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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. Manchado *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 Manchado, 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 β-cell antigen proinsulin ($NP_{ITE+Ins}$). Injection of NOD mice with $NP_{ITE+Ins}$ 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-β (*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, Lichtmannegger *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 chelaters, rescuing rats from severe acute liver failure, without signs of toxicity.

ORIGINAL ARTICLE Lichtmannegger, 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 $HER2^+$ breast cancer. *Cell Chem. Biol.* **23**, 678–688 (2016)