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Cell death induced by Bovine Viral Diarrhea Virus in neural cells has apoptotic and autophagic characteristics

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Several studies show interplay between apoptosis and autophagy in response to viral infection, and it has been demonstrated that viruses have evolved different strategies to antagonize, and potentially, to exploit the host autophagic and/or apoptotic machinery (1-3).

Bovine Viral Diarrhea Virus (BVDV), a small enveloped positive single-stranded RNA virus that belongs to the genus Pestivirus of the family Flaviviridae, is an important pathogen of cattle (4), and is commonly used as a surrogate model for Hepatitis C Virus (HCV) infection. It is already known that cytopathic strain of BVDV in Madin Darby bovine kidney (MDBK) cells induces apoptotic death by activation of caspases and non-apoptotic death by autophagy associated with cytoplasmic vacuolization via endoplasmic reticulum (ER) stress (5-7), as well as HCV-induced hepatocytes damage (8). Because both viruses seem to have cellular tropism also for neural tissue, here we have investigated the infection of mouse neuroblastoma (neuro-2a) cells with the cytopathic BVDV strain using indirect immunofluorescence. Apoptotic index, as quantified by acridine orange staining, revealed a significant increase in the percentage of apoptotic cells at 12 h post infection (p.i.) and reached a massive effect at 72 h p.i.. We have also observed, by Western blotting, increase in the activation of caspase -8, -9 and -3 with a peak at 8, 12 and 24 h of p.i., respectively. Furthermore, the infected cells appeared characterized by substantial autophagic vacuolization in the cytoplasm.

This findings suggested that BVDV is able to replicate on neural cells and utilizes machinery involving both cellular apoptotic and autophagic processes.

Keywords: neural cells, BVDV, apoptosis, autophagy.

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