Influence of BeWo trofoblast cells and *Toxoplasma gondii* infection in the modulation of cell death mechanisms in THP-1 cells

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During pregnancy, trophoblast cells interact with monocytes presents at maternal-fetal interface, modulating their functional activities, and it is determinant for gestational success. Furthermore, during this period, maternal organism becomes more susceptible to infections caused by pathogens, as *Toxoplasma gondii*, and these microorganisms directly interfere in the interactions established between these cells, which can cause gestational complications. The cell death mechanisms that occurs in cell populations present at maternal-fetal interface are involved in the gestational development and, in this way, this study aimed to evaluate the influence of trophoblast cell (BeWo line) and *T. gondii* infection in the modulation of death mechanisms in monocytes (THP-1 line). For this, THP-1 cells were stimulated or not with supernatants of BeWo cells (infected or uninfected with *T. gondii*) and then infected with *T. gondii.* After this, the mechanisms of cell death in THP-1 cells were analyzed. The results showed that both supernatants of BeWo cells increased the index of cell death and apoptosis in uninfected THP-1 cells, probably as a mechanism of defense developed by the trophoblast. Furthermore, THP-1 cells, when infected, presented index of cell death higher than uninfected THP-1 cells, but the index of apoptosis was lower, suggesting that the parasite prevents apoptosis, but induces cell death, probably necrosis, as strategies to parasite dissemination. Macrophage migration inhibitory factor (MIF) and transforming growth factor beta 1 (TGF-β1), both secreted by BeWo cells, induced cell death in uninfected THP-1 cells, while only TGF-β1 altered cell death in infected THP-1 cells, inhibiting it. Both of these soluble factors were able to reduce the index of apoptosis in uninfected THP-1 cells, but only TGF-β1 altered this index in infected THP-1 cells. The expression of Fas/CD95 and the secretion of FasL were higher in infected THP-1 cells than uninfected THP-1 cells, suggesting that this is an action mechanism of monocytes to control the parasitism. The intracellular proteins, phophorylated ERK1/2 and active caspase 3 were less expressed in infected THP-1 cells and both supernatants of BeWo cells, induced decreased of active caspase 3 expression, in uninfected and infected THP-1 cells. These results suggest that *T. gondii* inhibits THP-1 apoptosis by blocking active caspase 3 and inhibition of ERK1/2 phosphorylation. Together, our results showed that BeWo trophobast cells and *T. gondii* infection modulate the mechanisms of cell death in THP-1 cells, and, these alterations can be associated with gestational maintenance and success.

Keywords: *Toxoplasma gondii*; THP-1 cells; apoptosis

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