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4 - Energy homeostasis and metabolic adaptations of pancreas and placenta during late pregnancy: role of Peroxisome proliferator-activated receptor gamma

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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 (PPARγ) is involved in adipogenesis, glucose and lipid metabolism and modulation of insulin sensitivity. Moreover, PPARγ plays an important role in β-cell proliferation in other pathologic situations like obesity. Our aim was to study the role of PPARγ in β-cell adaptation and placental functionality during gestation in different study conditions. We have created two transgenic mouse models: PPARγ2knockout (PPARγ2KO) mice and specific PPARγ knockout mice in pancreatic β-cell (βγKO). At D15and D16 GTT or ITT were performed respectively and animals were sacrificed at D18 of gestation. βγKO females were also fed with high fat diet 3 weeks before pregnancy. Lack of PPARγ2 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 PPARγ2 induced morphological changes in pancreas and an altered metabolomic profile (carnitine metabolism) and lipid metabolism expression in placenta. Similarly, results in βγKO 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 βγKO and WT pregnant mice. These data indicated that an appropriate expression of PPARγ 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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