Nitric Oxide Down Modulation by PGE_2 and TGF-b in Glial Cells Infected by *Neospora caninum*

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Neospora caninum causes abortion in cattle and neuromuscular disorders in dogs. All animal tissues can be infected, but in central nervous system immunopathogenic mechanisms are differentiated, since the immune response to this parasite has an anti-inflammatory pattern that preserves the tissue, but unfortunately, maintains the infection. Previously, we have showed that *N. caninum* infected glial cultures release high levels of IL-10 and, upon IFN-γ stimulation, parasites number and nitrite liberation were reduced. In order to investigate the mechanisms involved in nitric oxide (NO) down modulation, this study evaluated TGF-β and PGE_2 production in this process. Rat glial cultures were treated with IFN-γ (300 IU/mL) and infected with *N. caninum* tachyzoites. After 72h, cultures supernatants were used to measure the levels of nitrite (by Griess method), TGF-β and PGE_2 (by a commercial sandwich ELISA). As expected, there was NO inhibition in infected glia and it was more evident in IFN-γ treated/infected cells. We also observed that the basal PGE_2 levels increased 17 and 25% respectively in infected and infected/IFN-γ treated cells, while TGF-β levels declined 32 and 45%, respectively, in IFN-γ treated and treated/infected cultures. Since TGF-β stimulates iNOS, and PGE_2 induces regulatory cytokines production, as such as IL-10, these results taken together contribute to clarify the anti-inflammatory pattern seen in *N. caninum* glial infection, and justify the NO down modulation observed in this model.

Key words: *Neospora caninum*, glia cells, NO, PGE_2, TGF-β