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IN BRIEF

THYROID CANCER

Positive results with lenvatinib for the treatment of advanced medullary thyroid cancer in a phase II trial

In a phase II clinical trial, 59 patients with progressive medullary thyroid cancer were treated with a 24 mg daily dose of the tyrosine kinase inhibitor lenvatinib over a 28-day period. Of these patients, 36% (95% CI 24–49%) reached the primary end point for lenvatinib treatment, defined as an objective response rate assessed by Response Evaluation Criteria In Solid Tumors v1.0 score and an independent imaging review. Overall, the disease control rate was high (80%, 95% CI 67–89%) and the time to response was only 3.5 months (95% CI 1.9–3.7). The median progression-free survival was 9.0 months. The incidence of adverse effects was low; they included diarrhoea, hypertension and decreased appetite, all of which were easily managed with medication or by modifying the dose of lenvatinib.

Original article Schlumberger, M. *et al.* A phase 2 trial of the multi-targeted tyrosine kinase inhibitor lenvatinib (E7080) in advanced medullary thyroid cancer (MTC). *Clin. Cancer Res.* doi:10.1158/1078-0432.CCR-15-1127

METABOLISM

Dietary iron regulates appetite and metabolism via a leptin-dependent mechanism

Iron deficiency is known to reduce appetite, but the mechanism by which this occurs is unclear. In a new study published in the *Journal of Clinical Investigation*, Gao and colleagues identified a negative correlation between levels of ferritin and leptin in 76 individuals who either had diabetes mellitus ($n = 36$) or were metabolically healthy ($n = 40$). This correlation was also found in mice fed a diet with a high iron content. Using 3T3-L1 adipocytes, the team found that iron decreased levels of leptin mRNA, which was dependent on the cAMP response element-binding protein (CREB). Two CREB binding sites were found in the leptin promoter, which when mutated abolished the effect of iron on leptin transcription. Finally, mice fed a high-iron diet had increased food consumption compared with mice fed a low-iron chow; importantly, this association was not seen in the leptin receptor-deficient *ob/ob* mouse.

Original article Gao, Y. *et al.* Adipocyte iron regulates leptin and food intake. *J. Clin. Invest.* doi:10.1172/JCI81860

OBESITY

The causal role of obesity in diabetic kidney disease—evidence from a Mendelian randomization study

Whether obesity is a direct cause of diabetic kidney disease (DKD) is unclear. Using a Mendelian randomization approach, Todd and colleagues assessed the association between BMI and DKD in 6,049 patients with type 1 diabetes mellitus, before comparing these data with results from cross-sectional and longitudinal observations. In the cross-sectional analysis, no association was seen between BMI and overall DKD. However, in the Mendelian randomization analysis, every 1 kg/m^2 increase in BMI was associated with an increased risk of developing DKD. Although supporting a causal role for obesity in the development of DKD, the investigators highlight that these data do not reveal the underlying mechanism of this association.

Original article Todd, J. N. *et al.* Genetic evidence for a causal role of obesity in diabetic kidney disease. *Diabetes* doi:10.2337/db15-0254

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