Resveratrol stimulates autophagosome formation and mitophagy in hepatic stellate cells (HSC)

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Autophagy is a high conserved cellular process responsible for organelles and cells protection against environment stress conditions. Mitochondrial dynamics and turnover are crucial for cellular homeostasis. Impaired mitochondria can contribute to the cell dysfunction or dead, and may be removed through mitochondrial autophagy, i.e. mitophagy. Resveratrol (3,5,4',btrihydroxystilbene; RSV), a phytoalexin related to the prevention of several pathologies, is known for its autophagy induction capacity through SIRT 1 deacetylase. Hepatic stellate cells (HSC) are known to play an important role in the liver fibrogenic process. The GRX cell line is a HSC model. Our previous results showed that GRX 50 µM RSV treatment promoted mitochondrial damage, which may leads to oxidative stress and cytotoxicity. This work investigated the relationship between mitochondria damage and mitophagy on GRX cells treated with 1 to 50 µM of RSV. Transmission electron microscopy (TEM) ultrastructural analysys was performed to access cellular organelles morphology and autophagossomes formation. To determine the mitochondria movement into acidic organelles, GRX cells were co-loaded with Mitotracker Green (MG) and Lysotracker Red (LR) probes and the mitochondria/lysosomes co-localization was analyzed by Confocal microscopy (CM). We found an increase of autophagosome number on GRX treated with 10 and 50 µM of RSV. CM images analysis showed co-localization between mitochondria and lysossoma in RSV treated cells, which may characterize the removal of damage mitochondria through mitophagy. This result could be related to GRX protection against the cytotoxic effect of RSV and may be related to cell survive. More studies are necessary to corroborate these findings.

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