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IN BRIEF

DIABETES

PPAR γ might have a role in the regulation of FGF21 action in pancreatic islets

So and co-investigators report that high glucose levels impair the action of fibroblast growth factor 21 (FGF21) in mouse pancreatic islets. The researchers show that in islets of adult *db/db* mice (a mouse model of obesity and type 2 diabetes mellitus) and islets from wild-type mice treated with high levels of glucose *ex vivo*, expression of β -klotho (a cofactor of FGF21) was reduced, FGF21 signalling was attenuated and expression of peroxisome proliferator-activated receptor γ (PPAR γ) was decreased. The thiazolidinedione drug rosiglitazone, which is a PPAR γ agonist, reversed the downregulation of β -klotho expression in both types of islets and, in consequence, restored FGF21 signalling. The investigators suggest that PPAR γ is involved in the negative regulation of β -klotho expression and FGF21 signalling that occurs in the islets in conditions of high glucose levels.

Original article So, W.Y. *et al.* High glucose represses β -klotho expression and impairs fibroblast growth factor 21 action in mouse pancreatic islets: involvement of peroxisome proliferator-activated receptor γ signaling. *Diabetes* doi:10.2337/db13-0645

REPRODUCTIVE ENDOCRINOLOGY

Insulin-like growth factor 2 and long-term placental programming of anxiety

A new study highlights the role of the placenta in the long-term programming of emotional behaviour. The researchers compared anxiety responses in mice that lacked the insulin-like growth factor 2 gene (*Igf2*) in the placenta only or in both the placenta and fetus. Intrauterine growth restriction occurs in both of these mouse models, but when *Igf2* is lacking from the placenta only, a mismatch is thought to exist between placental supply and fetal demand for nutrients during gestation. Enhanced responses to anxiety only occurred in the adult mice lacking *Igf2* in the placenta only, and these mice had specific changes in brain gene expression related to anxiety behaviours.

Original article Mikaelsson, M. A. *et al.* Placental programming of anxiety in adulthood revealed by *Igf2*-null models. *Nat. Commun.* doi:10.1038/ncomms3311

BONE

GSK-3 β in bone might also regulate whole-body metabolism

Bone has a central role in regulating body metabolism, suggest Gillespie and co-investigators in a study that describes the skeletal and metabolic phenotypes of mice with skeleton-specific inactivation of glycogen synthase kinase 3 β (GSK-3 β). This protein is an important negative regulator in many anabolic signalling pathways, including those involving Wnt and insulin. Mutant mice with skeleton-specific inactivation of GSK-3 β had reduced body fat and postnatal bone growth. In addition, the mice had reduced circulating levels of glucose and insulin, even though expression of GSK-3 β was normal in metabolic tissues. The researchers found that these metabolic effects were because of an increase in global insulin sensitivity in the mutant mice. Male mutant mice also seemed to be predisposed to develop type 2 diabetes mellitus and died prematurely.

Original article Gillespie, J. R. *et al.* GSK-3 β function in bone regulates skeletal development, whole body metabolism and male life span. *Endocrinology* doi:10.1210/en.2013-1155