Título en español: Leptina revierte el efecto apoptótico del cloruro de cobalto en células placentarias

Título en inglés: Placental apoptosis induced by cobalt chloride treatment is counteracted by leptin

Nataly de Dios est Ph.D[1], Malena Schanton Pd.D[1], Rodrigo Riedel Ph.D[1], Roberto Casale Esp.[2], Julieta Maymó Ph.D[2] and Cecilia Varone Ph.D[1]
1. Departamento de Química Biológica FCEN-UBA, Instituto de Química Biológica IQUIBICEN, CONICET, Buenos Aires, Argentina
2 Hospital Nacional Profesor Alejandro Posadas, Buenos Aires, Argentina

Leptin acts as a regulating hormone in the maternal fetal interface. We demonstrated that leptin promotes proliferation and survival of trophoblastic cells. Moreover, leptin prevents cellular stress under hypoxic condition in trophoblastic cells. In this sense, Leptin is incremented in different pathologies associated to pregnancies like as preeclampsia. In this work we aimed to elucidate the mechanisms involved in Leptin antiapoptotic effect on placental apoptosis induced by cobalt chloride ($CoCl_2$). This agent stabilizes HIF-1α transcription factor. We used Swan-71 cells, a cytotrophoblast human cell line and human term placental explants cultured under normoxia and hypoxia conditions. Swan-71 cells and placental explants were treated with $CoCl_2$ (50 or 100 µM) in presence or absence of leptin (100 ng/ml). The expression of HIF-1α, p53, Caspase-3, cPARP and Mdm2 was determined by Western blot or Immunofluorescence (IF). Apoptosis was determined by the visualization of apoptotic nuclei by IF. All procedures were approved by ethical review committee at the Alejandro Posadas National Hospital. We observed that HIF-1α stabilization increased apoptosis in Swan-71 cells. Treatment with $CoCl_2$ increased PARP-1 and Caspase-3 levels indicating that apoptosis was induced. Leptin treatment diminished this effect. Moreover, p53 protein expression and nuclear localization was enhanced by hypoxic condition. Leptin was capable to regulate p53 pathway, increasing Mdm2 expression, a p53 negative regulator. All these results suggest that HIF-1α stabilization enhances placental apoptosis and leptin is capable to protect these cells under hypoxia conditions.

Key words: Placenta, apoptosis, hypoxia, leptin

References

[1] Dos Santos E, Duval F, Vialard F, Dieudonne F.N. The roles of leptin and adiponectin at the fetal-maternal interface in humans, Hormone molecular biology and clinical investigation 24(1) (2015) 47-63.

[2] Magarinos M.P, Sanchez-Margalet V, Kotler M, Calvo J.C, Varone C.L, Leptin promotes cell proliferation and survival of trophoblastic cells, Biol Reprod 76(2) (2007) 203-10.

[3] Toro A.R, Perez-Perez A, Corrales Gutierrez I, Sanchez-Margalet V, Varone C.L, Mechanisms involved in p53 downregulation by leptin in trophoblastic cells, Placenta 36(11) (2015) 1266-75.

[4] Toro A.R, Maymo J.L, Ibarbalz F.M, Perez-Perez A, Maskin B, Varone C.L, et al. Leptin is an anti-apoptotic effector in placental cells involving p53 downregulation, PLoS One 9(6) (2014) e99187.