INDUCTION OF CELL DEATH BY TUNICAMYCIN AND BREFELDIN A IN RETINAL TISSUE BY ENDOPLASMIC RETICULUM STRESS

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Various neurodegenerative pathologies have been associated with endoplasmic reticulum (ER) stress. The aim of this work was to broaden our studies on ER stress and cell death in retinal tissue. For this purpose we used tunicamycin, an inhibitor of N-glicosylation and brefeldin A, a blocker of vesicular transport, both inducers of ER stress. We further investigated the expression of the transcription factor CHOP, which is involved with ER stress, as well as the participation of the ERK pathway. Retinal explants from 6 day-old rats were maintained for 24 hours *in vitro*, in the presence of tunicamycin or brefeldin A. Cell death was evaluated by counting condensed profiles either stained with neutral red or immunolabeled using anti-rhodopsin, a marker of rod photoreceptors. Protein expression and phosphorylation were examined by western blot. We observed that both 1µg/mL of tunicamycin and 3µM of brefeldin A induce cell death in retinal tissue, however we observed that photoreceptors were not sensitive to these treatments. We also verified an induction of the expression of CHOP and an increase in the amount of phospho-ERK. Inhibition of caspase activity with BAF (100µM), blocked tunicamycin-induced cell death. These results show that tunicamycin and brefeldin A induce cell death in retinal tissue, probably by ER stress, and suggest involvement of the ERK pathway. (Financial support: CNPq, FAPERJ, HHMI-GAR).