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IN BRIEF

OBESITY

FXR signalling mediates weight loss associated with bariatric surgery

Weight loss following vertical sleeve gastrectomy (VSG) occurs via an increase in total circulating levels of bile acids, which bind and signal through the nuclear receptor FXR. In a model of diet-induced obesity, the weight-loss effects of VSG were considerably reduced in *Fxr*-deficient mice compared with wild-type and sham-surgery control mice. Other VSG-associated metabolic outcomes were also diminished in *Fxr*-deficient mice, including altered gut microbiome composition and improved glucose tolerance.

Original article Ryan, K. K. *et al.* FXR is a molecular target for the effects of vertical sleeve gastrectomy. *Nature* doi:10.1038/nature13135

DIABETES

Genetic variants associated with HbA_{1c} are linked with diabetes mellitus in East Asian populations

Nine genetic variants associated with glycated haemoglobin (HbA_{1c}) have been identified in a large meta-analysis of genome-wide association studies in individuals of East Asian ancestry. The study assessed data from 16 cohorts that included 32,602 individuals. Four of the nine variants identified in the study were unique to East Asian populations compared with those of European ancestry. Six of the nine variants were found to be associated with erythrocyte function and not glycaemic control, which might have implications when using HbA_{1c} to diagnose diabetes mellitus.

Original article Chen, P. *et al.* Multiple non-glycaemic genomic loci are newly associated with blood level of glycated hemoglobin in East Asians. *Diabetes* doi:10.2337/db13-1815

CLINICAL TRIALS

Aleglitazar—no cardiovascular protection after acute coronary syndrome in patients with T2DM

In a large phase 3 randomized clinical trial, addition of the peroxisome proliferator-activated receptor agonist aleglitazar to standard medical therapy was ineffective in protecting against cardiovascular morbidity among patients with type 2 diabetes mellitus (T2DM) who were hospitalized after an acute coronary syndrome. The double-blind, placebo-controlled AleCardio study enrolled 7,226 patients in 720 hospitals in 26 countries, and was terminated prematurely at 104 weeks owing to a high rate of adverse events.

Original article Lincoff, M. D. *et al.* Effect of aleglitazar on cardiovascular outcomes after acute coronary syndrome in patients with type 2 diabetes mellitus. The AleCardio randomized clinical trial. *JAMA* doi:10.1001/jama.2014.332

METABOLISM

Endotrophin drives metabolic dysfunction in adipose tissue

Adipose-specific overexpression of endotrophin in mice that were fed a high-fat diet resulted in metabolic dysfunction, fibrosis of adipose tissues, insulin resistance and increased levels of circulating inflammatory mediators. Antibody-mediated neutralization of endotrophin effectively reversed these effects, even after long-term consumption of a high-fat diet. Endotrophin might be a potential therapeutic target for metabolic disease and associated pathologies.

Original article Sun, K. *et al.* Endotrophin triggers adipose tissue fibrosis and metabolic dysfunction. *Nat. Commun.* doi:10.1038/ncomms4485