

IN BRIEF

▶ METABOLIC DISEASE**Weight loss herb targets GPCR**

The African cactiform *Hoodia gordonii* exhibits anorexant properties, but the active components and molecular targets remain unclear. Here, a screen of 4,400 natural products identified Gordonoside F — a pregnane steroidal glycoside isolated from *Hoodia gordonii* — to activate GPR119, a GPCR highly expressed in pancreatic β cells and intestinal L cells which can stimulate both insulin and GLP-1 release. Synthesized Gordonoside F improved glucose tolerance, enhanced glucose-stimulated insulin secretion and reduced food intake in mice.

ORIGINAL RESEARCH PAPER Zhang, S. *et al.* Molecular matchmaking between the popular weight-loss herb *Hoodia gordonii* and GPR119, a potential drug target for metabolic disorder. *Proc. Natl Acad. Sci. USA* **111**, 14571–14576 (2014)

▶ TYPE 2 DIABETES**Personalizing therapy**

A single-nucleotide polymorphism in *ADRA2A*, rs553668A — which leads to overexpression of the α 2A-adrenergic receptor (α 2AAR) — has been associated with defective β cell function and increased risk of type 2 diabetes. Here, results of a randomized clinical study, in which 50 patients with type 2 diabetes were treated with the α 2AAR antagonist yohimbine, are reported. The study met its primary end point, with yohimbine markedly increasing insulin secretion in risk allele carriers at 30 minutes during an oral-glucose tolerance test, to a level similar to that in non-risk allele carriers.

ORIGINAL RESEARCH PAPER Tang, Y. *et al.* Genotype-based treatment of type 2 diabetes with an α 2A-adrenergic receptor antagonist. *Sci. Transl. Med.* **6**, 257ra139 (2014)

▶ NATURAL PRODUCTS**Global classification of NPGCs**

Systematic study of natural product biosynthetic gene clusters (NPGCs) encoded by actinobacteria has been complicated by their complex and repetitive nature. Here, the authors create a data set comprising NPGCs identified in 830 actinomycete genomes and apply similarity metrics to classify these gene clusters into families (GCFs). By correlating mass spectrometric detection of known small molecules with the presence or absence of their established biosynthetic gene clusters, they verify the GCF designation and demonstrate its application in the *de novo* correlation of natural products and biosynthetic genes.

ORIGINAL RESEARCH PAPER Doroghazi, J. R. *et al.* A roadmap for natural product discovery based on large-scale genomics and metabolomics. *Nature Chem. Biol.* **10**, 963–968 (2014)

▶ TYPE 2 DIABETES**New lipid class regulates glucose homeostasis**

Mice overexpressing the glucose transporter Glut4 in adipocytes (AG4OX mice) exhibit elevated lipogenesis and increased glucose tolerance, despite being obese with elevated circulating fatty acids. Yore *et al.* identified elevated levels of novel metabolically beneficial branched fatty acid esters of hydroxy fatty acids (FAHFAs) in adipose tissue (AT) from AG4OX compared with wild-type mice. The most highly upregulated FAHFAs in AG4OX AT were palmitic acid-hydroxy stearic acids (PAHSAs), which signal through GPR120. In humans, PAHSA levels correlated with insulin sensitivity, and in mice PAHSA administration lowered glycaemia, improved glucose tolerance and stimulated GLP-1 and insulin secretion.

ORIGINAL RESEARCH PAPER Yore, M. M. *et al.* Discovery of a class of endogenous mammalian lipids with anti-diabetic and anti-inflammatory effects. *Cell* **159**, 318–332 (2014)