

## IN BRIEF

**CANCER****Combination therapy for lung cancer**

Strategies to target the RAF–MAPK/ERK kinase (MEK)–extracellular signal-regulated kinase (ERK) pathway, which is activated in KRAS-mutant lung cancer, have been limited by adaptive drug resistance. Machado *et al.* therefore set out to identify potential combination targets for the MEK inhibitor trametinib. Using a pool-based short-hairpin RNA (shRNA) screen, fibroblast growth factor receptor 1 (FGFR1) inhibition was found to sensitize KRAS-mutant lung cancer cells to trametinib. In KRAS-mutant lung cancer xenografts, a KRAS-mutant patient-derived xenograft and a genetically engineered mouse model of mutant *Kras*-induced lung adenocarcinoma, FGFR1 inhibition using shRNA or ponatinib in combination with trametinib potently inhibited tumour growth and caused tumour regression.

**ORIGINAL ARTICLE** Machado, E. *et al.* A combinatorial strategy for treating KRAS-mutant lung cancer. *Nature* **534**, 647–651 (2016)

**AUTOIMMUNE DISEASE****Re-establishing immune tolerance**

Re-establishment of immune tolerance is a major goal for type 1 diabetes (T1D) treatment. Although cell-based therapies aiming to increase numbers of functional antigen-specific regulatory T ( $T_{reg}$ ) cells and restore immune tolerance are being investigated, their clinical translation is challenging. Now, Yeste *et al.* have engineered nanoparticles to co-deliver a tolerogenic molecule — the aryl hydrocarbon receptor ligand 2-(1'H-indole-3'-carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE) — and the  $\beta$ -cell antigen proinsulin (NP<sub>ITE+Ins</sub>). Injection of NOD mice with NP<sub>ITE+Ins</sub> suppressed spontaneous T1D development, inducing a tolerogenic dendritic cell phenotype and increasing  $T_{reg}$  cell differentiation.

**ORIGINAL ARTICLE** Yeste, A. *et al.* Tolerogenic nanoparticles inhibit T cell-mediated autoimmunity through SOCS2. *Sci. Signal.* **9**, 433ra61 (2016)

**RARE DISEASES****Bacterial peptide reverses Wilson disease**

Wilson disease is a rare autosomal-recessive disorder caused by mutations in ATPase copper-transporting- $\beta$  (*ATP7B*), resulting in excessive copper accumulation in the liver. Existing copper chelators exert adverse effects and are ineffective in patients with advanced liver disease. Here, Lichtmanegger *et al.* report the therapeutic potential of methanobactin (MB), a peptide produced by *Methylosinus trichosporium* OB3b, which has a high copper affinity. In *Atp7b*-deficient rats, short-term MB treatment markedly reduced total liver copper levels to a greater extent than existing copper chelators, rescuing rats from severe acute liver failure, without signs of toxicity.

**ORIGINAL ARTICLE** Lichtmanegger, J. *et al.* Methanobactin reverses acute liver failure in a rat model of Wilson disease. *J. Clin. Invest.* **126**, 2721–2735 (2016)

**BREAST CANCER****FASN inhibitor increases survival**

Fatty acid synthase (FASN) expression is elevated in several cancers and is associated with poor prognosis. Although several FASN inhibitors have been developed, they are associated with selectivity issues and toxicity. Alwarawrah *et al.* have now identified Fasnall, a novel, selective thiophenopyrimidine-based FASN inhibitor. Fasnall exhibited potent broad antitumour activity against various breast cancer cell lines and was well tolerated in mice. Moreover, Fasnall reduced tumour volume and increased survival in a mouse breast cancer model.

**ORIGINAL ARTICLE** Alwarawrah, Y. *et al.* Fasnall, a selective FASN inhibitor, shows potent anti-tumor activity in the MMTV-Neu model of HER2<sup>+</sup> breast cancer. *Cell Chem. Biol.* **23**, 678–688 (2016)