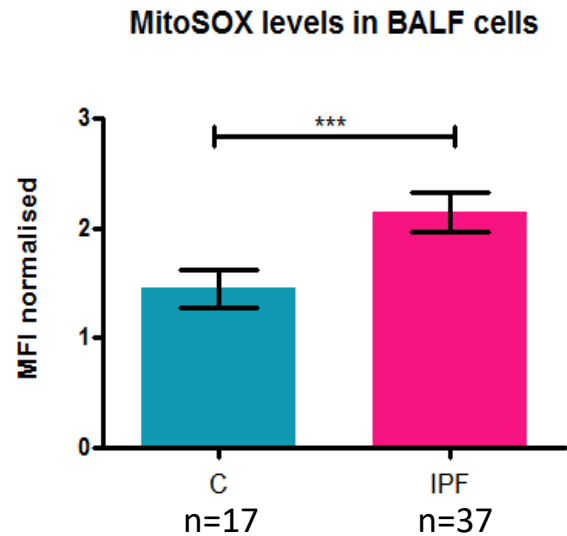
Mitochondrial oxidation levels

Autophagy process

Mitophagy –mitochondrial status

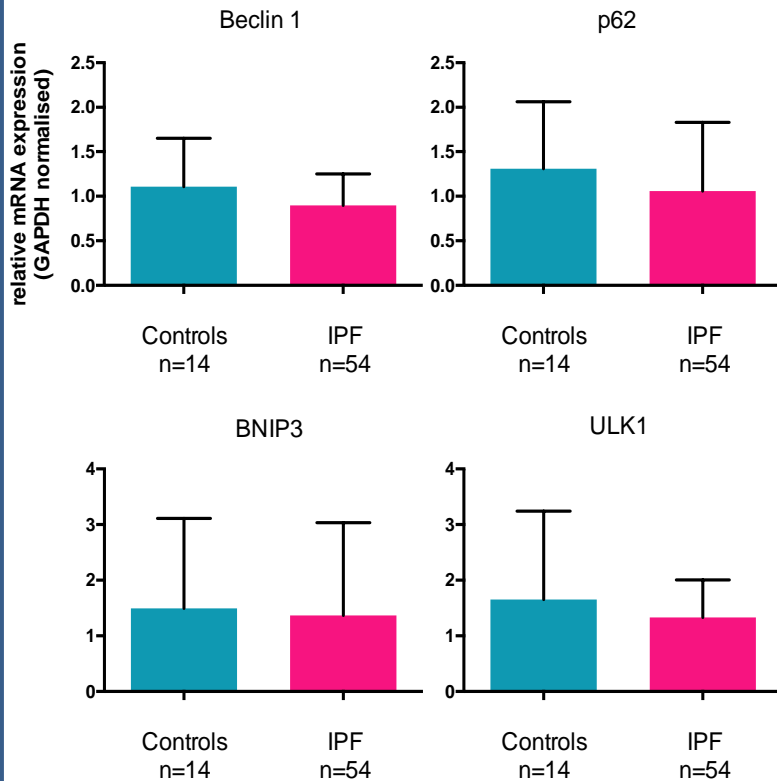
in IPF macrophages.

Increased mitochondrial ROS in BALF macrophages using MitoSOX.

