

IN BRIEF

► MALARIA

Novel antimalarial target identified

Current antimalarial strategies are limited by the complex life cycle of *Plasmodium* parasites and the emergence of drug-resistant strains. With these challenges in mind, Kato *et al.* screened a diverse panel of 100,000 compounds, which were produced using diversity-oriented synthesis (DOS), to identify new multistage antimalarial compounds exhibiting novel mechanisms of action. This screen led to the identification of a series of bicyclic azetidines that inhibited a new target, phenylalanyl-tRNA synthetase. The bicyclic azetidine BRD7929 prevented disease transmission, ensured prophylaxis and displayed single low-dose cure, with activity against all *Plasmodium* parasite life stages in multiple mouse models.

ORIGINAL ARTICLE Kato, N. *et al.* Diversity-oriented synthesis yields novel multistage antimalarial inhibitors. *Nature* <http://dx.doi.org/doi:10.1038/nature19804> (2016)

► ANTICANCER AGENTS

ACC inhibition suppresses lung cancer

Targeting the elevated rate of *de novo* fatty acid synthesis (FASyn), which often occurs in tumour cells, has emerged as a promising therapeutic strategy. However, efforts to inhibit acetyl-CoA carboxylase (ACC) — the rate-limiting enzyme in FASyn — have so far been unsuccessful. Svensson *et al.* now show that ACC1 is highly expressed in human non-small-cell lung cancer (NSCLC) cell lines and that activity of this enzyme maintains NSCLC cell growth and viability *in vitro* and *in vivo*. Chronic treatment of xenograft and genetically engineered mouse models of NSCLC with the small-molecule allosteric ACC inhibitor ND-646 significantly inhibited tumour growth.

ORIGINAL ARTICLE Svensson, R. U. *et al.* Inhibition of acetyl-CoA carboxylase suppresses fatty acid synthesis and tumor growth of non-small-cell lung cancer in preclinical models. *Nat. Med.* **22**, 1108–1119 (2016)

► LYSOSOMAL STORAGE DISEASES

HSP70 reverses lysosomal pathology

Existing treatment options for the lysosomal storage diseases (LSDs) known as sphingolipidoses are limited and have little efficacy against neurological manifestations. Here, Kirkegaard *et al.* report that recombinant human heat shock protein 70 (HSP70) enhances binding of sphingolipid-degrading enzymes to their essential cofactor bis(monoacylglycerophosphate) *in vitro*, an effect that reversed lysosomal pathology in primary fibroblasts from individuals with LSD. Administration of HSP70 or arimoclomol (an orally available small-molecule co-inducer of HSPs currently in clinical trials) attenuated sphingolipid accumulation, disease progression and neurological symptoms in mouse models of sphingolipidoses.

ORIGINAL ARTICLE Kirkegaard, T. *et al.* Heat shock protein-based therapy as a potential candidate for treating the sphingolipidoses. *Sci. Transl. Med.* **8**, 355ra118 (2016)

► AUTOIMMUNE DISEASE

CK2 blockade ameliorates EAE

T helper 17 ($T_{H}17$) cells infiltrating the central nervous system are believed to have a crucial role in experimental autoimmune encephalomyelitis (EAE) and multiple sclerosis. Here, Ulges *et al.* report that genetic ablation or pharmacological blockade of the protein casein kinase 2 (CK2) inhibits encephalitogenic human and mouse $T_{H}17$ cell development and effector function but promotes protective regulatory T cell development. In EAE-affected mice, daily intraperitoneal administration of the small-molecule CK2 inhibitor CX4945 reduced disease severity and protected mice from relapse.

ORIGINAL ARTICLE Ulges, A. *et al.* Protein kinase CK2 governs the molecular decision between encephalitogenic $T_{H}17$ cell and T_{reg} cell development. *Proc. Natl Acad. Sci. USA* **113**, 10145–10150 (2016)