The Effects of Peptides derived from Beta2 Glycoprotein I on Endothelial and Placental Tissue in Models of Preeclampsia

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Preeclampsia, a hypertensive disorder that affects nearly 10% of pregnant women, is the leading cause of maternal death and medically-induced preterm births in the US. Preeclampsia symptoms include high blood pressure, elevated protein in the mother's urine, and low birth weight. Although the exact cause remains unknown, evidence indicates that complement dysregulation caused by placental hypoxia plays a vital role in the development of preeclampsia. To simulate preeclampsia, a frequent model of placental ischemia and induced hypertension is the reduced uteroplacental perfusion pressure (RUPP) rat model. Beta2-glycoprotein I (β2-GPI) elicits an immune response during hypertension and mediates fetal loss and growth restrictions in other pregnancy conditions. We tested the hypothesis that β2-GPI binds hypoxic endothelial cells and peptides derived from mouse β2-GPI block binding in vitro and in preeclampsic rats. Rat endothelial cells, IEC-18, were incubated in either hypoxic or normoxic conditions for two hours prior to receiving one of four different peptide treatments during a 30 min reperfusion period. The treated cells were stained for β2-GP1 with immunohistochemistry. The results strongly indicate that hypoxic conditions induced β2-GPI binding to rat endothelial cells and peptides 296c-s and RD-p9 reduced binding compared to the control peptide or the untreated sample. Importantly, RD-p9 appeared to have a greater effect on the reduction of rat endothelial binding. Future experiments will examine IgM, C3, and β2-GPI deposited on rat placenta from rats treated with β2-GPI peptides prior to Sham or RUPP surgery to simulate preeclamptic conditions.