Apoptosis without fragmentation of the nucleus in murine microglia after UV irradiation

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Among the most characteristic features of apoptosis are chromatin condensation and marginalization, nuclear fragmentation, and formation of apoptotic bodies. Recently, we described in the microglial cell line BV-2 a new apoptotic phenotype. After UV irradiation the nucleus is degraded not by fragmentation, but by a combination of chromatin extrusion into the cytoplasm and shrinking of the nuclear envelope by vesicle formation [1].

In the present study, we extended our data about the fate of condensed chromatin and the nuclear envelope during apoptosis in UV-irradiated BV-2 cells by performing transmission electron microscopy using both chemical and high pressure freeze fixation, as well as immunogold-labelling of histone H3. Additionally, we investigated the ultrastructure of apoptotic primary microglia after UV irradiation.

Even though the cell ultrastructure was preserved differently depending on the fixation method used, we were able to confirm our previous morphological observations that nuclear degradation in apoptotic BV-2 cells is executed by dilation of the nuclear envelope, subsequent vesicle formation, and translocation of chromatin from nucleoplasm into cytoplasm by an unknown mechanism. Other prominent features of apoptotic BV-2 cells are changes in the morphology of ER cisternae, forming long sheets and convoluted structures in the cell periphery. Moreover, antibody-staining with anti-histone H3 labeled nuclear as well as cytoplasmic chromatin in apoptotic BV-2 cells. Agarose gel electrophoresis showed that DNA fragmentation starts already 1 h after apoptosis induction.

In murine primary microglia we observed similar changes in cell morphology as in BV-2 cells after UV irradiation. Apoptotic primary microglia are also characterized by condensed chromatin in the nuclear periphery, a strongly dilated nuclear envelope with numerous vesicles in its vicinity, and changes in the organization of ER similar to those observed in BV-2 cells. Our morphological data also suggest that chromatin in apoptotic primary microglia is translocated into the cytoplasm, but to a smaller extend as in BV-2 microglia.

1. S. Zierler et al., Brain Res. **1121(1)** (2006) p12-21.
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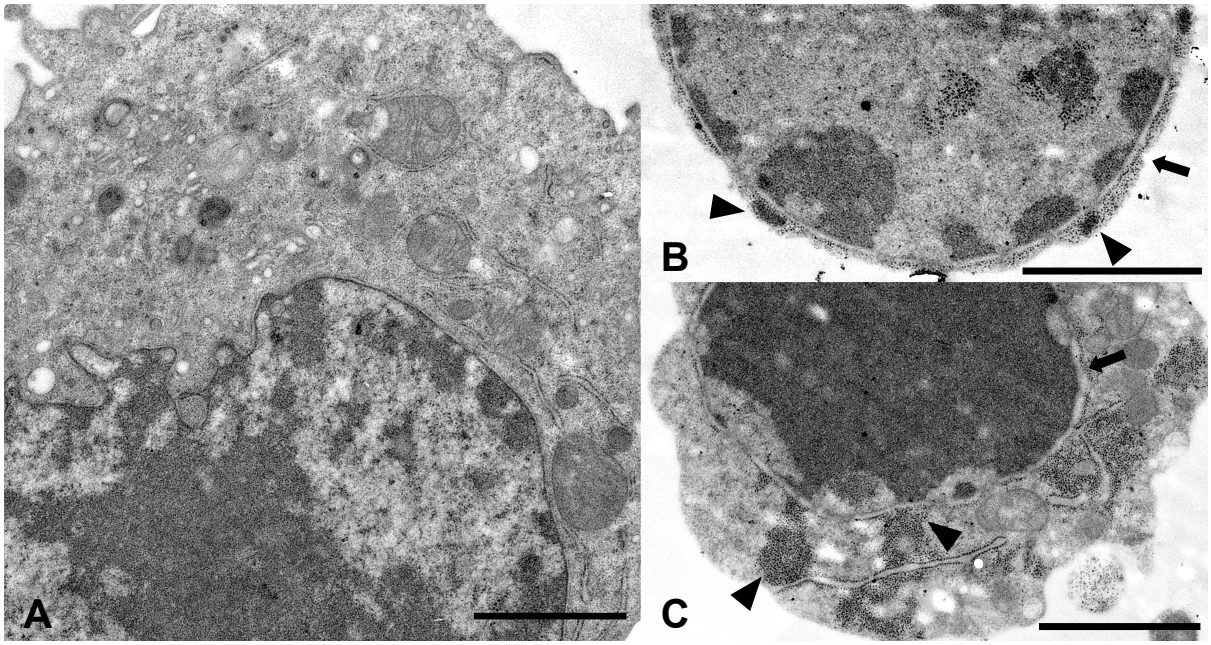

Figure 1. Electron micrographs of chemically fixed, untreated (**A**) and apoptotic (**B** and **C**) microglia of the cell line BV-2 after UV irradiation. Note the dilated nuclear envelope (arrows) and cytoplasmic chromatin (arrowheads). Bars 2 μm.

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