

*Nature Reviews Endocrinology* **10**, 640 (2014); published online 19 August 2014;  
doi:10.1038/nrendo.2014.152;  
doi:10.1038/nrendo.2014.153;  
doi:10.1038/nrendo.2014.154

## IN BRIEF

### THYROID FUNCTION

#### Subclinical hypothyroidism and thyroid autoimmunity increase the risk of miscarriage

Women with subclinical hypothyroidism and thyroid autoimmunity are thought to have an increased risk of adverse pregnancy outcomes; however, the risk of miscarriage is not well defined. Now, a study of 3,315 women in iodine-sufficient areas of China has assessed the effect of these conditions at 4–8 weeks gestation on subsequent risk of miscarriage. Compared with women with normal thyroid function, women with subclinical hypothyroidism and/or thyroid autoimmunity had an increased risk of miscarriage. The risk was greatest in women who had both conditions. In addition, miscarriages in women with these conditions occurred at an earlier gestational age than miscarriages in women who had normal thyroid function.

**Original article** Liu, H. *et al.* Maternal subclinical hypothyroidism, thyroid autoimmunity and the risk of miscarriage: a prospective cohort study. *Thyroid* doi:10.1089/thy.2014.0029

### DIABETES

#### RNA stress response links obesity and ageing to development of type 2 diabetes mellitus

A new study by Yan and colleagues reveals a mechanism that links obesity and ageing to hypothalamic inflammation, and thus to type 2 diabetes mellitus. In this study, an initial analysis found that production of transforming growth factor  $\beta$  (TGF- $\beta$ ) was excessive in obese and elderly mice. These excess levels of TGF- $\beta$  were shown to cause hyperglycaemia and glucose intolerance, an effect that was independent of changes in body weight. Excess levels of TGF- $\beta$  were demonstrated to induce a hypothalamic RNA stress response, which accelerated the mRNA decay of *I $\kappa$ B $\alpha$*  (an inhibitor of proinflammatory nuclear factor  $\kappa$ B). TGF- $\beta$  was mainly produced and released by astrocytes and affected hypothalamic neurons, which resulted in metabolic dysfunction.

**Original article** Yan, Y. *et al.* Obesity- and aging-induced excess of central transforming growth factor- $\beta$  potentiates diabetic development via an RNA stress response. *Nat. Med.* doi:10.1038/nm.3616

### DEVELOPMENT

#### Genome-wide association study reveals gene variants that are involved in the development of hypospadias

Hypospadias, in which the urethra opening is located on the underside of the penis, is a fairly common disorder of sex development. A genome-wide association study including 1,006 patients with hypospadias confirmed by surgery and 5,486 control individuals from Denmark that was replicated in 1,972 patients and 1,812 control individuals from Denmark, Sweden and the Netherlands has identified 18 loci that are associated with hypospadias. Several of the identified loci are close to genes known to be involved in embryonic development, such as *HoxA4*, *EYA1*, *IRX5* and *IRX6*. The identified loci were also demonstrated to be functionally connected. Pathway analysis identified potential genetic mechanisms underlying the development of hypospadias.

**Original article** Geller, F. *et al.* Genome-wide association analyses identify variants in developmental genes associated with hypospadias. *Nat. Genet.* doi:10.1038/ng.3063