SYNTHETIC RECEPTORS INDUCE AN ANTI ANGIOGENIC PROFILE ON HUMAN FIRST TRIMESTER CYTOTROPHOBLAST CELLS


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Purpose: Preeclampsia (preE) is a hypertensive disorder unique to pregnancy with abnormal placentation. We have demonstrated that marinobufagenin (MBG), a cardiotonic steroid (CTS), impairs cytotrophoblast (CTB) function, which is critical for placental development. However, the cell surface receptor for the CTS has not been identified yet. Synthetic receptors (SR) were used to explore the cell surface receptor or CTS on CTB cells. The human extra villous CTB cells used in this study were derived from first trimester chorionic villus tissue. Cells were treated with 0.1, 1, 10, and 100 nM SR for 48 h. CTB function was studied in the SR-treated cells. The levels of angiogenic and anti-angiogenic factors were measured in the cell culture media, while the cell lysates were utilized to measure the VEGF-1, AT1 and AT2 receptors expression. The sFlt-1 (Soluble fms-like tyrosine kinase-1) and sEnd (endoglin) were significantly increased while VEGF (vascular endothelial growth factor) and PIGF (placental growth factor) were decreased in the culture media of CTB cells treated with ≥ 1 nM SR. The AT2 receptor (Angiotensin II receptor type 2) expression was significantly up regulated in ≥ 1 nM SR-treated CTB cells in compared to basal; however, the AT1 and VEGFR-1 (VEGF receptor 1) receptors expression was down regulated. The anti-proliferative and anti-angiogenic effect of this compound on CTB cells are similar to the effect of CTS. The receptor/ligand affinity of SR on CTB cells provides us the clue to design a potent inhibitor to prevent the CTS-induced impairment of CTB cells.