Nature Reviews Endocrinology | Published online 20 November 2015

IN BRIEF

DIABETES

Fine mapping reveals regulation at T2DM susceptibility loci

Genetic fine mapping of 39 susceptibility loci — defined by genome-wide association studies — in 27,206 individuals with type 2 diabetes mellitus (T2DM) and 57,574 controls, has identified 49 distinct association signals, predominantly mapping to noncoding sequences. Comparison of these signals with chromatin immunoprecipitation sequence data identified a common role for hepatocyte nuclear factor 3β (HNF-3β, encoded by *FOXA2*) transcription-factor binding in the regulation of gene activity contributing to disease susceptibility. For example, an allelic variant associated with T2DM risk at the *MTNR1B* gene had higher HNF-3β transcriptional enhancer activity in human pancreatic islet and liver-derived cells than low-risk alleles. HNF-3β binding patterns could inform strategies for future research into the mechanisms underlying T2DM susceptibility.

ORIGINAL ARTICLE Gaulton, K. J. *et al.* Genetic fine mapping and genomic annotation defines causal mechanisms at type 2 diabetes susceptibility loci. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3437

REPRODUCTIVE ENDOCRINOLOGY

Effects of omega-3 fatty acids on serum FSH in women are dependent on BMI

Newly published results suggest that dietary supplementation with omega-3 polyunsaturated fatty acids (PUFA), which can delay ovarian ageing and promote oocyte quality in mice, could have similar benefits in women who are not obese. Women aged 28–34 years (15 with obesity and 12 with a normal BMI) received daily dietary supplementation with eicosapentaenoic acid and docosahexaenoic acid for 1 month. Compared with baseline, the ratio of plasma omega-6 PUFA to omega-3 PUFA decreased significantly in both groups. Similar levels of reduction in a number of proinflammatory cytokines were seen in both groups, but only the changes in IL-1β and TNF in women with obesity were significant. In women with a normal BMI, but not those with obesity, the follicle-stimulating hormone (FSH) response to gonadotropin-releasing hormone was significantly reduced following omega-3 PUFA supplementation.

ORIGINAL ARTICLE Al-Safi, Z. A. *et al.* Omega-3 fatty acid supplementation lowers serum FSH in normal weight but not obese women. *J. Clin. Endocrinol. Metab.* http://dx.doi.org/10.1210/jc.2015-2913

RISK FACTORS

Very low endogenous testosterone in men is associated with high risk of ischaemic stroke

A study of a Danish population has found that low testosterone is associated with increased risk of ischaemic stroke in men, but not in women. Levels of endogenous sex hormones were measured in 4,615 men and 4,724 women between 1981 and 1983. With up to 29 years of follow-up, 524 men and 563 women developed ischaemic stroke. No association was observed between the incidence of ischaemic stroke and levels of plasma oestradiol in either sex, or testosterone in women. However, the risk of ischaemic stroke was higher in men with testosterone concentrations up to the 10th percentile, compared with the 11th to 90th percentiles (HR 1.34). Partial mediation of this increased risk meant that the corresponding hazard ratio was 1.46 in men with hypertension and overweight or obesity.

ORIGINAL ARTICLE Holmegard, H. N. *et al.* Sex hormones and ischemic stroke: a prospective cohort study and meta-analyses. *J. Clin. Endocrinol. Metab.* http://dx.doi.org/10.1210/jc.2015-2687