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# SATURATED FREE FATTY ACIDS INDUCE TROPHOBLAST LIPOAPOPTOSIS AND SUBCELLULAR STRESS

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Maternal obesity, a metabolic condition, has become a major public health concern among the women of reproductive age owing to an increased risk for the development of pregnancy complications, including gestational diabetes, pre-eclampsia, maternal inflammation, intrauterine growth retardation and large-for-gestational-age infants. Studies have shown that maternal obesity could potentially impact the metabolic health of newborns and could increase the risk of future development of metabolic syndromes like obesity, diabetes and cardiovascular diseases in offspring. Studies in our lab showed that increased saturated free fatty acids in maternal circulation as a result of increased adipose tissue lipolysis induced trophoblast apoptosis, commonly known as lipoapoptosis. Trophoblasts exposed to physiological concentration of Palmitic (PA) and Stearic acid (SA) showed a concentration dependent increase in cell cytotoxicity and caspase 3/7 activity. While PA and SA increased trophoblast cytotoxicity, Oleic acid (OA), a monounsaturated fatty acid protected cell against PA and SA induced cell cytotoxicity. We showed increased cleaved caspase 3 and PARP levels in cells treated with PA and SA. To further characterize the mechanism behind cell cytotoxicity, we hypothesize that upon exposure to trophoblasts, free fatty acids induces organelle stress, in particular endoplasmic reticulum stress (ER stress) and MAPK activation, which could potentially mediate cell cytotoxicity by apoptosis. We used choriocarcinoma derived third trimester trophoblasts (JEG-3 and JAR) and exposed these cells to palmitic acid mediated cell injury for various times. Apoptosis was assessed with DAPI staning and by measuring Caspase 3/& activity. Immunoblot was performed to analyses activation of MAPKs and cell stress pathways. Initial results show that PA induces MAPK activation (JNK and ERK), phosphorylation of critical mediators of ER stress (IRE1) and nuclear localization of CHOP in trophoblasts, thereby potentially contributing to lipoapoptosis induction. Trophoblast undergo apoptotic cell death when induced with palmitic acid. Further, palmitic acid induces subcellular stress in form of MAPKs activation and ER stress.