Vacuole-mitochondrial crosstalk during apoptosis induced by acetic acid in yeast

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We have previously shown that acetic acid activates a mitochondria-dependent death process in *Saccharomyces cerevisiae* and that the ADP/ATP carrier (AAC) is required for mitochondrial outer membrane permeabilization and cytochrome *c* release. Mitochondrial fragmentation and degradation have also been shown in response to this death stimulus. We showed that vacuolar protease Pep4p is released from the vacuole into the cytosol in response to acetic acid treatment. Furthermore using yeast genetic approaches we found that the Pep4p and AAC proteins have a role in mitochondrial degradation. Depletion and overexpression of Pep4p, an orthologue of human cathepsin D, delays and enhances mitochondrial degradation, respectively. Moreover, AAC-deficient cells also show a decrease in mitochondrial degradation in response to acetic acid and are not defective in Pep4p release. Therefore, AAC proteins seem to affect mitochondrial degradation at a step subsequent to Pep4p release, possibly triggering degradation through their involvement in mitochondrial permeabilization. Since autophagy is not active in cells undergoing acetic acid-induced apoptosis, vacuolar membrane permeabilization associated with the release of Pep4p may act as an alternative mitochondrial degradation process. In the present communication, I will cover our recent studies with isolated vacuoles towards the understanding of the role of this organelle in acetic acid induced apoptosis. The validation in mammalian cell lines of the hypothesis postulated with the yeast model will be also discussed.

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