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IN BRIEF

CARDIOVASCULAR ENDOCRINOLOGY

A novel GLP-1R–ANP axis controls blood pressure

Kim *et al.* used *in vitro* and mouse studies to identify a gut–heart axis involved in the regulation of blood pressure. In this axis, activation of the glucagon-like peptide-1 receptor (GLP-1R) leads to secretion of atrial natriuretic peptide (ANP) and reduction in blood pressure. Furthermore, the Rap guanine nucleotide exchange factor Epac2 (also known as Rapgef4) was identified as a downstream target of GLP-1R in cardiomyocytes. The investigators call for more research on the metabolic and cardiovascular effects of ANP as a downstream target of GLP-1 action.

Original article Kim, M. *et al.* GLP-1 receptor activation and Epac2 link atrial natriuretic peptide secretion to control of blood pressure. *Nat. Med.* doi:10.1038/nm.3128

BONE

A key role for PPARβ/δ in bone homeostasis

PPARβ/δ, which regulates lipid metabolism and energy homeostasis, also has a role in bone homeostasis, report Scholtysek and co-workers. In mice deficient in PPARβ/δ, Wnt signalling activity and serum concentrations of osteoprotegerin were reduced, whereas osteoclast numbers and rates of osteopenia were increased. By contrast, in a mouse model of postmenopausal osteoporosis in which PPARβ/δ was pharmacologically activated, bone turnover was rebalanced and bone density was restored to normal. The researchers suggest that PPARβ/δ is a promising target for the treatment of osteoporosis.

Original article Scholtysek, C. *et al.* PPARβ/δ governs Wnt signaling and bone turnover. *Nat. Med.* doi:10.1038/nm.3146

OBESITY

T-bet has a role in obesity-associated insulin resistance

The T-helper-1-cell transcription factor T-bet has a role in obesity-associated insulin resistance, Stolarczyk *et al.* reveal. In mice deficient in T-bet, insulin sensitivity is improved despite increased visceral adiposity compared with wild-type mice. Further experiments in mice showed that T-bet acts in the adaptive immune system, and that its absence from this system leads to the improved insulin sensitivity. The researchers speculate that obesity could be uncoupled from insulin resistance through the absence of T-bet and, therefore, that T-bet is a potential target for the treatment of insulin resistance and type 2 diabetes mellitus.

Original article Stolarczyk, E. *et al.* Improved insulin sensitivity despite increased visceral adiposity in mice deficient for the immune cell transcription factor T-bet. *Cell Metabolism* **17**, 520–533 (2013)

DIABETES

Diabetes clinical trials are not addressing key issues

In a descriptive analysis of current diabetes-related trials, Lakey *et al.* found that studies are not adequately addressing important issues related to disease prevention, treatment or therapeutic safety. Most of the trials had small numbers of participants, were of short duration and assessed drug therapy instead of other types of interventions or preventive strategies. Moreover, the majority of trials excluded participants at the extremes of ages.

Original article Lakey, W. C. *et al.* Are current clinical trials in diabetes addressing important issues in diabetes care? *Diabetologia* doi:10.1007/s00125-013-2890-4