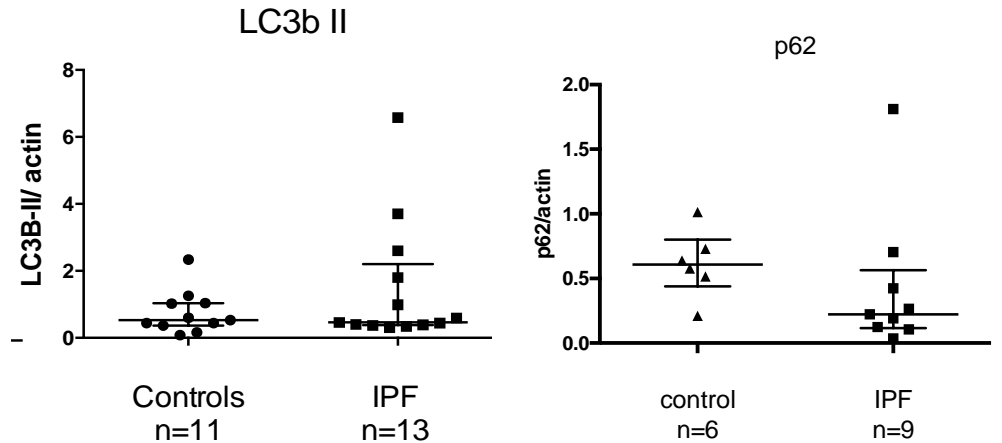


Autophagy in IPF BALF cells

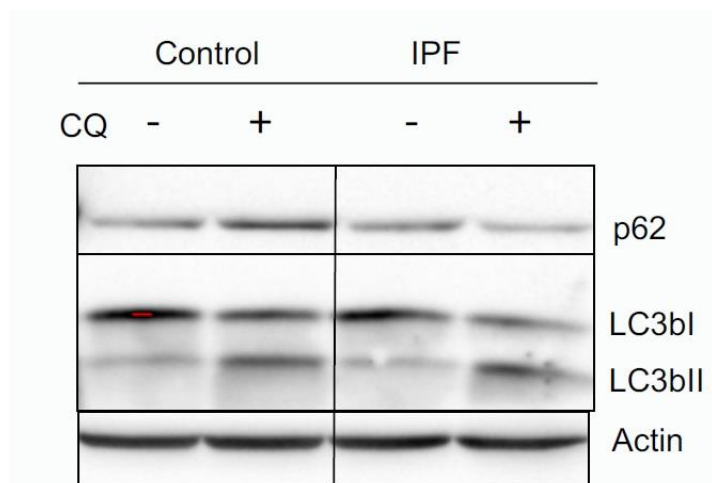
Autophagy gene expression



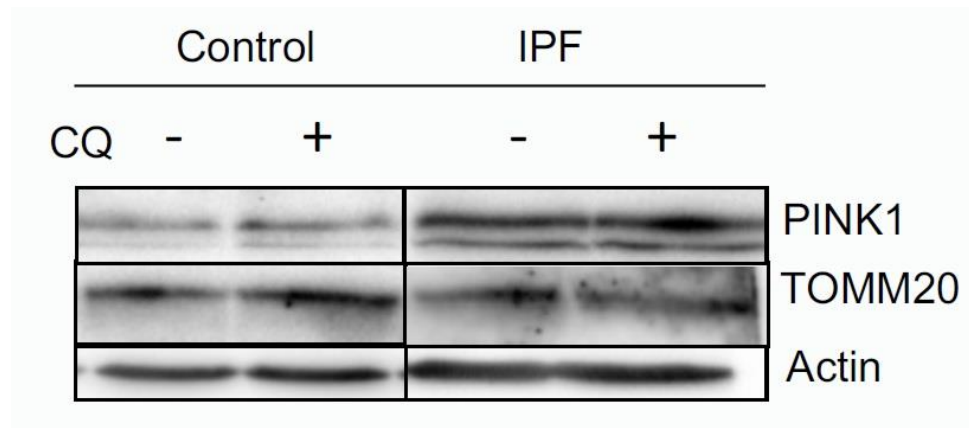
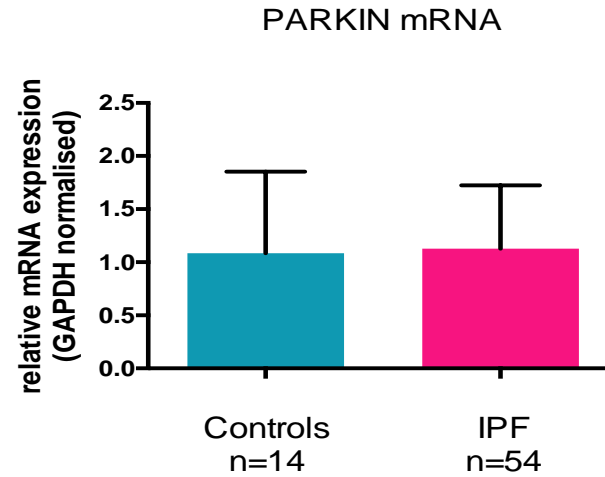
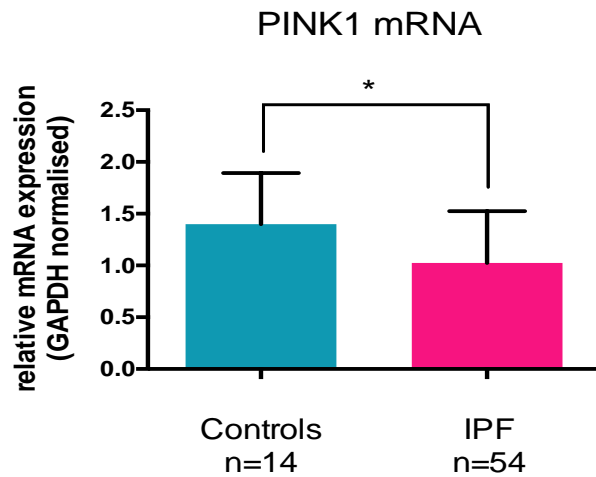
Levels of LC3-membrane associated forms and p62 protein levels



