ERK1/2 phosphorylation and low levels of IL-6 induce high susceptibility to *Toxoplasma gondii* infection in human extravillous trophoblast cells (HTR-8/SVneo line)

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During pregnancy, *T. gondii* can trigger serious manifestations and potentially affect the fetal development. During the early placentation, cytotrophoblast proliferate and differentiate by fusion to form multinucleated syncytiotrophoblast layer. The extravillous trophoblast invade the uterine wall in the deciduous region. It is important evaluate differences in susceptibility of these cells to *T. gondii* for establish new therapeutic approaches capable of interfering in control fetal infection by *T. gondii* without compromising pregnancy success. This study aimed to evaluate the susceptibility of cytotrophoblast, syncytiotrophoblast and extravillous trophoblast to *T. gondii*. In order to obtain syncytiotrophoblast, BeWo cells were submitted to treatment (Forskolin and PMA), while BeWo cells without these treatments were used as cytotrophoblast, and HTR-8/SVneo were used as extravillous trophoblast cells. Next, cells were cultured in coverslips into 6-well plates and infected by *T. gondii* for additional 24 h. In parallel, the three cell populations were treated with ERK1/2 inhibitor (PD98059) for 3 h and infected by *T. gondii* for 24 h. The supernatants were collected to measure cytokine profile, and the cells analyzed for infection index, total number of parasites, and MAPKs phosphorylation. Our data showed that HTR-8/SVneo was the most susceptible cells to *T. gondii* infection when compared to syncytiotrophoblast and cytotrophoblast. In addition, syncytiotrophoblast was the cell type more resistant to parasite infection. Also, cytotrophoblast and syncytiotrophoblast cells produced significantly more IL-6 than HTR-8/SVneo cells. In another hand, HTR-8/SVneo cells showed higher ERK1/2 phosphorylation than cytotrophoblast and syncytiotrophoblast cells. The ERK1/ inhibition reduced the *T. gondii* infection and increased the IL-6 production in HTR-8/SVneo cells. It is possible to speculate that HTR-8/SVneo cells are more susceptible to *T. gondii* infection since these cells present higher ERK1/2 phosphorylation and lower IL-6 levels, showing that these mediators are important to favor the parasite infection in this kind of trophoblast.

Keywords: *Toxoplasma gondii*, extravillous trophoblast, cytokines

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