DEPTOR is a novel mTOR interacting protein and has the capacity to form complexes with mTOR and negatively regulate mTORC1 and mTORC2 complexes. Recently it has been suggested that the changes in placental mTOR signalling components in an ovine model could be driven by fetal stress. Indeed, pregnancy-specific stress is a powerful contributor to birth outcomes. In this study we tested the hypothesis that maternal stress might affect DEPTOR expression. Two human choriocarcinoma cell lines (JEG-3 and BeWo) were used as placental models treated with the stress-hormone cortisol in a dose-dependent manner over 24 hrs. Quantitative RT-PCR and immunofluorescent analyses demonstrated for first time that DEPTOR is expressed at both mRNA and protein level in these cell lines. Fluorescent microscopy revealed that DEPTOR is exclusively expressed in the cytoplasm in both JEG-3 and BeWo cells. When BeWo cells were treated with cortisol 10nM, 100nM or 1000nM the expression of DEPTOR was significantly down-regulated by 50%, 41% and 39% respectively when compared with basal levels. Treatment of JEG-3 cells with cortisol, lead to a significant decrease of DEPTOR expression at 100nM (39%) and at 1000nM (73%) when compared with basal levels as well. These in vitro findings suggest that cortisol can be a potent modulator of DEPTOR. As a result, it is attractive to speculate that maternal stress might affect subsequent placental mTOR-mediated signalling events.