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IN BRIEF

DIABETES

Mechanistic insights from islet genome regulation

Dysregulation of *cis*-regulatory elements that drive pancreatic islet cell gene transcription could underlie diabetes mellitus, a new study suggests. Researchers have identified genomic sequences that reside predominantly in clusters of enhancers and form functional 3D chromatin domains. These enhancers were bound by key β-cell transcription factors, such as FoxA2 and PDX-1, and drove islet-specific gene expression in human islet samples. Sequence variation in these regions was associated with an increased risk of type 2 diabetes mellitus and variation in fasting glycaemia levels.

Original article Pasquali, L. *et al.* Pancreatic islet enhancer clusters enriched in type 2 diabetes risk-associated variants. *Nat. Genet.* doi:10.1038/ng.2870

NUTRITION

Short-chain fatty acids regulate intestinal gluconeogenesis

The short-chain fatty acids (SCFAs) propionate and butyrate —both products of gut microbiota-driven fermentation of soluble dietary fibre—activate intestinal gluconeogenesis via two distinct mechanisms in mice. European investigators showed that butyrate acts on intestinal gluconeogenesis gene expression through a cAMP-dependent pathway. By contrast, propionate mediated its beneficial metabolic effects by activating the expression of intestinal gluconeogenesis genes through a gut–brain neural circuit. The study suggests that intestinal gluconeogenesis is a causal link for the benefits of dietary fibre on energy and glucose homeostasis.

Original article De Vadder, F. *et al.* Microbiota-generated metabolites promote metabolic benefits via gut–brain neural circuits. *Cell* doi:10.1016/j.cell.2013.12.016

CANCER

Pathogenetics of craniopharyngiomas unravelled

Identification of subtype-specific mutations in the genes *CTNNB1* and *BRAF* in craniopharyngiomas could have implications for the diagnosis and treatment of patients with these brain tumours. Whole-exome sequencing identified mutations in *CTNNB1* (which encodes β-catenin) in 92% of analysed adamantinomatous craniopharyngiomas, a subtype of craniopharyngiomas that is typically found in children. By contrast, all neoplasms of the papillary subtype, which is more frequent in adults, exhibited mutations in *BRAF*.

Original article Brastianos, P. K. *et al.* Exome sequencing identifies BRAF mutations in papillary craniopharyngiomas. *Nat. Genet.* doi:10.1038/ng.2868

PHARMACOTHERAPY

Efficacy of lysine deacetylase inhibitors in T1DM

Findings in mice indicate that the immunomodulating lysine deacetylase inhibitors might be effective for treating patients with type 1 diabetes mellitus (T1DM). Addition of the lysine deacetylase inhibitors vorinostat and givinostat to the drinking water of nonobese diabetic mice at low doses markedly reduced diabetes incidence and counteracted inflammatory cell damage. These effects were mediated through hyperacetylation of transcription factors, which prevented transcription factor binding and reduced proinflammatory gene expression in leucocytes and β cells.

Original article Christensen, D. P. *et al.* Lysine deacetylase inhibition prevents diabetes by chromatin-independent immunoregulation and β-cell protection. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1320850111