Measurement of autophagy flux

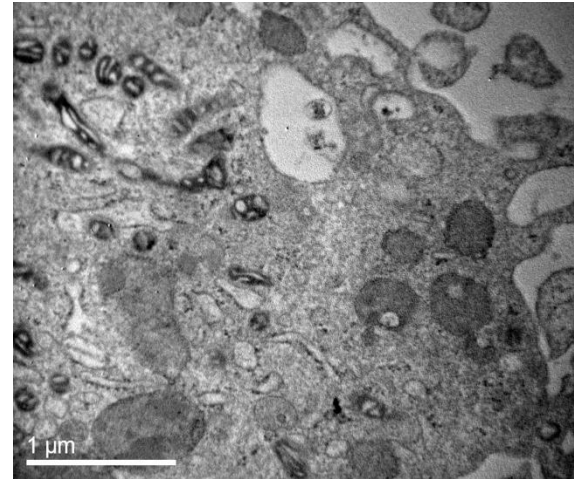
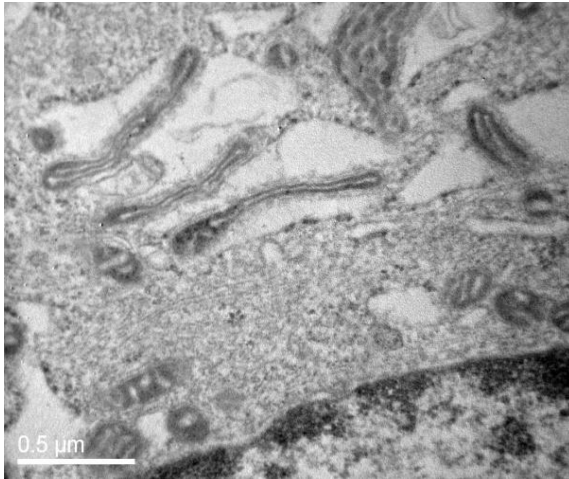


Mitophagy in IPF BALF cells

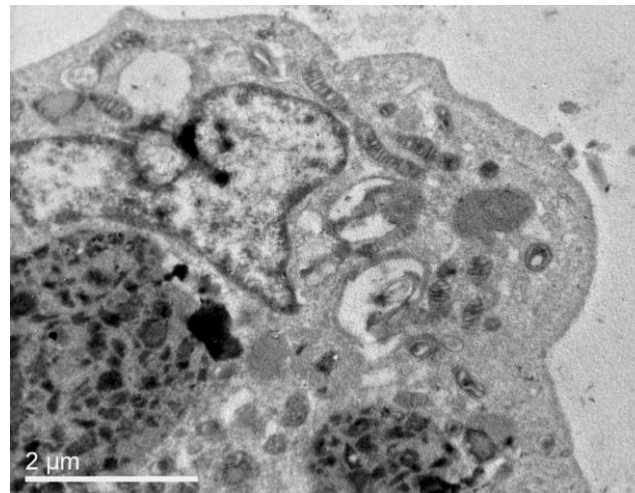


TEM - abnormal mitochondria in IPF BALF cells

- IPF subjects



- control



Conclusions

- Increased MitoSOX levels in IPF macrophages are associated with disease severity.
- Further work is needed to delineate the role of autophagy in the accumulation of oxidised mitochondria in IPF.
- LC3 membrane association appears intact, however cargo degradation maybe deregulated in IPF.
- Impairment of lysosomal function?



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