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c-FLIP is involved in autophagosome biogenesis and regulates autophagy-dependent cell death

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In the present study we investigate the role of c-FLIP in autophagosome biogenesis. c-FLIP is an apoptosis modulator [1] and plays a complex role in cellular homeostasis [2]. In the last few years a cross-talk between autophagy and apoptosis has been highlighted [3], but this complex mechanism still remains partially unknown. In c-FLIP-/- MEFs (mouse embryonic fibroblasts) compared to WT MEFs we analysed two well-known autophagy markers, LC3 and p62, under different autophagy-inducing stimuli (torin 1, starvation and tunicamycin). We found a strong reduction of the autophagic flux in c-FLIP-/- MEFs. We then studied the activation state of specific markers at each stage of the autophagic process and c-FLIP was found to participate in the nucleation stage and to bind key factors in the autophagosomes nucleation. Then we analysed the autophagic flux at increasing times and doses after treatment with autophagic inducers. A positive correlation was observed between death increase and autophagic flux induction in WT MEFs. Cell death was partially reversed by combining drug treatments with autophagy inhibitors. On the contrary, autophagy inhibition did not affect the basal low-level death of c-FLIP-/- MEFs. Further experiments are currently ongoing to better characterize the involved mechanisms and we can conclude that c-FLIP protein absence reduces autophagy-dependent cell death.

References

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Key words

Autophagosome, mouse embryonic fibroblasts, apoptosis.