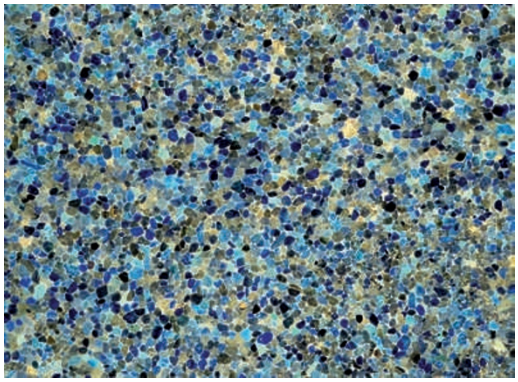
IN BRIEF

CANCER

B-cell-derived lymphotoxin promotes castration resistant prostate cancer

Ammirante, M. *et al. Nature* **464**, 302–305 (2010)

The mechanisms underlying the emergence of castration-resistant prostate cancer (CRPC) are poorly understood. Ammirante and colleagues show that androgen ablation causes infiltration of leukocytes, including B cells, into regressing androgen-dependent tumours, where activation of IκB kinase-β results in the production of cytokines that enhance androgen-free survival of CRPC cells. These data suggest that individuals who produce high levels of lymphotoxin are more likely to develop CRPC and so could benefit from anti-lymphotoxin therapy.



STEM CELLS

High-throughput screening in embryonic stem cell-derived neurons identifies potentiators of AMPA-type glutamate receptors

McNeish, J. *et al. J. Biol. Chem.* 8 Mar 2010 (doi/10.1074/jbc.M109.098814)

This paper reports one of the first stem cell-based screens to identify biologically active lead molecules. A screen of more than 2.4 million small molecules in neuronal precursor cells derived from differentiated mouse embryonic stem cells identified hit compounds that potentiated AMPA-type glutamate receptor currents, several of which underwent validation in human embryonic cell-derived neurons. This approach could be used for other CNS drug targets that are not easily reconstituted using traditional expression systems.

DIABETES

Leptin therapy in insulin-deficient type 1 diabetes

Wang, M.-Y. *et al. Proc. Natl Acad. Sci. USA* **107**, 4813–4819 (2010)

In type 1 diabetes, injected insulin does not replicate the metabolic homeostasis produced by endogenous insulin. Wang and colleagues showed that in non-obese mice with type 1 diabetes, leptin therapy alone or combined with low-dose insulin reversed the catabolic state via suppression of hyperglucagonaemia, mimicked the anabolic actions of insulin monotherapy and normalized haemoglobin A1c with less variability in glucose levels. In contrast to insulin, leptin reduced plasma and tissue lipids, suggesting that it may offer advantages over insulin monotherapy.

CANCER

Genetic dissection of the oncogenic mTOR pathway reveals druggable addiction to translational control via 4EBP-eIF4E

Hseih, A. C. *et al. Cancer Cell* **17**, 249–261 (2010)

The oncogenic PI3K–AKT–mTOR pathway activates two prominent downstream translational regulators: eIF4E binding proteins and ribosomal protein S6. This paper showed that it is the 4EBP-eIF4E arm of the pathway that controls cap-dependent translation, cell growth, and cancer initiation and progression. An ATP active-site mTOR inhibitor blocked 4EBP-eIF4E hyperactivation and suppressed growth of AKT-mediated tumours that were resistant to the approved mTOR inhibitor rapamycin, suggesting that targeting this pathway could be beneficial in cancer therapy.

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