



Endocrinología y Nutrición



4 - ENERGY HOMEOSTASIS AND METABOLIC ADAPTATIONS OF PANCREAS AND PLACENTA DURING LATE PREGNANCY: ROLE OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA

P. Corrales-Cordón^a, M. Díez-Hochleitner^b, Y. Vivas^a, A. Izquierdo-Lahuerta^a, D. Horrillo^a, J. Sevillano^b, M. Ricote^c, M. Ros^a, P. Ramos^b y G. Medina-Gómez^a

^aUniversidad Rey Juan Carlos. Alcorcón. España. ^bUniversidad San Pablo-CEU. Madrid. España. ^cCentro Nacional de Investigaciones Cardiovasculares. Madrid. España.

Resumen

Pregnancy requires a progressive adaptation of maternal energy metabolism, which includes pancreatic β -cell adaptation and the correct placental development and function. Insulin resistance develops predominantly during late gestation, as part of the metabolic adaptations that support fetus development and growth. Peroxisome proliferator-activated receptor γ (PPAR γ) is involved in adipogenesis, glucose and lipid metabolism and modulation of insulin sensitivity. Moreover, PPAR γ plays an important role in β -cell proliferation in other pathologic situations like obesity. Our aim was to study the role of PPAR γ in β -cell adaptation and placental functionality during gestation in different study conditions. We have created two transgenic mouse models: PPAR γ 2knockout (PPAR γ 2KO) mice and specific PPAR γ knockout mice in pancreatic β -cell ($\beta\gamma$ KO). At D15 and D16 GTT or ITT were performed respectively and animals were sacrificed at D18 of gestation. $\beta\gamma$ KO females were also fed with high fat diet 3 weeks before pregnancy. Lack of PPAR γ 2 induced higher insulin resistance associated with lower serum adiponectin levels than WT mice (1.07 ± 0.08 vs 4.40 ± 0.34) during late pregnancy. Indeed, ablation of PPAR γ 2 induced morphological changes in pancreas and an altered metabolomic profile (carnitine metabolism) and lipid metabolism expression in placenta. Similarly, results in $\beta\gamma$ KO mice have shown decreased pancreatic β -cell mass despite high serum levels of insulin during pregnancy. Their pancreatic weight was lower compared with the WT animals. There were also differences in placenta morphology and metabolites between $\beta\gamma$ KO and WT pregnant mice. These data indicated that an appropriate expression of PPAR γ is necessary to ensure a normal pancreas and placenta metabolism during gestation, particularly within the late phase of pregnancy when a state of insulin resistance is established.

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