IN BRIEF

ANTICANCER DRUGS

Double boost for doxorubicin therapy

This study showed that conjugating the anticancer drug doxorubicin to squaline, a natural lipid precursor of cholesterol, improved its anticancer efficacy and reduced its cardiotoxicity. Doxorubicin–squalene (SQ–Dox) conjugates formed nanoassemblies that reduced pancreatic tumour growth by 95% when administered to a mouse model, compared to a 29% reduction with normal doxorubicin. Moreover, murine lung tumours that did not respond to normal doxorubicin treatment were inhibited by 90% with SQ–Dox. In addition, the nanomedicine had a fivefold higher maximum tolerated dose than the unmodified drug, and unlike doxorubicin it did not cause myocardial lesions.

ORIGINAL RESEARCH PAPER Maksimenko, A. *et al.* A unique squalenoylated and nonpegylated doxorubicin nanomedicine with systemic long-circulating properties and anticancer activity. *Proc. Natl Acad. Sci. USA* **111**, E217–E226 (2014)

EPIGENETICS

Banishing bad memories

It is difficult to diminish long-term traumatic memories with behavioural therapy, making it challenging to treat anxiety disorders. This study showed that administration of a histone deacetylase 2 (HDAC2) inhibitor to mice during a specific phase of traumatic memory recall — known as memory reconsolidation — rendered month-old memories susceptible to attenuation by behavioural therapy. The HDAC2 inhibitor epigenetically primed the expression of genes related to neuronal plasticity and increased the synaptic and structural plasticity of neurons. So, HDAC2 inhibitors could be used with behavioural therapy to eliminate long-term traumatic memories.

ORIGINAL RESEARCH PAPER Gräff, J. *et al.* Epigenetic priming of memory updating during reconsolidation to attenuate remote fear memories. *Cell* **156**, 261–276 (2014)

TARGET IDENTIFICATION

Targeting neuronal loss in Gaucher's disease

Approved enzyme replacement therapies for Gaucher's disease do not help neurological symptoms. Vitner *et al.* used a mouse model of Gaucher's disease to show that neuronal cell death hinged on a pathway of programmed cell necrosis that involved the kinases RIPK1 (receptor-interacting protein kinase 1) and RIPK3. Mice that were deficient in RIPK3 had less neuronal loss and liver injury, improved motor coordination and a longer lifespan than mouse models with normal RIPK3 expression, suggesting that RIPK3 could be a new target for the disorder.

ORIGINAL RESEARCH PAPER Vitner, E. B. *et al.* RIPK3 as a potential therapeutic target for Gaucher's disease. *Nature Med.* **20**, 204–208 (2014)

AUTOIMMUNE DISEASE

Antidiabetic mechanisms uncovered

Low concentrations of histone deacetylase (HDAC) inhibitors have immunomodulatory effects, but their mechanism of action is unclear. This paper showed that the clinically used HDAC inhibitors vorinostat and givinostat protected against the development of type 1 diabetes in a mouse model by increasing the numbers of regulatory T cells and decreasing the numbers of inflammatory dendritic cells and cytokines. Further work showed that these effects were probably mediated through HDAC inhibitor-mediated hyperacetylation of transcription factors, rather than hyperacetylation of nuclear histones.

ORIGINAL RESEARCH PAPER Christensen D. P. *et al.* Lysine deacetylase inhibition prevents diabetes by chromatin-independent immunoregulation and β-cell protection. *Proc. Natl Acad. Sci. USA* **111**, 1055–1059 (2014)