IN BRIEF

OBESITY

N-acylphosphatidylethanolamine, a gut-derived circulating factor induced by fat ingestion, inhibits food intake

Gillum, M. P. *et al. Cell* **135,** 813–824 (2008)

N-Acylphosphatidylethanolamines (NAPEs) are a group of plasma lipids with previously unknown physiological significance. This paper shows that NAPEs are secreted into the circulation from the small intestine in response to ingested fat and are able to enter the brain, concentrating in the hypothalamus. Chronic NAPE infusion in rats resulted in a reduction of food intake and body weight, suggesting that NAPEs could provide new opportunities for obesity treatments.

CANCER

Small molecule-mediated disruption of Wnt-dependent signaling in tissue regeneration and cancer

Chen, B. *et al. Nature Chem. Biol.* 4 Jan 2009 (doi:10.1038/nchembio.137)

WNT–β-catenin signalling proteins play a key part in tissue homeostasis and tumorigenesis. By screening a synthetic chemical library, Chen and colleagues discovered two new classes of small molecules that disrupted discrete regulatory steps in the WNT–β-catenin pathway. Using these compounds, they demonstrated a transient, reversible suppression of the WNT–β-catenin pathway response in zebrafish and established a mechanism-based approach to target cancerous cell growth *in vitro*. So, such signal transduction mechanisms could be exploited for chemical genetics and therapeutic targeting.

ATHEROSCLEROSIS

Disrupting functional interactions between platelet chemokines inhibits atherosclerosis in hyperlipidemic mice

Koenen, R. R. *et al. Nature Med.* **15,** 97–103 (2009)

Chemokine-driven mononuclear-cell recruitment leads to arterial-wall inflammation in atherosclerosis, but directly antagonizing chemokine receptors could lead to immunological side effects. These authors determined structural features of heteromers of the chemokine ligands CCL5 and CXCL4 and designed stable peptide inhibitors that specifically disrupted proinflammatory CCL5–CXCL4 interactions. In mice, one CCL5–CXCL4 inhibitor attenuated monocyte recruitment and reduced atherosclerosis, establishing the potential of targeting heteromer formation to achieve therapeutic effects.

ANTICANCER DRUGS

Effective use of PI3K and MEK inhibitors to treat mutant *Kras* G12D and *PIK3CA* H1047R murine lung cancers

Engelman, J. A. *et al. Nature Med.* **14**, 1351–1356 (2008)

To more closely mimic human lung cancer, Engelman and colleagues developed transgenic mouse models of lung tumours. Treatment of tumours driven by mutant phosphoinositide 3-kinase (PI3K) with NVP-BEZ235 — a dual pan-PI3K and mTOR (mammalian target of rapamycin) inhibitor — led to marked tumour regression. In mouse lung cancers driven by mutant *Kras* — a tumour type associated with poor prognosis — NVP-BEZ235 combined with a mitogen-activated protein kinase kinase inhibitor led to a marked synergy in shrinking these tumours.